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Current legislation in respect to food applications of nanomaterials worldwide

Chi-Hao Lee

Food Satety Division, Food and Drug Administration, Ministry of Health and Welfare, Taipei, Taiwan

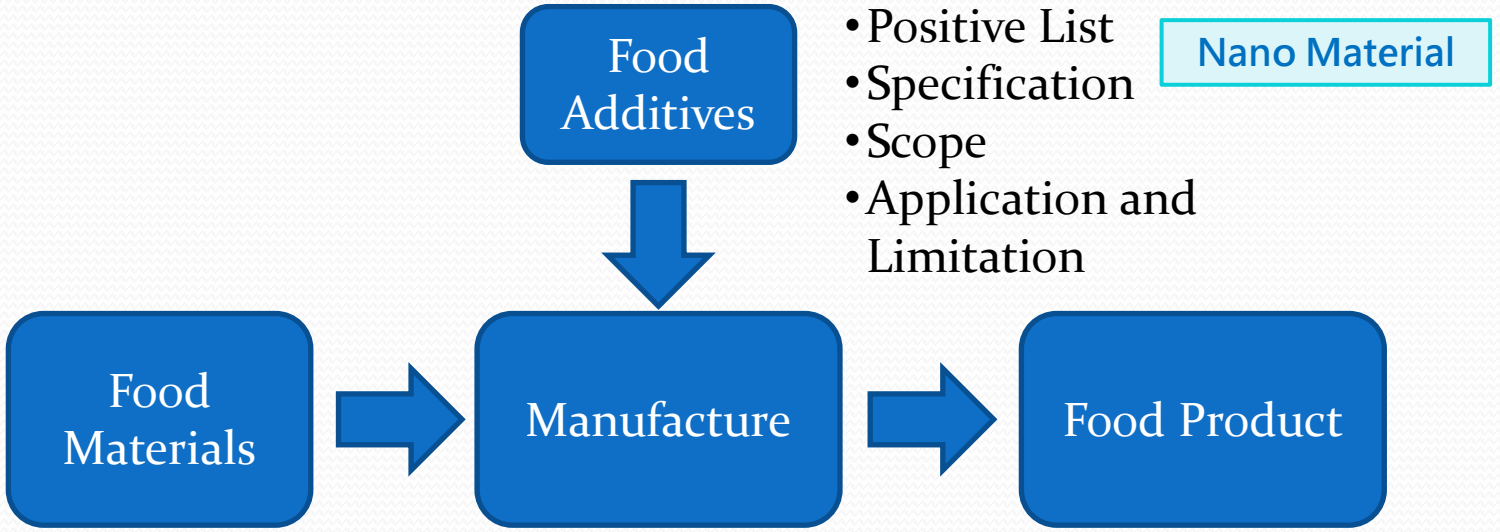
FDA 衛生福利部食品藥物管理署
Taiwan Food and Drug Administration

Outline

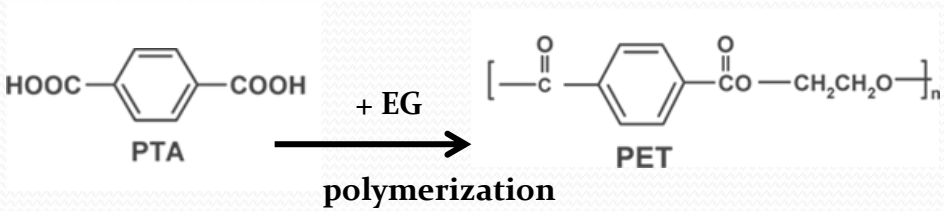
- Management System of Food, Food additives and Food Utensils, Containers and packaging
- Several regulations and guidances of nanomaterials on food application
- Current management system of food applications of nanomaterial

Management System of Food, Food additives and Food Utensils, Containers and packaging

Management System of Food and Food additives



Management System of Food Utensils, Containers and Packaging



Molding

Shaping

migration

Food contact substances (FCS)

Food contact materials (FCM)

Food contact articles

Indirect food additives

The inertness and inherent toxicity of FCS is important.

FCS approvals/authorization

Nano Technology

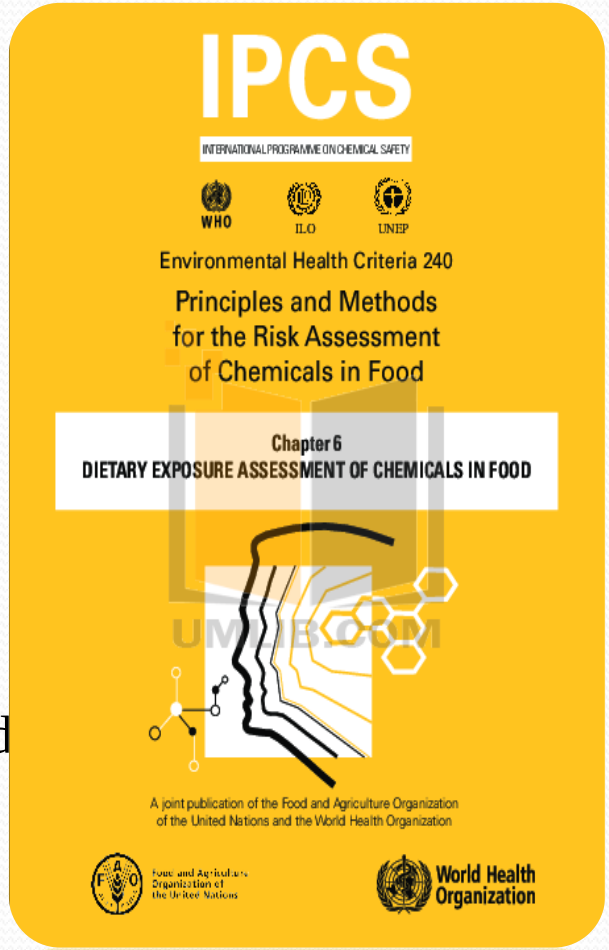
Quality assurance by Migration assay

Nano Material Migration

Environmental Health Criteria 240 FAO/WHO IPCS (2009)

Principles and Methods for the Risk Assessment of Chemicals in Food

- The scope and methods of risk assessment for food additives, chemical contaminants, animal drug residues and natural food ingredients.
- Combines food consumption data with data on the concentration of chemicals in food.
- The resulting dietary exposure estimate may then be compared with the relevant health based guidance value for the food chemical of concern (ADI)



- Chapter 1 : Introduction
- Chapter 2 : Risk Assessment and its Role in Risk Analysis
- Chapter 3 : Chemical Characterization, Analytical Methods and the Development of Specifications
- Chapter 4 : Hazard Identification and Characterization; Toxicological and Human Studies
- Chapter 5 : Dose-Response Assessment and Derivation of Health-Based Guidance Values
- Chapter 6 : Dietary Exposure Assessment of Chemicals in Food
- Chapter 7 : Risk Characterization
- Chapter 8 : Maximum Residue Limits for Pesticides and Veterinary Drugs
- Chapter 9 : Principles Related to Specific Groups of Substances

Several regulations and guidances of nanomaterials on food application

EU regulation

- 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.(EU) No 1169/2011
- To ensure a high level of protection of human health and consumers' interests, food consisting of engineered nanomaterials should also be considered a novel food under this Regulation. (EU) No 2015/2283

EFSA Guidance(2018)

GUIDANCE

EFSA Journal

ENDORSED: 29 May 2018

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Guidance on risk assessment of the application of nanoscience and nanotechnologies in the food and feed chain: Part 1, human and animal health

EFSA Scientific Committee,
Anthony Hardy, Diane Benford, Thorhallur Halldorsson, Michael John Jeger,
Helle Katrine Knutsen, Simon More, Hanspeter Naegeli, Hubert Noteborn, Colin Ockleford,
Antonia Ricci, Guido Rychen, Josef R. Schlatter, Vittorio Silano, Roland Solecki,
Dominique Turck, Maged Younes, Qasim Chaudhry, Francesco Cubadda, David Gott,
Agnes Oomen, Stefan Weigel, Melpo Karamitrou, Reinhilde Schoonjans and Alicja Mortensen

Abstract

The European Food Safety Authority has produced this Guidance on human and animal health aspects (Part 1) of the risk assessment of nanoscience and nanotechnology applications in the food and feed chain. It covers the application areas within EFSA's remit, e.g. novel foods, food contact materials, food/feed additives and pesticides. The Guidance takes account of the new developments that have taken place since publication of the previous Guidance in 2011. Potential future developments are suggested in the scientific literature for nanoencapsulated delivery systems and nanocomposites in applications such as novel foods, food/feed additives, biocides, pesticides and food contact materials. Therefore, the Guidance has taken account of relevant new scientific studies that provide more insights to physicochemical properties, exposure assessment and hazard characterisation of nanomaterials. It specifically elaborates on physicochemical characterisation of nanomaterials in terms of how to establish whether a material is a nanomaterial, the key parameters that should be measured, the methods and techniques that can be used for characterisation of nanomaterials and their determination in complex matrices. It also details the aspects relating to exposure assessment and hazard identification and characterisation. In particular, nanospecific considerations relating to *in vivo*/*in vitro* toxicological studies are discussed and a tiered framework for toxicological testing is outlined. It describes *in vitro* degradation, toxicokinetics, genotoxicity as well as general issues relating to testing of nanomaterials. Depending on the initial tier results, studies may be needed to investigate reproductive and developmental toxicity, immunotoxicity, allergenicity, neurotoxicity, effects on gut microbiome and endocrine activity. The possible use of read-across to fill data gaps as well as the potential use of integrated testing strategies and the knowledge of modes/mechanisms of action are also discussed. The Guidance proposes approaches to risk characterisation and uncertainty analysis, and provides recommendations for further research in this area.

1.2.3. Definition of engineered nanomaterial

Engineered nanomaterials are a subset of the 'nanomaterial' that is defined in the European Commission's Recommendation of 2011. As outlined in the Novel Food Regulation (EU) No 2015/2283[7] and referring to Regulation (EU) No 1169/2011[8] on the Provision of Food Information to Consumers, Engineered nanomaterial means 'any intentionally produced material that has one or more dimensions of the order of 100 nm or less or 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, including structures, agglomerates or aggregates, which may have a size above the order of 100 nm but retain properties that are characteristic of the nanoscale. Properties that are characteristic of the nanoscale include:

i) those related to the large specific surface area of the materials considered; and/or
ii) specific physicochemical properties that are different from those of the corresponding conventional material of the same chemical composition.'

EFSA (2018)

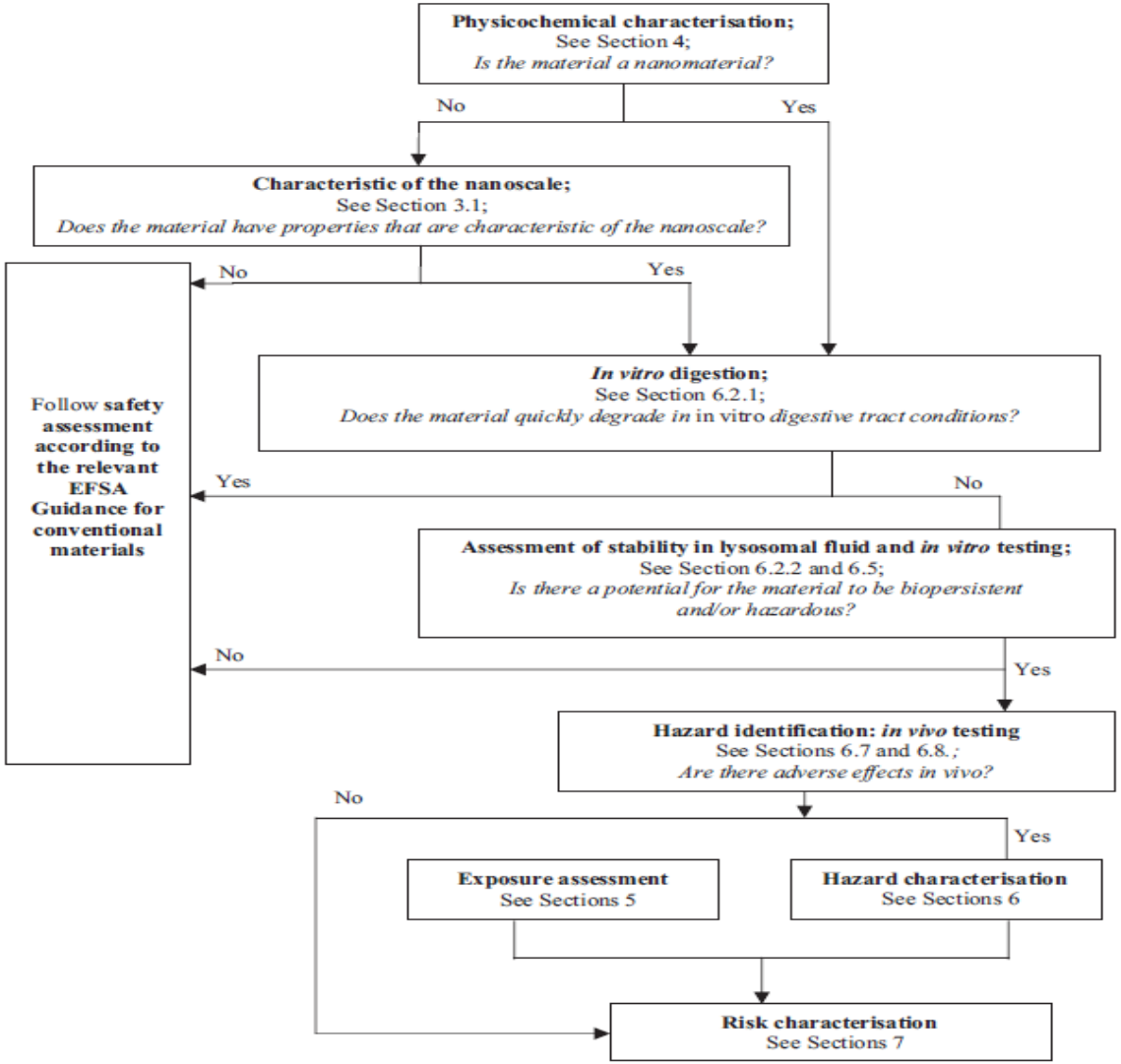

Figure 1: Schematic outline for risk assessment of ingested[11] nanomaterials for human and animal health, focussing on hazard characterisation. A complementing outline for the exposure part of the assessment is presented in Figure 2.

EFSA (2018)

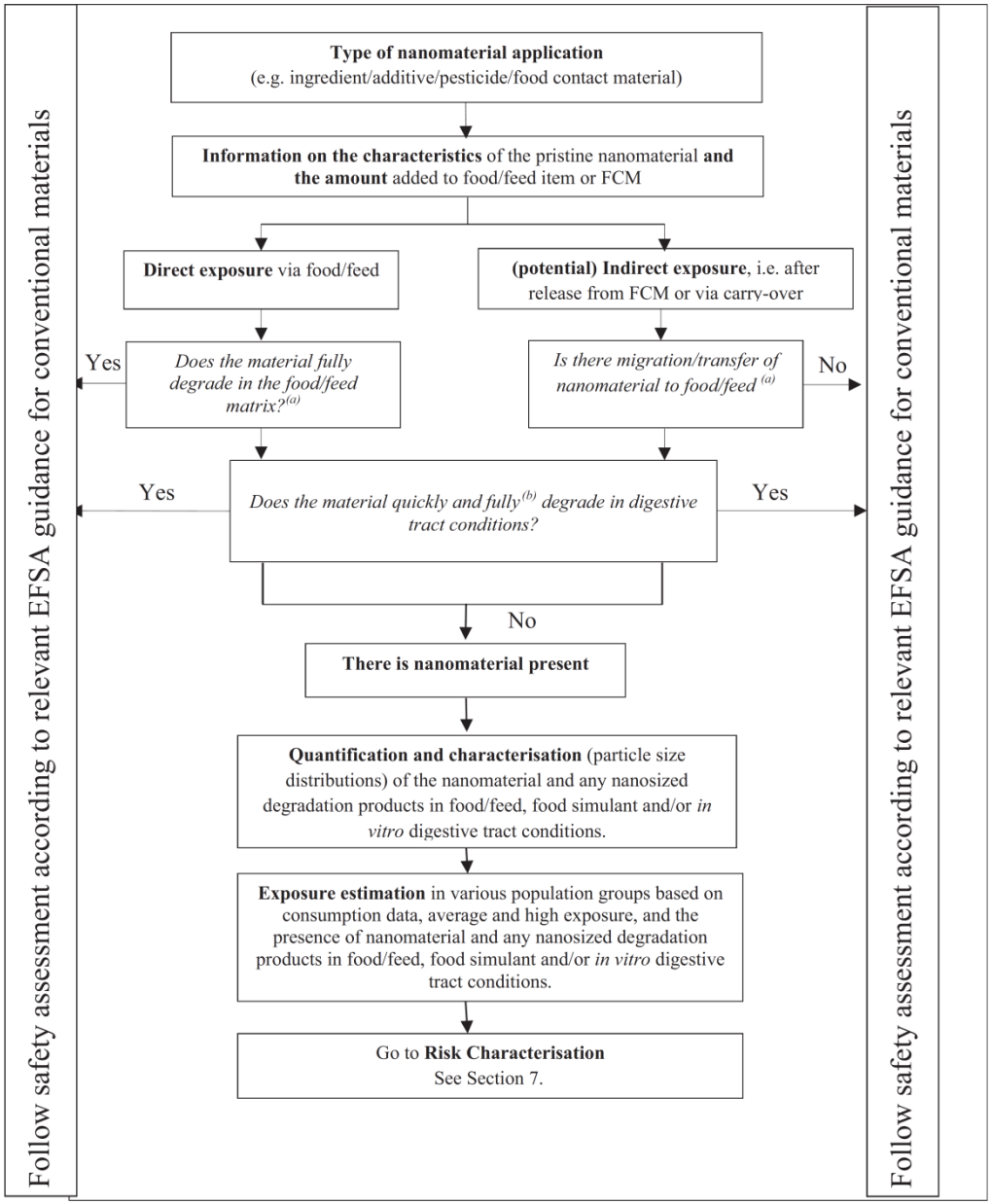

Figure 2: Steps in oral exposure assessment

The arrows going out (left and right) indicate that nanospecific considerations are not needed , and risk assessment for the non-nanomaterials can follow the standard approach (i.e. the relevant EFSA Guidances for conventional materials)

EFSA (2018)

Several nanomaterials allowed used in plastic FCM in EU (EC 10/2011)

- Carbon black (No. 411)
- Silicon dioxide (No. 87 & 504)
- Titanium nitride (No. 998)

- Use as additive or polymer production aid.
- These nanomaterials shall not migrate into food in detectable quantities.

Re-evaluation several food additives may have nanoparticles (EFSA)

- Calcium carbonate (E 170)
- Titanium dioxide (E 171)
- Iron oxides and hydroxide (E 172)
- Silver (E 174)
- Gold (E 175)

- There are insufficient data to prove these food additives are harmful for human health
- Specifications should include a characterization of particles in the nanoscale
- Need specific safety data of responding nanomaterial

USFDA

Guidance for Industry
Considering Whether an FDA-Regulated Product Involves the Application of Nanotechnology

Contains Nonbinding Recommendations

June, 2014

Additional copies are available from:
Office of Policy
Office of the Commissioner
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
Phone: 301-796-4830
http://www.fda.gov/RegulatoryInformation/Guidances/ucm257698.htm

You may submit electronic or written comments regarding this guidance at any time. Submit written comments on the guidance to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to http://www.regulations.gov. All comments should be identified with the docket number (FDA-2010-D-0530) listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this document contact: Office of the Commissioner, Food and Drug Administration, 10903 New Hampshire Avenue, Silver Spring, MD 20993, 301-796-4830.

U.S. Department of Health and Human Services
Food and Drug Administration
Office of the Commissioner

June 2014

Contains Nonbinding Recommendations

Guidance for Industry
Considering Whether an FDA-Regulated Product Involves the Application of Nanotechnology[1]

This guidance represents the Food and Drug Administration's (FDA's or the Agency's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the telephone number listed on the title page of this guidance.

I. INTRODUCTION AND SCOPE

Nanotechnology is an emerging technology that can be used in a broad array of FDA-regulated products, including medical products (*e.g.* to increase bioavailability of a drug), foods (*e.g.*, to improve food packaging) and cosmetics (*e.g.* to affect the look and feel of cosmetics). Materials in the nanoscale range (i.e., with at least one dimension in the size range of approximately 1 nanometer (nm) to 100 nm) can exhibit different chemical or physical properties, or biological effects compared to larger-scale counterparts. For example, dimension-dependent properties or phenomena may be used for functional effects such as increased bioavailability, decreased dosage, or increased potency of a drug product, decreased toxicity of a drug product, better detection of pathogens, more protective food packaging materials, or improved delivery of a functional ingredient or a nutrient in food (Refs. 1-6). These effects may derive from altered chemical, biological, or magnetic properties, altered electrical or optical activity, increased structural integrity, or other unique characteristics of materials in the nanoscale range not normally observed or expected in larger-scale materials with the same chemical composition (Ref. 7). Materials or end products may also exhibit similar properties or phenomena attributable to a dimension(s) outside the nanoscale range of approximately 1 nm to 100 nm (Refs. 27-30; see also discussion in Section II.B.5).

USFDA (2014)

A. Points to Consider

At this time, when considering whether an FDA-regulated product involves the application of nanotechnology, FDA will ask:

1. Whether a material or end product is engineered to have at least one external dimension, or an internal or surface structure, in the nanoscale range (approximately 1 nm to 100 nm);

In addition, as we explain in more detail below, because materials or end products can also exhibit related properties or phenomena attributable to a dimension(s) outside the nanoscale range of approximately 1 nm to 100 nm that are relevant to evaluations of safety, effectiveness, performance, quality, public health impact, or regulatory status of products, we will also ask:

2. Whether a material or end product is engineered to exhibit properties or phenomena, including physical or chemical properties or biological effects, that are attributable to its dimension(s), even if these dimensions fall outside the nanoscale range, up to one micrometer (1,000 nm).[6]

USFDA (2014)

III. CONCLUSION

The two Points to Consider elaborated in this guidance should be applied when considering whether an FDA-regulated product involves the application of nanotechnology. An affirmative finding to either of the Points to Consider, elaborated in this guidance, might suggest the need for particular attention to the product by FDA and/or industry for potential implications for safety, effectiveness, public health impact, or regulatory status of the product. We will consider future revisions to our approach, including developing regulatory definitions relevant to nanotechnology, as warranted and in keeping with evolving scientific understanding.

There remains a need to learn more about the potential role and importance of dimensions in the physical and chemical characteristics and biological effects exhibited by FDA-regulated products that involve the application of nanotechnology.[15] Product-specific premarket review, when required, offers an opportunity for FDA to better understand the properties and behavior of products that involve the application of nanotechnology. Where products that involve the application of nanotechnology are not subject to premarket review, we urge industry to consult with the Agency early in the product development process. In this way, any questions about the products' regulatory status, safety, effectiveness, or public health impact can be appropriately and adequately addressed. FDA has and, as needed, will continue to provide additional guidance to industry in more targeted guidance documents to address these considerations.

U.S. FDA (2014)

Health Canada

2. Objectives

The objectives of this Policy Statement are to:

1. Establish a working means of identifying nanomaterials;
2. Assist Health Canada to collect information and establish internal inventories regarding regulated substances, products, and any component material, ingredient, device, or structure that are nanomaterials;
3. Support communications about nanomaterials with the broader community of interested stakeholders; and,
4. Support the administration of the legislative and regulatory frameworks under the authority of Health Canada and to help further the development of policy, guidance and programs applicable to nanomaterials.

3. Scope

Nanomaterials that are manufactured and intended to be sold or represented for use as, or as part of a regulated product or substance, or that otherwise fall within Health Canada's mandate, are within the scope of this Policy Statement.

Health Canada(2011)

4. Policy Statement

4.1 Health Canada's Working Definition of Nanomaterial

Health Canada considers any manufactured substance or product and any component material, ingredient, device, or structure to be nanomaterial if:

a. It is at or within the nanoscale in at least one external dimension, or has internal or surface structure at the nanoscale, or;

b. It is smaller or larger than the nanoscale in all dimensions and exhibits one or more nanoscale properties/phenomena.

For the purposes of this definition:

i. The term "nanoscale" means 1 to 100 nanometres, inclusive;

ii. The term "nanoscale properties/phenomena" means 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; and,

iii. The term "manufactured" includes engineering processes and the control of matter.

Health Canada(2011)

TFDA

Guidance on the Registration of Nano-Food (2014)

Introduction：

The physical and chemical properties of nanomaterials are different relative to bulk materials, and those differences could have toxic effects. Since the safety/toxicity of nanomaterials still involve uncertainties, safety evaluations of the applications of nanotechnology to food products (so called nano-food) needs to be revisited. This guidance refers to international practices for evaluating the safety of nano-food in Taiwan.

Definition of Nano-foods:

There are two categories of nano-foods:

(a) "Nano-food ingredients" or "Nano-food additives" are defined as:

- Food ingredients or food additives that comprise of manufactured (not natural) particles with one or more external dimensions in the range 1-100 nm, and 50 % or more of the particles in the number size distribution.
- When a food ingredient or food additive is engineered to exhibit specific properties or phenomena, including physical or chemical properties or biological effects, that are attributable to its dimension(s), even if these dimensions fall outside the nanoscale range, up to one micrometer (1,000 nm).

(b) "Nanomaterial food" is defined as:

The constituents of "nanomaterial food" should meet definition (a) above. The weight or volume of (a) should be 50% or more of total constituent materials.

Guidance on the Registration of Nanomaterial-containing Food Utensils, Containers and Packaging (2017)

Introduction:

With technological advances, many novel materials have been developed for food-contact items. In this field, the application of nanotechnology can well improve thermal resistance and barrier functions; however, nanomaterials inside containers or packaging might also leach/migrate into food or beverages. Since the database on nanomaterials migration is insufficient, a safety assessment is required. This guidance references international safety assessment practices for food-contact materials/articles to assess the safety of "nanomaterial-containing food utensils, containers and packaging" in Taiwan.

TFDA(2017)

Definition:

(a) Food contact substance (nano-form) or FCS (nano-form):

The single, pure chemicals applied with nanotechnology can be regarded as constituents of food utensils, containers and packaging. For example, the constituents can be monomers, other initial substances, and macromolecules after microbial fermentation, additives and poly-production aid. The

(b) Food contact materials (FCM):

All materials in contact with food products can be made into food utensils, containers and packaging.

(c) Nanomaterial-containing food-contact materials:

This involves the addition of FCS (nano-form) or the application of nanotechnologies that result in general FCM exhibiting novel properties or functions, which can be made into "nanomaterial-containing food utensils, containers and packaging."

(d) Nanomaterial-containing food utensils, containers and packaging:

The application of nanotechnologies on general food utensils, containers and packages must exhibit novel properties or functions.

TFDA(2017)

Current management system on food applications of nanomaterials

- Most of them are guidances
- Definition of engineered nanomaterials are similar
- Including food, food additives, food packaging
- Base on risk assessment principles and methods
- Need method to assess nanomaterial (size distribution, physical chemical properties, and existence etc.)
- Need more safety data of nanomaterials (toxicity, ADME etc.)
- Other field regulation (Occupational Safety, Pollution, Ecosystem etc.) should be considered

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2. European Union, 2011, REGULATION (EU) No 1169/2011 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL.
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Thanks for your attention!