Scientific Committee on Emerging and Newly Identified Health Risks

SCENIHR

OPINION ON

THE SCIENTIFIC ASPECTS OF THE EXISTING AND PROPOSED DEFINITIONS RELATING TO PRODUCTS OF NANOSCIENCE AND NANOTECHNOLOGIES

Scientific Committees
on consumer products
on emerging and newly identified health risks
on health and environmental risk

The SCENIHR adopted this opinion at the 21st plenary on 29 November 2007

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ABSTRACT

This Opinion is concerned with the development of a conceptual framework for definitions in the areas of nanoscience and nanotechnologies. It is recognised that there is a need for an overarching framework for such definitions. This framework is based on an analysis of existing definitions in these areas, taking into account the need to avoid the promulgation of unnecessary terms and the requirements that it should be based on sound principles of lexicology. In view of the mandate of SCENIHR, this framework has been developed in the context of risk assessment procedures. Most of the concepts and behaviour patterns seen at the very small dimensions associated with nanotechnology are not new, and can be described by the existing terminology used at larger scales. It is recognised that it is impossible to stop individuals producing new words and definitions, but it is crucial that a new language is not adopted unnecessarily by the scientific community, and that on those occasions where it is required, it is consistent with established terminology.

The framework takes into account a number of key factors. First, the selection of the size limits associated with the prefix 'nano' in all aspects of nanoscience and the nanotechnologies is somewhat arbitrary, and there does not appear to be any sharp change in either toxicokinetic or toxicodynamic properties of substances at any particular size. Secondly, many of the terms used in nanoscience are based on commonly used words such as 'substance', 'matter' and 'material' and terms in nanoscience should not conflict with the general meaning of such words. Thirdly, certain physico-chemical properties of the products of nanotechnologies are anticipated to have a major impact on their behaviour in the environment. Some of these properties of substances may be size dependent and, therefore, determinants for both exposure and interactions with living systems and the environment. Fourthly, it is recognised that certain forms of substances that have characteristics with very small dimensions are found naturally in the environment such that exposure of man and other species is inevitable. However, there has been, and will continue to be, a significant increase in the use of manufactured and engineered products of nanotechnologies, and it is this increased production which requires consideration of potential new words and definitions. Finally, with respect to small individual components, as size decreases, it may be necessary to distinguish between different sizes of particles and molecules for a variety of reasons. This does not imply, however, that there is, a priori, any greater toxicological, public health, or environmental health concern associated with any one size range.

The majority of terms that need to be considered in the context of nanoscience and nanotechnology are those that start with the prefix 'nano-', which specifically means a measure of 10^{-9} units, the nature of this unit being determined by the word that follows. There is absolutely no need to change the meaning of any scientific term, such as metre or material just because it is pre-fixed by 'nano-'. The majority of terms used in nanotechnology are broadly self-explanatory. There are, however, some situations in which explanations are required in the development of a suitable framework for this terminology, especially for risk assessment purposes.

The framework involves a hierarchy of terms, principal of which is 'nanoscale', which is considered here to be characterised by dimensions of the order of 100 nm or less. The framework builds on this concept of the nanoscale and develops series of definitions, appropriate for risk assessment purposes, based on considerations of size, shape and properties. Key words defined in this framework include nanomaterial and nanoparticle, with particular emphasis on the limits to the nanoscale, the features that characterise a nanomaterial, the distinction between different geometric shapes at the nanoscale, and the potential for harm of released discrete free particles and/or their decomposition products.

The Opinion has established a framework for relevant definitions concerned with nanoscience, nanotechnologies and the products of nanotechnology, based on a sound scientific rationale that emphasises the specific needs for clarity of terminology in relation to risk assessment.

Keywords: SCENIHR, opinion, nanomaterial, nanoparticle, safety, risk, definition

To be cited as:

SCENIHR (Scientific Committee on Emerging and Newly-Identified Health Risks), 29 November 2007, the existing and proposed definitions relating to products of nanotechnologies

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1. BACKGROUND

Nanotechnologies are enabling technologies manipulating matter at the atomic scale and exploiting new properties and functionalities for new applications that may bring benefits to the whole society. Industry is increasingly using nanotechnology in sectors such as healthcare (targeted drug delivery, regenerative medicine, diagnostics), electronics, cosmetics, textiles, food, information technology, seed production, pesticides, and the environmental protection. The EU Strategy [COM (2004) 338] and the Action Plan [COM (2005) 243] for Nanotechnology define the EU approach and actions in nanosciences and nanotechnologies and 3.5 billion euros in the 7th Framework Programme for Research and Technological development in 2007-2013 is allocated in these fields. Some nanotechnology applications are already being marketed and citizen's trust and acceptance are essential for their further development and market uptake of new applications.

The communication between different disciplines of nanosciences and nanotechnologies and between various actors and operators as well as general public call for clear and scientifically coherent terminologies, reflecting also the risk assessment needs.

For the moment a multitude of definitions related to nanosciences and nanotechnologies exist and are under development. In 2004, the UK Royal Society and the Royal Academy of Engineering defined the key terms for nanoscience, nanotechnologies and nanomaterials in their report and the British Standardisation Institute adopted the first nomenclature for the definitions relating to products of nanoscience and nanotechnologies shortly after that.

These definitions are being applied and further modified in different international organisations (such as ISO/CEN, OECD) and individual countries as well as amongst various actors such as e.g. academia, business associations. There are various approaches and viewpoints on the key concepts and further on definitions may be related to different aims, regulatory, funding, standardisation, testing etc. The need for consistent recognised definitions and terminology is widely shared and work is in progress at international level in that respect.

The Commission participates in the on-going dialogue at international level, with a view to establishing a framework of shared principles for the safe, sustainable, responsible and socially acceptable development and use of nanotechnologies in large variety of applications such as chemicals, food, pharmaceuticals, medical devices etc. The SCENIHR is requested to provide a scientific review on definitions and base concepts in the area of nanotechnologies. The SCENIHR opinion on the subject will help Commission services to contribute within the appropriate fora to establish scientifically sound terminology for nanoscience and nanotechnologies.

2. TERMS OF REFERENCE

The SCENIHR is asked:

1. *To define a conceptual framework to assess the proposed definitions relating to nanoscience, nanotechnologies and products of nanotechnologies;*
2. *To make, on the basis of the framework, a scientific review of the strengths and weaknesses of existing and proposed definitions relating to nanosciences, nanotechnologies and products of nanotechnologies including those pertaining to risk assessment, taking also into account the growing importance of active nanosystems and the various needs of different users for defining the key concept and terms.*
3. *To identify a minimum set of essential criteria to be referred to when developing definitions relating to products of nanoscience and nanotechnologies or seeking to improve them. A short justification should accompany each criterion as well as the set itself.*

3. SCIENTIFIC RATIONALE

3.1. Introduction

It is understood that several different organisations, both national and international, are giving serious consideration to the definitions used in the areas of nanoscience and the nanotechnologies. It is recognised that there is a need for an overarching framework for such definitions. The promulgation of different definitions in different sectors should be avoided, and should be based on sound etymological principles such that meanings are consistent with existing scientific terminology and with the principles of lexicology.

Agreement on definitions is important for scientific and legal purposes and as an aid to communications between disciplines and across national borders. In the rapidly developing areas within nanotechnology, definitions may need to be reviewed from time to time as science and technology progress. However, most of the concepts and behaviour patterns seen at very small dimensions are not new, and can be described by the existing terminology also used at larger scales. It is recognised that it is impossible to stop individuals producing new words and definitions, but it is crucial that a new language is not adopted unnecessarily by the scientific community, and that on those occasions where it is required, it is consistent with established terminology. Many definitions are already widely used in the basic physical, chemical and biological sciences that already embrace the concepts of 'substances' and 'matter' that are essential to the description of the characteristics of nanoscience. The potential risks associated with substances and materials used in nanotechnologies are currently under intensive discussion and clearly a detailed assessment of terminology used in this process of risk assessment is needed. It is noted that the increasingly diverse nature and use of the products of nanotechnologies means that there is an increasing need for the identification of appropriate risk assessment strategies. This requires a precise set of definitions that are both scientifically sound and useful for practical purposes. Current definitions have not, generally, been developed with risk assessment strategies in mind and it is important that consistency and relevance is achieved in this process of harmonising definitions.

In view of the rapidly emerging nature of this subject, it is not surprising that the development of various definitions by different organisations has led to some confusion and some inconsistencies, possibly caused by the conflicting purposes of these organisations and the variable uses that would be made of the definitions. The mandate of the Working Group required that existing definitions, produced by various organisations should be examined, and strengths and weaknesses identified. SCENIHR has therefore assessed the existing definitions from the perspectives of the risk assessment, which is the responsibility of the Committee but has finally decided to refrain from presenting individual strength and weaknesses. However, aconceptual framework has been developed, within which definitions that may be needed for risk assessment purposes, and the parameters that need to be covered by each of these definitions, are identified.

3.2. Conceptual framework

The process of risk assessment is intended to provide an estimation of the risk associated with exposure to substances and products, which includes the possible harm inflicted by such substances or products and the likely extent of exposure to them. This may be performed both with respect to human health and the environment.

Definitions that help to characterise products of nanotechnologies, and which are therefore important to risk assessment, may be based on physical and chemical properties, and on their fate within biological environments. A number of key issues arise.

First, from a risk assessment perspective, it is acknowledged that the selection of the size limits associated with the prefix 'nano' in all aspects of nanoscience and the nanotechnologies is somewhat arbitrary. From the scientific evidence so far available, there does not appear to be any sharp change in either toxicokinetic or toxicodynamic properties of substances at any particular size. This has to be taken into account when considering the preciseness of any definitions.

Secondly, as noted below, many of the terms used in nanoscience are based on commonly used words such as 'substance', 'matter' and 'material'. It is important that the development of terms in theses areas does not conflict with the general meaning of such words. However, it is also necessary to interpret the general meanings as precisely as possible in these new areas of science and technology. In particular some terms used in risk assessment may be defined in slightly different ways to those in the general language. For example, for the purposes of risk assessment in European Union chemicals regulation (1907/2006/EC), the term 'substance'[1] has a more precise and detailed definition than normally encountered. Such usage has to be taken into account.

Thirdly, some physico-chemical properties of the products of nanotechnologies are anticipated to have an impact on their behaviour in the environment and, therefore, on the exposure of man and the environment to them. In particular, some physico-chemical properties may be size dependent and, therefore, help to determine both exposure and interactions with living systems and the environment. Such interactions may result in harmful effects with respect to the environment, and to human health. These considerations, largely determined by and consistent with the recent SCENIHR Opinions on risks associated with nanotechnologies (SCENIHR, 2006; SCENIHR, 2007; SCCP, 2007) have guided the selection of a number of the key words identified in this Opinion.

Fourthly, it is recognised that certain forms of substances whose characteristics involve very small dimensions are found naturally in the environment, such that exposure of man and other species is inevitable. In addition, human activities (energy production, combustion, etc.) may lead to the release of similar substances into the environment. However, there has been, and will continue to be, a significant increase in the use and diversity of manufactured and engineered products of nanotechnologies with uncertain consequences. It is therefore necessary that there are more detailed descriptions of definitions of the words used.

Finally, with respect to small individual components, as size decreases, it may be necessary to distinguish between different sizes of particles and molecules for a variety of reasons. This does not imply, however, that there is, a priori, any greater toxicological, public health, or environmental health concern associated with any one size range. There is an urgent need to develop a classification system for particles based on their potential hazardous properties, although the available data are insufficient to achieve this with any confidence at present.

In establishing a framework for definitions, it is important to take into account the work on terms and definitions performed in key organisations such as OECD and ISO/CEN. The SCENIHR is particularly concerned with the identification of definitions with respect to the terms used for risk assessment purposes. The following criteria, with respect to the parameters for selection of terms and their definition, have been used to guide the work of SCENIHR on these definitions:

[1] Substance: means a chemical element and its compounds in the natural state or obtained by any manufacturing process, including any additive necessary to preserve its stability and any impurity deriving from the process used, but excluding any solvent which may be separated without affecting the stability of the substance or changing its composition.

Criteria used in the selection of terms:

- Compatibility: the term should not be inconsistent with existing terms used in related areas of science;
- Uniqueness: if there is a suitable alternative in common use, that should be used rather than a new term created;
- Relevance: the term must be essential for risk assessment or related purposes;
- Focus: overlapping terms should be avoided;
- Ease of translation: the term should be capable of translation into many languages without affecting the intended meaning.

Criteria used in the definition of terms:

- Scientific nature: definitions should be based on fundamental principles and processes;
- Clarity: definitions should be short and unambiguous;
- Practicality: definitions should be practical and useable, especially in the context of current methodologies and measurement accuracy;
- Completeness: definitions should stand alone as far as possible, not relying on other definitions in order to be understood;
- Ease of translation: definitions should be capable of translation into many languages without affecting the intended meaning.

3.3. Considerations of Terms and Definitions

3.3.1 Background of the meaning of 'nano'

The majority of terms that need to be considered in the context of nanoscience and nanotechnology are those that start with the prefix 'nano-', followed by a noun, such as in nanoscience and nanotechnology themselves. The prefix 'nano-' specifically means a measure of 10^{-9} units, the nature of this unit being determined by the word that follows. Thus a nanosecond is 10^{-9} seconds and a nanometre is 10^{-9} metres. There is absolutely no need to change the meaning of any scientific term (e.g. second, metre, material, tube, particle, etc.) just because it is pre-fixed by 'nano-'. There is also no special reason to be prescriptive in the meanings of 'science' and 'technology' as applied to nanoscience and nanotechnology as these very general words do not require definition in any standards or regulatory frameworks.

There are certain situations in which explanations are required in the development of the framework for the terminology, and where the use of the prefix 'nano' is not intuitively obvious or understandable. For example, clarification may be needed on how precisely the term refers to the 10^{-9} measure. Also the addition of the prefix 'nano-' to a noun may not adequately explain exactly to what the 10^{-9} measure refers. For instance, with the word 'nanomaterial', to what structural feature of a material should the prefix 'nano-" refer? Are crystal size, grain size, domain size, surface topology or any other feature included? It is also important to avoid introducing ambiguities when word combinations involving terms of nanotechnology are used.

3.3.2 The Meaning of 'nano-' in Nanoscience and Nanotechnology

It is widely accepted that although the prefix nano specifically refers to 10^{-9} units, in the context of nanoscience the units should only be those of dimensions, rather than of any other unit of scientific measurement, such as for time, energy or power. Moreover, it is unrealistic, for practical purposes, to consider the prefix 'nano-' to solely and precisely refer to 10^{-9} metres, just as it is not considered that 'micro-' specifically and solely concerns something with a dimension of precisely 10^{-6} metres. It is further widely agreed that one of the characteristics that confers special properties to products of nanotechnologies is the large surface area to volume ratio that is encountered at very small dimensions and that those of the order of 100 nm and below are most likely to be associated with such properties.

3.3.3 Key words relevant to nanoscience and nanotechnology

The definitions required for risk assessment purposes have to include those that refer to the qualitative and quantitative description of the size and shape of products of nanotechnologies and to relevant features of their behaviour. Combining the strengths of some currently used definitions with this conceptual framework, the following terms and definitions are considered essential for risk assessment purposes.

3.3.3.1 Size considerations

Based on the considerations mentioned above, the main word in the hierarchy of terminology in nanotechnology and nanoscience related to size is 'nanoscale'. It follows that the definition of nanoscale should be:

> ***Nanoscale: A feature characterised by dimensions of the order of 100 nm or less.***

Since the changes in characteristics that are seen on reducing dimensions do not occur uniquely at the 100 nm dimension, some of the derivatives of the nanoscale have to allow for a range of dimensions at this level. It is important that some latitude is allowed in this definition with respect to the meaning of 'the order of' and it is considered that common sense should prevail. It is accepted that technically 'nanometrescale' is a more precise term since it refers only to dimensions and not any other property, but 'nanoscale' is already being used to describe size in this range and it is unlikely to be replaced in common usage by the more cumbersome 'nanometrescale'. In this Opinion, nanoscale is determined to be the preferred term.

In the hierarchy of terms, the noun 'nanostructure' and the adjective 'nanostructured', follow on from nanoscale. The term 'structure' is generally held to mean 'a complex entity composed of many parts'. It is logical, therefore, to consider that 'nanostructure' implies a complex entity composed of discrete functional parts, many of which will be at the nanometre scale. Reference here is made to the functionality of the component parts. This is required since it is not the mere presence of very small entities that determines that a substance is nanostructured (all substances consist of atoms that exist at the nanoscale), but rather the existence of such entities that control the properties and functions that are unique to the nanoscale for that substance.

It follows that most substances will have internal structures that individually could be considered as being at the nanoscale, for example molecules, crystals or domains, but these do not, a priori, qualify for classification as nanostructures. For example, simply because a polymeric material may consist of individual molecules of nanometre dimensions does not necessarily confer nanostructure status on that substance.

Nanostructure should therefore be defined as follows:

> ***Nanostructure: Any structure that is composed of discrete functional parts, either internally or at the surface, many of which have one or more dimensions of the order of 100 nm or less.***

Often used in a similar manner to nanostructure is the word 'nanomaterial'. A material is normally defined as a 'substance useful for making objects', and there is little to be gained from deviating from this when the word is used to describe materials comprised mainly of nanoscale components. A preferred format is to use the expression '*nanostructured material*, the meaning of which is obvious from the combined meanings of nanostructure and material. However, the commonly used term for 'nanostructured material' is nanomaterial, which should be defined as.

Nanomaterial: Any form of a material that is composed of discrete functional parts, many of which have one or more dimensions of the order of 100 nm or less.

It follows from this that a nanocrystalline material should be defined as follows:

Nanocrystalline material: A material that is comprised of many crystals, the majority of which have one or more dimensions of the order of 100 nm or less.

It also follows that a nanocomposite should be defined as follows:

Nanocomposite: A multi-phase material in which the majority of the dispersed phase components have one or more dimensions of the order of 100 nm or less.

Some terms have been introduced into nanotechnology in order to describe some general types of process or product. The only ones of significance are those that relate to engineered or manufactured nanostructures. There is no need to re-define manufactured nanomaterials, manufactured nanoparticles or any other manufactured entity since their meaning is obvious. The terms engineered nanostructure and engineered nanoparticle are a little different but it is difficult at this stage to be too prescriptive with the meaning. However, as the term engineered nanomaterials is commonly used, a definition is provided. Generally, these terms should be defined in a similar manner to the following.

Engineered nanomaterial: Any material that is deliberately created such that it is composed of discrete functional parts, either internally or at the surface, many of which will have one or more dimensions of the order of 100 nm or less.

In practice, the products of nanotechnology rarely consist of a single entity with one or more dimensions of 100 nm or less, or of large numbers of identical entities with identical sizes. Rather, they consist of large numbers of similar but non-identical entities, as, for example, in a powder. It is here that difficulty arises with the size definition, since rarely will the sample be monodisperse or homogeneous. Moreover, some samples may have the majority of entities of less than 100 nm size, but a significant minority greater than 100 nm. These are important factors for risk assessment purposes, since a sample has to be carefully and accurately characterised, and described by representative size distributions of its components. One of the key characteristic that has to be described, therefore, is the size distribution of the sample. It should be noted that the term bulk material is in common use to describe the same material in other, more conventional, physical forms. This term is helpful for risk assessment purposes**.**

3.3.3.2 Shape considerations

It is helpful to have terms that differentiate between discrete entities having either one, two or three dimensions in the nanoscale. The use of the term 'nanoparticle' here has created some difficulties. Areas in which there is inconsistency in language includes the traditional biological domains where entities exist at a nanoscale (such as vesicles, proteins, liposomes), but where the term nanoparticle is not commonly used. Moreover, in risk assessment, a particle is usually taken to be one which has three dimensions of approximately comparable size. However in nanotechnology the term 'nanoparticle' is used as a collective term for any material consisting of discrete entities with one, two or three dimensions of the order of 100 nm or less. It is considered that for risk assessment purposes it is preferable to consider a nanoparticle to have a comparable scale in all three dimensions. The following are therefore recommended.

> ***Nanosheet: A discrete entity which has one dimension of the order of 100 nm or less and two long dimensions.***

Note: Other entities such as nanofilm, nanoplate and nanolayer comply with this definition, but may differ from each other by other characteristics (e.g. sheet is usually free and a layer is usually supported; there may be considerable differences in flexibility).

> ***Nanorod: A discrete entity which has two dimensions that are of the order of 100 nm or less, and one long dimension***

Note: Other entities such as nanofibre, nanowire, nanowhisker comply with this definition, but may differ from each other by other characteristics (e.g. rotational symmetry, flexibility).

In general a nanorod or nanofibre can be characterised by the aspect ratio, which is the ratio between length and diameter of the structure.

> ***Nanotube: A discrete hollow entity which has two dimensions of the order of 100 nm or less and one long dimension***.

Particles are considered to be individual discrete entities. It is inappropriate to discuss heterogeneous collections of nanoparticles simply as nanoparticles. It is suggested that the preferred terminology in the case of deliberately manufactured products containing nanoparticles is 'nanoparticulate matter'. However as nanoparticle is the more commonly used term, it needs to be defined as follows:

> ***Nanoparticle: A discrete entity which has three dimensions of the order of 100 nm or less***.

> ***Nanoparticulate matter: A substance comprising of particles, the substantial majority of which have three dimensions of the order of 100 nm or less***.

It should be noted here that this definition of nanoparticle deviates from that used in previous SCENIHR Opinions (SCENIHR, 2006; SCENIHR, 2007) and also the position taken in the Royal Society and Royal Academy report on nanotechnology (Royal Society and Royal Academy of Engineering, 2004), which refers to substances with one or more rather than all three dimensions being of the order of 100 nm or less. It is accepted that the latter position is compatible with the generic interpretation of the nanoscale, but the definition given in this Opinion is more consistent with terminology in particle toxicology and hence is more relevant to risk assessment.

It is also accepted that for some materials the definitions may introduce uncertainty as to whether, for risk assessment purposes, they should be actually considered to be nanomaterials. This is the case with the fullerenes for which sometimes the term 'nanoparticle' is used while they are in fact molecules. It is proposed that, as a general rule, if a material has distinctly different properties from the bulk material as a consequence of its occurrence as discrete entities (nanoparticles, nanosheets, nanorods or nanotubes) with one or more dimensions of 100 nm or less, it should be considered as a nanomaterial.

3.3.3.3 Property Considerations

Of all the possible configurations of nanostructured materials, it is the nanoparticles that are by far the most significant as far as human health and the environment are concerned. In order to facilitate risk assessment with nanoparticulate products, the behaviour of the nanoparticles themselves within the various compartments of the environment have to be considered, and certain terms are important for this purpose. This concerns the manner in which particles diffuse in media, how they interact amongst themselves, where they may reversibly or irreversibly combine into groups of particles and their susceptibility to solubilitisation or degradation. The following terms and definitions relate to these behavioural characteristics.

Coalescence: The formation of a new homogeneous entity out of two initial ones, e.g. after the collision of two nanoparticles.

Agglomerate: A group of particles held together by weak forces such as van der Waals forces, some electrostatic forces and or surface tension.

It should be noted that an agglomerate will normally retain a high surface to volume ratio.

Aggregate: A group of particles held together by strong forces such as those associated with covalent or metallic bonds.

It should be noted that an aggregate may retain a high surface to volume ratio.

Degradation: A change in the chemical structure, physical properties or appearance of a material.

Solubilisation: The process of dissolution.

It should be noted that the amount of substance that can be dissolved in a liquid under specified conditions characterises its solubility. Specifically for nanomaterials, the solubility is of critical importance in view of potential persistence. Within biological systems, the dissolution kinetics (including timing, distribution within the biological system, allocation etc.) greatly affect the possibility of adverse effects.

3.4. Evaluation of currently used definitions

As noted in the Terms of Reference, SCENIHR was requested to construct this framework on the basis of an analysis of the strengths and weaknesses of existing definitions. However, it became clear that, although existing definitions had to be considered carefully, a separate discussion of individual strengths and weaknesses could not assist in establishing a conceptual framework. It became illogical to dissect and criticise individual pre-existing definitions in order to develop this framework. Indeed during the internal peer review of this Opinion, the Working Group was advised to avoid inclusion of such an analysis. SCENIHR considers that the conceptual framework and its associated definitions stand alone without the need for considerations of strengths and weaknesses of other definitions.

3.5. Conclusions

3.5.1 Framework for definitions on nanotechnology

The majority of terms that need to be considered in the context of nanotechnology are those that start with the prefix 'nano-', which specifically means a measure of 10^{-9} units. There is no need to change the meaning of any scientific term (e.g. metre, material) just because it is pre-fixed by 'nano-', and, in a general sense, the majority of terms used in nanotechnology are broadly self-explanatory. There are, however, some situations in which explanations are required in the development of a suitable framework for this terminology, especially for risk assessment purposes. Clarification may be needed on how precisely the term refers to the 10^{-9} measure. Also the prefix of 'nano-' to a noun may not adequately explain exactly to what the 10^{-9} measure refers as with the word nanomaterial, and it may be necessary to consider word combinations, such as engineered nanoparticles, where the meaning is not intuitively obvious. This Opinion has therefore developed a framework, based on the existing understanding of terms, on common sense, and on the need to reflect the needs of risk assessment. The definitions required for risk assessment purposes have to include those that refer to the qualitative and quantitative description of the size and shape of products of nanotechnologies and to relevant features of their behaviour, which are all taken into account in the framework.

3.5.2 Suitable existing definitions from internationally recognised bodies

A number of definitions that had been previously published by or are currently under discussion within international bodies, many of which are considered useful for a better understanding of nanotechnology. This Opinion has taken note of these, for example nanoscale, nanostructure, nanomaterial, nanorod, nanotube and nanoparticulate products. In some of the terms there is a logical explanation of meaning through the conventional meaning of the constituent parts of the term such as with nanocrystalline material and nanocomposite.

Considering the complex nature of nanoparticle interactions, some terms are necessary to describe the various interactions that may occur between nanoparticles including coalescence, agglomeration and aggregate, and the behaviour of nanoparticles in the environment, and these have been included in this framework.

3.5.3 Definitions in relation to risk assessment

The definitions provided in Section 3.3 that arise from this framework should be appropriate for the use in risk assessment. The most important aspects of risk assessment are the description and characterization of the nanomaterial under consideration and the evaluation of potential for harm of released discrete free particles and/or their decomposition products. The definitions given in this Opinion provide a tool for this characterization and description.

3.5.4 Possible areas of further work

It has to be realised that some of the definitions in the literature have not been systematically generated but act more like descriptors. One of the issues that need to be addressed is the limitation of certain definitions. While the nanometre scale is a descriptor of the size or dimension, other definitions refer to the chemical and physical interactions and the aggregation state of matter. In terms of the release of decomposition products through free particles or solute chemical compounds this is also an important discriminator in the context of risk assessment. A challenge however remains in the determination of these relevant parameters from routine assessments.

4. OPINION

Several different organisations, both national and international, are giving serious consideration to the definitions used in the areas of nanoscience and the nanotechnologies and it is recognised that there is a need for an overarching framework for such definitions. The promulgation of different definitions in different sectors should be avoided, and should be based on sound etymological principles such that meanings are consistent with existing scientific terminology and with the principles of lexicology. Most of the concepts and behaviour patterns seen at the very small dimensions associated with nanotechnology are not new, and can be described by the existing terminology used at larger scales. It is recognised that it is impossible to stop individuals producing new words and definitions, but it is crucial that a new language is not adopted unnecessarily by the scientific community, and that on those occasions where it is required, it is consistent with established terminology.

The potential risks associated with substances and materials used in nanotechnologies are currently under intensive discussion and clearly a proper assessment of terminology used in this process of risk assessment is needed. It is noted that the increasingly diverse nature and use of the products of the nanotechnologies imply that there is an increasing need for the identification of appropriate risk assessment strategies, which require a precise series of definitions that are both scientifically sound and useful for practical purposes. Current definitions have not, generally, been developed with risk assessment strategies in mind and it is important that consistency and relevance is achieved in this process of harmonising definitions.

A conceptual framework has been developed, within which definitions that may be needed for risk assessment purposes, and the parameters that need to be covered by each of these definitions, are identified.

The process of risk assessment is intended to provide an estimation of the potential risk associated with exposure to substances and products, which includes both the estimation of the both the possible harm inflicted by such substances or products and the likely extent of exposure to them, both with respect to human health and the environment. Definitions that help to characterise products of nanotechnologies, and which are therefore important to risk assessment, may be based on physical, chemical, and biological properties. A number of key issues arise.

First, the selection of the size limits associated with the prefix 'nano' in all aspects of nanoscience and the nanotechnologies is somewhat arbitrary. From the scientific evidence so far available, there does not appear to be any sharp change in either toxicokinetic or toxicodynamic properties of substances at any particular size. Secondly, as noted below, many of the terms used in nanoscience are based on commonly used words such as 'substance', 'matter' and 'material'. It is important that the development of terms in nanoscience do not conflict with the general meaning of such words, although it is recognised that some terms used in risk assessment may be defined in slightly different ways to those in the general language. Thirdly, certain physico-chemical properties of the products of nanotechnologies are anticipated to have a major impact on their behaviour in the environment and therefore on the exposure of man and the environment to them. In particular, some physico-chemical properties of substances may be size dependent and, therefore, determinants for both exposure and interactions with living systems and the environment. Such interactions may result in harmful effects with respect to the environment and to human health. These considerations have guided the development of the framework and the selection of a number of the key words identified in this Opinion.

Fourthly, it is recognised that certain forms of substances that have characteristics with very small dimensions are found naturally in the environment such that exposure of man and other species is inevitable. However, there has been, and will continue to be a significant increase in the use of manufactured and engineered products of nanotechnologies, and it is this increased production which requires consideration of potential new words and definitions. Finally, with respect to small individual components, as size decreases, it may be necessary to distinguish between different sizes of particles and molecules for a variety of reasons. This does not imply, however, that there is, a priori, any greater toxicological, public health, or environmental health concern associated with any one size range.

In establishing a framework for definitions certain criteria, with respect to the parameters for selection of terms and their definition, have been established. Criteria used in the selection of terms include their compatibility with other terms used in science, their uniqueness and lack of suitable alternatives, their relevance to risk assessment or related purposes, and their ease of translation. Criteria used in the definition of terms include scientific validity, clarity, the need for practicality and their ability to stand alone.

The majority of terms that need to be considered in the context of nanoscience and nanotechnology are those that start with the prefix 'nano-' ', which specifically means a measure of 10^{-9} units, the nature of this unit being determined by the word that follows. There is absolutely no need to change the meaning of any scientific term, such as metre or material just because it is pre-fixed by 'nano-'. The majority of terms used in nanotechnology are broadly self-explanatory. There are, however, some situations in which explanations are required in the development of a suitable framework for this terminology, especially for risk assessment purposes. Clarification may be needed on how precisely the term refers to the 10^{-9} measure. Also the prefix of 'nano-' to a noun may not adequately explain exactly to what the 10^{-9} measure refers as with the word nanomaterial, and it may be necessary to consider word combinations, such as engineered nanoparticles, where the meaning is not intuitively obvious. This Opinion has therefore developed a framework, based on the existing understanding of terms, on common sense, and on the need to reflect the needs of risk assessment. The definitions required for risk assessment purposes have to include those that refer to the qualitative and quantitative description of the size and shape of products of nanotechnologies and to relevant features of their behaviour, which are all taken into account in the framework.

It is widely accepted that although the prefix nano specifically refers to 10^{-9} units, in the context of nanoscience, the units should only be those of dimensions. Moreover, it is unrealistic, for practical purposes, to consider the prefix 'nano-' to solely and precisely refer to 10^{-9} metres, just as it is not considered that 'micro-' specifically and solely concerns something with a dimension of precisely 10^{-6} metres.

The definitions required for risk assessment purposes have to include those that refer to the qualitative and quantitative description of the size and shape of products of nanotechnologies and to relevant features of their behaviour.

Based on the considerations mentioned above, the main word in the hierarchy of terminology in nanotechnology and nanoscience related to size is 'nanoscale'. It follows that the definition of nanoscale should be:

> ***Nanoscale: A feature characterised by dimensions of the order of 100 nm or less***

In the hierarchy of terms, the noun 'nanostructure' and the adjective 'nanostructured', follow on from nanoscale. The term 'structure' is generally held to mean 'a complex entity composed of many parts'. It is logical, therefore, to consider that 'nanostructure' implies a complex entity composed of discrete functional parts, many of which will be at the nanometre scale. Reference here is made to the functionality of the component parts. This is required since it is not the mere presence of very small entities that determines that a substance is nanostructured (all substances consist of atoms that exist at the nanoscale), but rather the existence of such entities that control the properties and functions that are unique to the nanoscale for that substance.

It follows that most substances will have internal structures that individually could be considered as being at the nanoscale, for example molecules, crystals or domains, but these do not, a priori, qualify for classification as nanostructures. For example, simply because a polymer may have individual molecules of nanometre dimensions does not necessarily confer nanostructure status on that substance.

The following definitions are based on this concept of the nanoscale, and the characteristics required for specific functionality at this scale:

> ***Nanostructure: Any structure that is composed of discrete functional parts, either internally or at the surface, many of which have one or more dimensions of the order of 100 nm or less.***
>
> ***Nanomaterial: Any form of a material that is composed of discrete functional parts, many of which have one or more dimensions of the order of 100 nm or less.***
>
> ***Nanocrystalline material: A material that is comprised of many crystals, the majority of which have one or more dimensions of the order of 100 nm or less.***
>
> ***Nanocomposite: A multi-phase material in which the majority of the dispersed phase components have one or more dimensions of the order of 100 nm or less.***
>
> ***Engineered nanomaterial: Any material that is deliberately created such that it is composed of discrete functional parts, either internally or at the surface, many of which will have one or more dimensions of the order of 100 nm or less.***

In practice, the products of nanotechnology rarely consist of a single entity with one or more dimensions of 100 nm or less, or of large numbers of identical entities with identical sizes. Rather, they consist of very large numbers of similar but non-identical entities, as, for example, in a powder. Rarely will the sample be monodisperse or homogeneous. This is important factor for risk assessment purposes, since a sample has to be carefully and accurately characterised, and described by representative size distributions of its components. One of the key characteristics that has to be described, therefore, is the size distribution of the sample.

It is helpful to have terms that differentiate between nanomaterials that occur as discrete entities having either one, two or three dimensions in the nanoscale. The use of the term 'nanoparticle' is particularly problematic. In risk assessment, a particle is usually taken to be one which has three dimensions of approximately comparable size. However in nanotechnology the term 'nanoparticle' is used as a collective term for any material consisting of discrete entities with one, two or three dimensions of the order of 100 nm or less. For risk assessment purposes it is preferable to consider a nanoparticle to have a comparable scale in all three dimensions. The following are therefore recommended.

> ***Nanosheet: A discrete entity which has one dimension of the order of 100 nm or less and two long dimensions.***
>
> ***Nanorod: A discrete entity which has two dimensions that are of the order of 100 nm or less, and one long dimension.***

Nanotube: A discrete hollow entity which has two dimensions of the order of 100 nm or less and one long dimension.

Nanoparticle: A discrete entity which has three dimensions of the order of 100 nm or less.

Nanoparticulate matter: A substance comprising of particles, the substantial majority of which have three dimensions of the order of 100 nm or less.

It is recognised that certain other terms currently in use comply with some of these definitions, including nanofibre, nanowire and nanowhisker, which are analogous to nanorod, and nanofilm and nanofibre, which are analogous to nanosheet, in each case there being minor differences in characteristics, such as flexibility, which further qualifies the term.

It should be noted here that this definition of nanoparticle deviates from that used in previous SCENIHR Opinions and also the position taken in the Royal Society and Royal Academy report on nanotechnology which refer to substances with one or more rather than all three dimensions being of the order of 100 nm or less. In consideration of the plethora of other terms introduced into nanoscience and nanotechnologies (e.g. nanodevice, nanobubble) it is suggested that official documents avoid their use as far as possible since satisfactory terms and definitions already exist. There are many other scientific terms that are used in nanoscience and nanotechnologies (micelle, liposome, vesicle, etc), and where attempts have been made to redefine them in the nanoscale context. It is suggested that this practice should be avoided where well established definitions are clearly adequate.

Of all the possible configurations of nanostructured materials, it is the nanoparticles that are by far the most significant as far as human health and the environment are concerned. In order to facilitate risk assessment with nanoparticulate products, the behaviour of the nanoparticles themselves within the various compartments of the environment have to be considered, and certain terms are important for this purpose:

Coalescence: The formation of a new homogeneous entity out of two initial ones, e.g. after the collision of two nanoparticles.

Agglomerate: A group of particles held together by weak forces such as van der Waals forces, some electrostatic forces and the surface tensions.

Aggregate: A group of particles held together by strong forces such as those associated with covalent or metallic bonds.

Degradation: A change in the chemical structure, physical properties or appearance of a material.

Solubilisation: The process of dissolution.

In conclusion, we believe that the definitions discussed in this Opinion and the conceptual framework within which they have been established should be appropriate for the use in risk assessment. The most important aspects of risk assessment are the description and characterization of the nanomaterial under consideration and the evaluation of potential for harm of released discrete free particles and/or their decomposition products. The definitions given in this Opinion provide a tool for this characterization and description.

With respect to the terms of reference and the mandate, the following comments may be made.

Question 1: Define a conceptual framework to assess the proposed definitions relating to nanoscience, nanotechnologies and products of nanotechnologies.

The Opinion has established a framework for relevant definitions concerned with nanoscience, nanotechnologies and the products of nanotechnology, based on a sound scientific rationale that emphasises the specific needs for clarity of terminology in relation to risk assessment, as defined in the above paragraphs of this Opinion.

Question 2: Make, on the basis of the framework, a scientific review of the strengths and weaknesses of existing and proposed definitions relating to nanosciences, nanotechnologies and products of nanotechnologies including those pertaining to risk assessment, taking also into account the growing importance of active nanosystems and the various needs of different users for defining the key concept and terms.

As noted above SCENIHR considered it unhelpful to construct and use a strength and weakness analysis of existing definitions in the establishment of this framework.

Question 3: Identify a minimum set of essential criteria to be referred to when developing definitions relating to products of nanoscience and nanotechnologies or seeking to improve them. A short justification should accompany each criterion as well as the set itself.

A set of essential criteria for the selection of terms and their definition is presented in Section 3.2 of the scientific rationale of this Opinion. Criteria used in the selection of terms include their compatibility with other terms used in science, their uniqueness and lack of suitable alternatives, their relevance to risk assessment or related purposes, and their ease of translation. Criteria used in the definition of terms include scientific validity, clarity, the need for practicality and their ability to stand alone.

It is recommended that the adaptation of definitions that already exist in other areas of science for use in nanotechnology should be avoided wherever possible.

5. MINORITY OPINION

None

6. REFERENCES

Several organisations have worked on or have work in progress concerning definitions in the area of nanoscience and the nanotechnologies, including, in alphabetical order, the following:

ANSI-NSP (American National Standards Institute)
http://www.ansi.org

ASTM (American Society for Testing and Materials): Committee E56
http://www.astm.org

BSI (British Standards Institution)
http://www.bsi-global.com
PAS 131 Terminology for medical, health and personal care applications of nanotechnology
PAS 132 Terminology for the bio-nano interface
PAS 133 Terminology for common nanoscale measurement terms including instrumentation
PAS 134 Terminology for carbon nanostructures
PAS 135 Terminology for nanofabrication
PAS 136 Terminology for nanomaterials

European Commission Communication "Towards a European Strategy for Nanotechnology" COM(2004) 338, at ftp://ftp.cordis.europa.eu/pub/nanotechnology/docs/nano_com_en.pdf

European Commission Action Plan "Nanosciences and nanotechnologies: An action plan for Europe 2005-2009" (COM(2005) 243), at
ftp://ftp.cordis.europa.eu/pub/nanotechnology/docs/nano_action_plan2005_en.pdf

ISO (International Standards Organisation): Technical Committee 229, at
http://www.iso.org/iso/iso_technical_committee.html?commid=381983

OECD (Organisation for Economic Cooperation and Development)
http://www.oecd.org/sti/nano

Royal Society and Royal Academy of Engineering, UK, July 2004, Nanoscience and nanotechnologies: opportunities and uncertainties, at
http://www.nanotec.org.uk/finalReport.htm

SCCP (Scientific Committee on Consumer Products). 19 June 2007, Preliminary Opinion on Safety of Nanomaterials in Cosmetic Products, at
http://ec.europa.eu/health/ph_risk/committees/04_sccp/docs/sccp_o_099.pdf .

SCENIHR (Scientific Committee on Emerging and Newly Identified Health Risks), 10 March 2006, modified opinion on: The appropriateness of existing methodologies to assess the potential risks associated with engineered and adventitious products of nanotechnologies, at
http://ec.europa.eu/health/ph_risk/committees/04_scenihr/docs/scenihr_o_003b.pdf

SCENIHR (Scientific Committee on Emerging or Newly-Identified Health Risks), 21-22 June 2007, The Appropriateness of the Risk Assessment Methodology in Accordance with the Technical Guidance Documents for New and Existing Substances for Assessing the Risks of Nanomaterials, at
http://ec.europa.eu/health/ph_risk/committees/04_scenihr/docs/scenihr_o_010.pdf.