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Comparative assessment of nanomaterial definitions and safety evaluation considerations

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ABSTRACT

Nanomaterials continue to bring promising advances to science and technology. In concert have come calls for increased regulatory oversight to ensure their appropriate identification and evaluation, which has led to extensive discussions about nanomaterial definitions. Numerous nanomaterial definitions have been proposed by government, industry, and standards organizations. We conducted a comprehensive comparative assessment of existing nanomaterial definitions put forward by governments to highlight their similarities and differences. We found that the size limits used in different definitions were inconsistent, as were considerations of other elements, including agglomerates and aggregates, distributional thresholds, novel properties, and solubility. Other important differences included consideration of number size distributions versus weight distributions and natural versus intentionally-manufactured materials. Overall, the definitions we compared were not in alignment, which may lead to inconsistent identification and evaluation of nanomaterials and could have adverse impacts on commerce and public perceptions of nanotechnology. We recommend a set of considerations that future discussions of nanomaterial definitions should consider for describing materials and assessing their potential for health and environmental impacts using risk-based approaches within existing assessment frameworks. Our intent is to initiate a dialogue aimed at achieving greater clarity in identifying those nanomaterials that may require additional evaluation, not to propose a formal definition.

1. Introduction

Definitions of nanomaterials and their use in regulatory evaluations have been, and continue to be, an area of active scientific and policy debate (ICCA, 2010; Maynard, 2011; Stamm, 2011; Bleeker et al., 2013). Nanomaterials may exhibit properties different from their non-nano forms, and these different properties have raised questions about potential human health and environmental risks. The International Organization for Standardization (ISO) has defined "nanomaterial" as a "material with any external dimension in the nanoscale or having internal structure or surface structure in the nanoscale" (ISO, 2010) and "nanoparticle" as a "nano-object with all three external dimensions in the nanoscale" where nanoscale is defined as the size range from approximately 1–100 nm (ISO, 2008). These technical definitions, based on size only, may be insufficient from a risk evaluation standpoint because they do not include other important elements that should be considered when determining whether a nanomaterial may need additional review.

Discussions about developing a definition for nanomaterials have been challenging because of the need to satisfy two diverging considerations. A definition should be broad enough to define

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materials that may warrant additional evaluation, yet it should not be so broad as to include those materials for which additional examination or evaluation would not be meaningful in terms of protecting human health or the environment. A balance is necessary to ensure appropriate allocation of resources to most effectively protect the health and safety of humans and the environment. Definitions proposed to date have taken a variety of approaches in attempting to strike a suitable balance, but while they may satisfy specific jurisdictional mandates, their frequently contradictory inclusions and exclusions present a complex regulatory maze for producers of nanomaterials and products containing them. Difficulties associated with attempting to comply with contradictory nanomaterial definitions and potential regulations can impede international trade and, more fundamentally, reduce public confidence in the adequacy of regulatory protections.

Nanomaterials are neither inherently hazardous nor inherently safe (Auffan et al., 2009; Donaldson and Poland, 2013), and it has been broadly recognized that they should not be treated as such in evaluation programs (SCENIHR, 2007; Holdren, 2011; Hamburg, 2012). Likewise, the informational elements of a nanomaterial definition presented in this paper are not intended to identify inherently hazardous or non-hazardous materials. Rather, they are intended to be used in conjunction with available hazard and exposure information to identify nanoscale materials which may be of interest for potential priority setting, risk assessment, and risk management activities. While the elements we identify in this paper can help strengthen or inform developing definitions, they should not be viewed as a comprehensive list of factors to be considered in a safety assessment of nanomaterials. Regardless of the definition that is applied, there is an obligation of both regulators and the regulated community to ensure that a material is evaluated appropriately to determine whether it poses a risk to human health or the environment. This evaluation should be based not only on the intrinsic hazard potential of the material but on consideration of exposure potential (e.g. during manufacturing, use, and disposal) as well.

The purpose of this paper is twofold: (1) to compare and contrast existing nanomaterial definitions and (2) to present a set of informational elements to be considered as discussions on the need for definitions and nanomaterial regulatory frameworks continue. The intent is not to propose a formal definition for nanomaterials, but to initiate a dialogue aimed at achieving greater clarity in identifying those nanomaterials that may require additional evaluation. That process should account for each of the elements presented in this paper at some point in the evaluation, while seeking to eliminate differences that create further ambiguity. The ideas expressed in this paper apply to the commercial manufacturing and use of nanomaterials.

2. Comparison/contrast of current definitions

Numerous definitions for nanomaterials have been proposed by various government, industry, and standards organizations. These definitions are often inconsistent in their elements and scope, which can lead to confusion in determining whether a material is or is not considered to be a “nanomaterial.” To better understand the similarities and differences among definitions, we performed a comprehensive comparative assessment of 14 definitions from various regulatory authorities (Table 1). The assessment included formal regulatory definitions as well as definitions stated in guidance or policy documents (“advisory definitions” in Table 1). The definitions are generally intended to address safety impacts to people and the environment, though there may appear to be a particular emphasis on human health impacts. The elements considered in this analysis are applicable for human and environmental safety, as well as toxicological and ecotoxicological effects.

Size (or external dimensions) was the only common element across all of the definitions, though the upper size limits were sometimes variable among the definitions. Several important core elements that were not consistently mentioned included: consideration of agglomerates and aggregates, distributional thresholds, novel properties, and solubility. Other important differences included number size distributions versus weight distributions and the inclusion of natural and incidental nanomaterials along with those manufactured intentionally. A summary of these core elements and the similarities and differences among the 14 definitions is presented in Table 2. This comparative assessment highlights some of the key differences that can lead to a lack of clarity and consistency with respect to the term “nanomaterial” and what materials may be subject to existing or developing regulations. What follows is a discussion on some of the factors that should be considered when developing regulatory definitions or identifying nanomaterials that may be of interest, with a focus on those elements identified through the comparative assessment in Table 2.

3. Core elements for describing nanomaterials

3.1. Size

Size is the fundamental defining characteristic of all nanomaterials. While size is an easy concept to understand, it is more difficult to apply because there are no natural physical or chemical boundaries that delineate the “nanoscale.” By convention, 1–100 nm is the size range most commonly used in reference to nanomaterials, but there is no bright line that clearly demarks the nanoscale from a chemical or biological perspective. At the lower end of the range, 1 nm is intended to distinguish between individual molecules and nanomaterials, although some molecules (e.g., some proteins and biomolecules) may have at least one dimension larger than 1 nm. Many nanomaterial definitions explicitly include materials that may have dimensions below 1 nm (e.g., fullerenes and graphene; Table 2). At this lower end of “nanoscale,” the characteristics and properties of the material are largely defined by the chemistry of the molecule and not by the physical nature of the formed nanoscale materials.

The upper end of the “nanoscale” at 100 nm is an arbitrary cut-off since the size-dependent behavior of materials does not stop or begin abruptly at 100 nm. Many properties characteristic of the nanoscale, such as solubility, light scattering, and surface area effects, are predictable and continuous characteristics of the bulk materials (Donaldson and Poland, 2013). In an attempt to be inclusive of all the characteristics that may be important for regulatory oversight, some authorities have expanded the upper range of the nanoscale well beyond 100 nm (Table 2) (Health Canada, 2011; US FDA, 2011; Taiwan, 2012).

While size limits are somewhat arbitrary, there is general agreement that any unique nano-specific phenomena of particulates are most likely to occur between 1 and 100 nm. For instance, the properties of inorganic particles were evaluated by Auffan et al. (2009) who found that novel, size-dependent properties of nanoscale materials, such as catalytic properties of gold, the photocatalytic activity of TiO_2, and the tunable fluorescent behavior of quantum dots, occur below 30 nm (see the Novel Properties section of this paper for further discussion). Most regulatory authorities have used 1–100 nm to define the nanoscale, which is consistent with the ISO standard (ISO, 2008). We agree that this provides a reasonable range, provided there is recognition that particle size alone is not sufficient for the evaluation of a nanomaterial and that