11
Nanomaterials in Food and Food Contact Materials – Potential Implications for Consumer Safety and Regulatory Controls

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11.1
Background

Recent advances in nanosciences and nanotechnologies have led to great interest in the study and potential manipulation of the properties of materials and substances at the nanoscale. Like other sectors, the new technological developments are promising to revolutionize the food sector – from production to processing, packaging, distribution, storage and consumption. The main focus of research and development in the food processing area relates to the development of processed nanostructures in food, and nano-sized food additives. The use of engineered nanomaterials to improve properties of plastic polymers has opened up another major application area for the development of innovative food packaging materials. Similar developments in the agricultural sector, although mainly at research and development stage at present, could offer many more potentially large-scale applications of nanotechnologies for food production. Despite the promise of enormous benefits, such developments have also raised a number of safety, ethical, policy, and regulatory questions. In particular, the likelihood of consumer exposure to potentially harmful engineered nanomaterials through consumption of nano-enabled foods and drinks has led to calls for a moratorium, or an outright ban, on the use of nanotechnologies until they are proven to be safe to consumers and the environment [1–3].

As for conventional substances, any risk to consumers from the use of engineered nanomaterials will be dependent on the toxicological properties of the materials, as well as the likelihood, extent, and frequency of any exposure. This will inevitably depend on the properties of the engineered nanomaterials used, and the nature of each application. In some applications, for example in food packaging, engineered nanomaterials may be incorporated in a fixed, bound or embedded form, and thus may not pose a significant risk of exposure to the consumer. Other applications may, on the other hand, contain free nanoparticles and therefore pose a relatively greater risk to the consumer.

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This chapter discusses the potential implications of nanotechnology applications for consumer safety in the light of the different existing and anticipated applications in the food and related sectors. The chapter also discusses the relevance of existing regulatory frameworks in relation to controlling the potential risks of nanotechnology applications to the consumer.

11.2 Nanomaterials Likely to be Used in Food and Related Applications

Based on the available information, the engineered nanomaterials likely to be used in nano-enabled food products fall into three main categories: inorganic, surface functionalized, and organic engineered nanomaterials [4]. In addition to the deliberately manufactured engineered nanomaterials, there is also a possibility that some micronized materials may also contain a nanoscale fraction due to a natural variation in the size range of manufactured materials [5]. Some engineered nanomaterials may also end up in food products as a result of environmental contamination, migration from packaging, contact with active surfaces, or from the use of nano-sized agrochemicals (e.g., pesticides or veterinary medicines).

11.2.1 Inorganic Nanomaterials

A number of inorganic engineered nanomaterials are known to be used in food and health food products and food packaging applications. These include engineered nanomaterials of transition metals (such as silver, titanium dioxide and iron), alkaline earth metals (such as calcium and magnesium), and non-metals (such as selenium and silicates) [4, 6]. Food packaging is currently the major area of application of inorganic metal and metal oxide engineered nanomaterials. Example applications include plastic polymers with nanoclay as a gas barrier, nano-silver and nano-zinc oxide for antimicrobial action, nano-titanium dioxide for ultraviolet (UV) protection, nano-titanium nitride as a processing aid, and nano-silica for surface coating.

Nano-silver is increasingly used as an antimicrobial, antiodorant, and (proclaimed) health supplement. Although the current use of nano-silver relates mainly to health food and packaging applications, its use as an additive in antibacterial wheat flour is the subject of a recent patent application [7].

Amorphous silica has been used for many years in food applications, such as in clearing of beers and wines, and as a free-flowing agent in powdered soups. The conventional bulk form of silica is a permitted food additive (SiO_2 INS 551). Porous silica is used in nano-filtration to remove undesired components in food and beverages – such as undesirable tastes in some plant extracts. Amorphous nano-silica is also known to be used in food contact surfaces and food packaging applications.

The conventional bulk form of titanium dioxide is already approved as an additive for food use (TiO_2 INS 171). Nano-titanium dioxide is currently used in a number of consumer products (e.g., paints, coatings, cosmetics, water treatment) but its use may extend to foodstuffs. For example, a US Patent (US 5741505) describes the potential application of nanoscale inorganic coatings directly on food surfaces to provide a barrier to moisture and oxygen to improve shelf-life, and/or the flavor impact of foods. The materials described for the nano-coatings, which are intended to be applied in a continuous process as a thin amorphous film of 50 nm or less, include titanium dioxide, along with silicon dioxide and magnesium oxide. The main intended applications described in the patent include confectionary products. However, to our knowledge, this technology has not so far been used in any commercial application.

Nano-iron is available commercially as a health supplement. Zero-valent nano-iron is also used in the treatment of contaminated water, where it is claimed to decontaminate water by breaking down organic pollutants and killing microbial pathogens. Nano-selenium is being marketed as an additive to a green tea product in China, with a number of (proclaimed) health benefits resulting from the enhanced uptake of selenium. Nano-calcium salts are subject to patent applications for intended uses in chewing gums (WO/2004/028262, and US Patent 20060034975 – Coated Chewing Gum – Sustech GmbH & Co. KG, Darmstadt, Germany). Nano-calcium and nano-magnesium salts are also available commercially as health supplements.

11.2.2 Surface-Functionalized Nanomaterials

Surface-functionalized nanomaterials are the second-generation engineered nanomaterials that can add certain functionality to the matrix, such as antimicrobial activity or a preservative action, for example, through absorption of oxygen. For food packaging materials, functionalized engineered nanomaterials are used to bind with the polymer matrix to offer mechanical strength or a barrier against movement of gases, volatile components (such as flavors) or moisture. One such example is the use of functionalized nanoclays to develop food packaging materials with enhanced gas barrier properties. The nanoclay mineral is mainly montmorillonite (also termed bentonite), which is a natural clay obtained from volcanic ash/rocks. Nanoclay has a natural nanoscale layer structure and is organically modified to bind to polymer matrices. Compared to unmodified engineered nanomaterials, the surface-functionalized engineered nanomaterials are more likely to react with different food components, and therefore become bound to food matrices. They are thus less likely to be available in free particulate forms in food, and also unlikely to migrate from packaging materials.

11.2.3 Organic Nanomaterials

A number of organic nano-sized materials, many of them naturally occurring, have been developed for use in food and feed products. These include vitamins, antioxidants, colorants, flavoring agents, and preservatives, which may be encapsulated in nano-delivery systems. The main proclaimed benefits of using a nano-sized organic additive over conventional forms are better dispersion of insoluble substances in foodstuffs without the need for additional fat, increased uptake and absorption, and improved bioavailability in the body. There are a wide range of available food additives (e.g., benzoic acid, citric acid, ascorbic acid) and supplements (e.g., vitamins A and E, isoflavones, β-carotene, lutein, omega-3 fatty acids, coenzyme-Q10). A synthetic nano-sized water-dispersible form of lycopene, a naturally occurring carotenoid in tomatoes, is also available commercially with a reported particle size in the range of 100 nm. Lycopene has been notified as of GRAS (generally regarded as safe) status to the Food and Drug Administration (FDA) in the USA (GRAS Notice GRN000119/2002), and a recent European Food Safety Authority (EFSA) opinion has also considered its use in food and beverages as safe [8]. However, the evaluations by both EFSA and the Joint FAO/WHO Expert Committee on Food Additives (JECFA) do not include the use of nano-sized forms. It is not known if the nano-form of the material is currently used in any food or beverage product.

11.3 Potential Consumer Safety Implications

It is known that materials manufactured at a nanometer scale can behave differently from their conventional equivalents, in terms of physicochemical properties, behavior, and interactions with other substances. For example, properties of engineered nanomaterials in the lower range of the nanometer scale are likely to be influenced by quantum effects compared to larger-sized equivalents. It is also possible that such changes in properties can lead to a significant deviation in the anticipated effects and impacts of engineered nanomaterials on biological systems. Studies have already suggested a change in the toxicity profile for some engineered nanomaterials compared to conventional equivalents [9, 10]. For example, exposure to some engineered nanomaterials has been shown to cause induction of oxyradical generation in both *in vitro* and *in vivo* studies, which may lead to oxidative stress and inflammatory reactions [11–13].

Another important aspect in relation to the potential harmful effects of engineered nanomaterials is their ability (especially of free nanoparticles) to penetrate biological membranes that act as barriers to the entry of particulate substances into cells and tissues [14, 15]. This adds a new dimension to the toxicology of particulate materials, as certain insoluble and potentially reactive or biopersistent nanoparticles may reach new targets in the body, where the entry of larger equivalents would be restricted [16–22].

Owing to their enormous surface free energies, engineered nanoparticles can adsorb or bind different compounds and moieties on their surfaces [23]. This, combined with their ability to cross cellular barriers, poses a potential risk of such particles acting as a carrier of harmful substances into the circulatory system, and to other unintended organs in the body. Depending on the surface chemistry, it is also known that systemically introduced engineered nanomaterials can interact with various biological entities, such as plasma proteins, platelets, and cells [23, 24]. In biological environments, nanoparticles may become coated with different biomolecules, especially proteins [25]. Such coatings may also direct them to specific parts of the body. For example, coating of nanoparticles with apolipoprotein E has been associated with their transport to the brain [26]. This suggests that engineered nanomaterials can undergo various interactions and transformations in both food and biological systems, which can influence their absorption, distribution, metabolism, and excretion (ADME) properties [27], and may lead to a deviation in their biological effects.

While there is a growing literature on the inhalation toxicity of engineered nanomaterials, only a limited number of studies have been carried out so far on the translocation and distribution of nanoparticles to various organs and tissues, and their effects following oral administration. The diffusion rate of particulate materials through the gastrointestinal (GI) mucus is reported to be dependent on a number of factors, such as size, charge [28], and surface coating [29]. The translocation from the gastrointestinal tract has been found to be greater for nano-sized particles than for larger ones [20, 30]. Engineered nanomaterials in the smaller nanometer range have also been found to cross the mucus layer faster than the larger ones [17, 18]. Within the gastrointestinal tract, the rate of uptake of nanoparticles has been reported to be between 2 and 200 times greater in the Peyer's patches compared to that in the enterocytes [20], despite the fact that Peyer's patches only represent around 1% of the total intestinal surface area.

Jani *et al.* [22] demonstrated that titanium dioxide nanoparticles (rutile, 500 nm) translocated to systemic organs, such as the liver and spleen, following oral gavage (forced feeding) for 10 days to female Sprague–Dawley rats. The nanoparticles were also detected in the lungs and peritoneal tissues, but not in the heart and kidney. Oral administration of colloidal gold nanoparticles (58, 28, 10, and 4 nm) to mice has been shown to result in an increasing distribution of smaller nanoparticles to different organs [17]. Following repeated oral administration of nanosilver (60 nm) at different dose levels, accumulation of the nanoparticles has been observed in the GI tract of Sprague–Dawley rats, followed by the kidney and liver, lungs, testes, brain and blood [31].

The insoluble, biopersistent engineered nanomaterials are typically taken up by the M-cells of Peyer's patches and passed to underlying macrophages, where they accumulate and appear as pigmentation in cells at the base of human intestinal lymphoid aggregates [32]. The few studies carried out so far have not found a clear association between dietary particulates (micro- or ultra-fine) with the initiation or exacerbation of gut diseases, such as Crohn's disease or irritable bowel syndrome [33, 34]. In an *in vitro* study on human epithelial cell cultures, Chen and von Mikecz [35] have shown that fluorescently labeled silica nanoparticles smaller than 70 nm could enter cell nuclei. The study also found protein accumulation in the nuclei and indication for impairment of deoxyribonucleic acid (DNA) replication and transcription. However, the relevance of the findings to potential *in vivo* effects of orally ingested nano-silica is not certain. Some engineered nanomaterials, such as nano-silver, are also known to have strong antimicrobial activity. The ingestion of such engineered nanomaterials via food may have a deleterious effect on the gut natural microflora. However, there is no published research at present on the potential effects of nano-silver or other antimicrobial engineered nanomaterials on the gut microflora.

A healthy digestive system allows the absorption of nutrients from the gastrointestinal tract after digestion of the food components. The gut wall is designed to let the digested dietary nutrients through, but to prevent translocation of larger-sized materials or foreign substances into the circulatory system. Our food is composed of complex natural polymers, such as proteins, carbohydrates, and fats. Many of these food components either exist, or are metabolized, at a nanoscale. In that sense, it seems that our bodies are used to dealing with nanostructures all the time. However, most of these materials are those that are either digested in the gastrointestinal tract, or are excreted from the body, and hence are not biopersistent. Many engineered nanomaterials falling in such "soft" categories would be expected to be dealt with in the body in a similar way as the conventional equivalents, and therefore should not pose any different risk to the consumer. The exception may be those engineered nanomaterials that are composed of a harmful substance, but such materials are highly unlikely to be used for food applications.

The consumer safety concerns relate mainly to the potential exposure to those engineered nanomaterials that are insoluble, indigestible, and biopersistent. If such "hard" nanomaterials are used for food applications, consumption of the food products will provide a direct route of entry of the engineered nanomaterials into the body. Although the potential use of "hard" engineered nanomaterials has raised a number of consumer safety concerns, there are major knowledge gaps in this area at present to allow an adequate assessment of any risk. For example, the behavior, interactions, fate, and effects of most engineered nanomaterials inside and outside the gastrointestinal tract are currently not known. It is possible that many "hard" engineered nanomaterials, when added to food products, will not remain in a free particulate form due to agglomeration, aggregation, binding with other food components, transformations due to reaction with stomach acid or digestive enzymes, and so on, and hence will not be available for translocation from the gastrointestinal tract. The lack of validated methodologies for detection and characterization of engineered nanomaterials in food matrices is also currently a major barrier in regard to further developments in this area.

11.4
Current and Projected Applications for Food

A number of recent reports and reviews have highlighted the current and projected uses of engineered nanomaterials for food and food packaging applications [4, 5, 36–40]. A review by Chaudhry *et al.* [4] has identified the following main categories of known and projected applications of nanotechnologies for the food and related areas:

- processed nanostructures in foodstuffs;
- nano-sized food additives;
- incorporation of engineered nanomaterials into coatings, packaging materials, and (bio)nanosensors;
- nano-enabled pesticides, veterinary medicines and other agrochemicals.

11.4.1 Processed Nanostructures in Foodstuffs

The advent of new probe microscopy tools in the early 1980s, such as atomic force microscopy, enabled the study and better understanding of the structures of food components close to the molecular level. This further enabled the development of new food textures through rational design of natural nanostructures, rather than by empirical guesswork [41]. This knowledge is driving the development of innovative food products based on nanostructures (also termed nanotextures), in the form of stable nano-micelles and liposomes. The methods commonly used for this purpose involve development of nano-emulsions, surfactant micelles, emulsion bilayers, double or multiple emulsions or reverse micelles [42].

The nanostructured food products are expected to offer novel or improved food tastes, textures, and mouth sensations. A typical example of this technology can be envisaged in the form of a low-fat food, which because of nanostructuring has a creamy texture and taste that is similar to its full-fat equivalent. At present there is no known example of a commercially available nanostructured food, although a number of products are understood to be in the research and development pipeline – some of which may be near market. An example of a product currently under research and development is a mayonnaise that is composed of an emulsion that contains nano-sized droplets of water inside. The mayonnaise would offer taste and texture attributes similar to the full-fat equivalent, but with a significant reduction in the fat content [43]. It can be envisaged from the nature of these applications that developments in this area will be aimed at those food products that are traditionally high in fat content, such as spreads, mayonnaises, creams, ice creams, sauces, dressings, and so on. Depending on their safety, scale of market penetration, and acceptance by the consumers, the nanostructured food products could provide a useful means to the consumer to reduce their dietary intake of fat, while still enjoying tasty foodstuffs.

This area of application is expected to involve mainly the use of “soft” nanomaterials that are likely to be digested in the gastrointestinal tract. As discussed in Section 11.1, this application area should not raise any special consumer safety concerns, and as such need not be branded “nanotechnology”. The safety evaluations for such applications should, however, consider whether nanoscale processing of some food ingredients could lead to a drastic change in the digestibility, uptake, and bioavailability of the resulting nanostructures in the body.

11.4.2
Nano-sized Food Additives

The development of nano-sized food additives and supplements represents an emerging area of nanotechnology applications, which could potentially exploit a much wider range of food and health food products. The applications involve the use of nano-sized or nano-encapsulated food additives, such as colors, preservatives, flavoring agents, and supplements. A number of nano-sized additives are already available in some countries. Examples include minerals, antimicrobials, vitamins, and antioxidants. Virtually all such additives and supplements claim improved absorption and bioavailability in the body compared with their larger-sized equivalents [4]. The technology employed for this purpose involves the development of nano-sized substances, or nano-encapsulating them in the form of micelles, liposomes or biopolymer-based carrier systems. These methods have also been used to develop delivery systems for additives and supplements for use in food and beverage products.

Nano-encapsulation offers benefits similar to micro-encapsulation, that is, in terms of preserving the ingredients and additives during processing and storage, masking unpleasant tastes and flavors, controlling the release of additives, improving the dispersion of water-insoluble food ingredients and additives, and improving the uptake of encapsulated nutrients and supplements. The concept of nano-delivery systems seems to have originated from medical research into targeted delivery of drugs and therapeutics. While the use of nano-carrier technology in food and related applications can offer a number of benefits, such as increased absorption and uptake, and improved bioavailability of nutrients and supplements, it also has the potential to alter the ADME characteristics of the substances in the body.

For example, using this approach, a water-soluble food additive can be rendered fat dispersible, or vice versa. Such transformations may not have an adverse health implication, provided that the nano-carrier breaks down and releases its contents in the gastrointestinal tract. In such a case, the risk of the encapsulated substance will not be any different from that of its conventional equivalent. However, if a nano-carrier is capable of delivering a substance to the circulatory system and other parts of the body, the altered ADME characteristics of some additives may pose an increased risk to the consumer's health. The safety considerations for this technology should also need to ensure that a nano-carrier does not act as a "Trojan horse", in terms of facilitating the translocation of potentially harmful or foreign materials from the GI tract to other unintended parts of the body.

As discussed in Section 10.1, the main risk to consumers from nano-additives in food is, however, expected to arise from the use of insoluble and biopersistent "hard" engineered nanomaterials.

11.4.3 Applications for Food Packaging

Nanotechnology applications for food contact materials (FCMs) and especially food packaging materials constitute the largest market share of the current and short-term predicted applications for the food sector [4, 44]. While most nanotechnology applications in the food and agriculture sectors are currently at research and development or near-market stages, the applications for food packaging seem to have become a commercial reality in some countries. The likely benefits of the technology include nano-enabled packaging materials that are lightweight but strong, and/or that can prolong shelf-life of the packaged foodstuffs. Considering the fixed or embedded nature of engineered nanomaterials in plastic polymers, this area of application is not expected to pose any significant risk to the consumer due to lack of migration into the packaged foodstuffs. A variety of nano-enabled packaging materials are currently available worldwide. The main applications in this area fall into the following broad categories [4, 45]:

- engineered nanomaterial–polymer composites (including biodegradable composites) with improved packaging properties in terms of flexibility, gas barrier properties, and temperature and moisture stability;
- active food contact materials incorporating engineered nanomaterials with antimicrobial or oxygen scavenging properties;
- intelligent or smart packaging concepts, incorporating nanosensors that can monitor and report food quality during transportation and storage.

Nanoclays have been incorporated into a variety of polymer composites for improved gas barrier properties. These include polyamides, polyolefins, polystyrene, ethylene–vinyl acetate copolymer, epoxy resins, polyurethane, polyimides, and polyethylene terephthalate. Known applications of the nanoclay–polymer composites include multilayer film packaging, bottles for beer and carbonated drinks, and thermoformed containers.

Metal and metal oxide engineered nanomaterial–polymer composites have been developed for a range of purposes, such as antimicrobial surfaces, abrasion resistance, ultraviolet absorption, or mechanical strength. The main engineered nanomaterials used in this area include nano-silver and nano-zinc oxide for antimicrobial action, nano-titanium dioxide for ultraviolet protection, nano-titanium nitride as a processing aid, and nano-silica for surface coating. For example, a number of "active" food contact materials incorporating nano-silver are available commercially that are claimed to preserve the food materials by inhibiting the growth of microorganisms on the food contact material surface. These include plastic food storage containers and bags. Nano-silver is also reported to have been incorporated into the plastic linings of many domestic refrigerators to prevent microbial growth, to maintain a clean environment, and to aid cleaning. In this regard, the discovery of antimicrobial properties of nano-zinc oxide and nano-magnesium oxide provides more affordable materials for applications in food packaging [46]. A plastic wrap containing nano-zinc oxide is currently available in Taiwan, which is claimed to sterilize under indoor lighting conditions. Any significant extension in the shelf-life of packaged food products should contribute toward reducing the waste of foodstuffs.

A range of coatings containing engineered nanomaterials is available for antimicrobial, scratch-resistant, anti-reflective, or corrosion-resistant surfaces. Examples of these include silver nano-coating on kitchenware, cutting boards, teapots, and other kitchen objects. Antibacterial nano-coatings on food preparation surfaces, such as meat cutting machinery in abattoirs, and food preparation and processing surfaces and conveyer belts, could also help to maintain hygiene during food processing. This may have special benefits for complex or hard-to-reach parts that are difficult to clean in place.

Nanotechnology has also enabled the development of nanosensors that can be applied as labels or coatings to add an intelligent function to food packaging in terms of ensuring the integrity of the package through detection of leaks (e.g., for foodstuffs packed under vacuum or inert atmosphere), indications of time–temperature variations (e.g., freeze–thaw–refreezing), or microbial safety (deterioration of foodstuffs). Food safety also requires confirmation of the authenticity of products. This is where application of nano-barcodes incorporated into printing inks or coatings has shown the potential for use in tracing the authenticity of the packaged product [47].

Any consumer safety concerns from nano-enabled food packaging and labels will only arise if engineered nanomaterials migrate into the packaged foodstuffs. Currently, there are only a few published studies on the migration of engineered nanomaterials from packaging materials. Avella *et al.* [48] determined the migration of Fe, Mg, and Si from a biodegradable starch–nanoclay nanocomposite film into packaged vegetables (lettuce and spinach). The results showed an insignificant increase in the levels of Fe and Mg in the packaged vegetables, while a consistent increase in Si (the main component of nanoclay) was noted.

A recent study by Šimon *et al.* [49] modeled the potential migration of engineered nanomaterials from different food contact materials on the basis of physicochemical parameters. The modeling predicted that any detectable migration of engineered nanoparticles from packaging polymers to packaged foodstuffs will take place only: (i) in the case of very small nanoparticles with a radius in the lower nanometer range; (ii) for polymers with a low dynamic viscosity such as polyolefins; and (iii) with no nanoparticle–polymer binding.

Another recent (unpublished) study by Bradley *et al.* (FERA, York) determined the migration of nanoclay components from commercial beer bottles that had a nanoclay composite embedded between polyethylene terephthalate (PET) layers. The study also determined the migration of nano-silver from commercial food containers made of polypropylene–nano-silver composite. The study found no detectable migration of nanoclay from PET bottles, and noted only a very low migration of silver (less than the limit of quantification) from food containers made of polypropylene–nano-silver composite. In either case, the presence of the engineered nanomaterials did not affect migration of other non-nano-components from the packaging materials. While these few studies provide some reassurance in the safety of nano-enabled food packaging materials, more tests will be needed to establish migration patterns for other engineered nanomaterial–polymer composites.

11.4.4 Applications in Food Production

The likely benefits of substituting active ingredients or carriers with nano-sized equivalents has opened up new avenues for research into potential applications of engineered nanomaterials to develop novel formulations of pesticides, veterinary medicines, and other agrochemicals, such as fertilizers and plant growth regulators [50, 51]. The anticipated benefits include a potential reduction in the use of certain agrochemicals, better dispersions, and control of dosage and applications of the nano-formulations in the field.

Theoretically, any nano-sized mineral, vitamin, or other additive or supplement developed for a food application can equally be used for animal feed. There are a few examples of available products where a nano-sized additive has been specifically developed (or is under development) for animal feed. For example, certain nano-grade vitamin mixes are available commercially for use in poultry and livestock feed. Examples of research and development in this area include a feed additive comprising a natural biopolymer from yeast cell walls that can bind mycotoxins to protect animals against mycotoxicosis, and an aflatoxin-binding nano-additive for animal feed, which is derived from modified nanoclay [52]. A polystyrene nanoparticle, with polyethylene glycol (PEG) linker and mannose targeting biomolecule, has also been developed that adheres to *Escherichia coli*. Administration of the nanoparticle through feed is likely to be helpful in removing food-borne pathogens in the gastrointestinal tract of the animals [53].

Research is also being carried out into the development of various nano-sized agrochemicals, such as fertilizers, pesticides, and veterinary medicines. The use of nano-sized active ingredients has been suggested to offer improved delivery of the agrochemicals in the field, better efficacy of pesticides, and better control over dosing of veterinary products. For example, nano-encapsulated and solid lipid nanoparticles have been explored for the delivery of agrochemicals [54], such as slow- or controlled-release fertilizers and pesticides. One example is a combined fertilizer and pesticide formulation encapsulated in nanoclay for the slow release of growth stimulants and bio-control agents [2]. Fertilizer compositions, claimed to contain nano-sized micronutrients, and micronized (volcanic) rock dust, are available commercially for remineralization of soil.

Despite a great deal of industrial interest in the use of nanotechnologies in the food production area, examples of the available products at present are very few and far between. Most of the developments seem to be currently at the research and development stage. However, such applications have the potential for large-scale use in the future, which is also likely to increase the potential exposure to agrochemicals used in food production.

11.5 Implications for Regulatory Frameworks

In many countries, regulatory frameworks exist for pre-market evaluation for food products. Despite some regulatory uncertainties [55, 56], the new developments in nanotechnology are taking place in a regulatory vacuum, as the potential risks will be controlled under the existing frameworks [57]. These relate to a plethora of regulatory frameworks on general food safety, food additives, novel foods, specific health claims, chemical safety, food contact materials, water quality, and other specific regulations on the use of certain chemicals in food production and protection, such as biocides, pesticides, veterinary medicines, and so on. Environmental regulations are also likely to capture the use of engineered nanomaterials in food packaging, and agri-food production applications.

Examples of general food laws include the Federal Food, Drug, and Cosmetic Act (the FDC Act) in the USA, which is administered by the Food and Drug Administration,[1] the European Commission's Food Law Regulation 178/2002, which sets down the general principles and requirements of food law within the European Union and provides for the establishment of the European Food Safety Authority (EFSA), and the Australia New Zealand Food Standards Code (the Food Standards Code).[2]

Most countries also have legislation relating to food contact materials, setting out (approved) materials and additives that can be used for food packaging, and acceptable levels of migration of substances from packaging into foodstuffs. The legislation takes different forms in different countries, but the principles – to help ensure consumer protection and avoid contamination of foodstuffs – are universal. The relevant regulations require that food contact materials should be made and used in such ways that they do not transfer constituents to food in quantities that could:

a) endanger human health;
b) bring about an unacceptable change in composition; or
c) bring about deterioration in organoleptic characteristics thereof.

There are also certain cross-cutting horizontal regulations that are relevant to nanotechnology applications for food and food packaging. An example of this in Europe is the Directive 2001/95/EC of 3 December 2001 on General Product Safety (in force since 14 January 2004, replacing Directive 92/59/EC). This legislation embodies the main principle that only safe products can be placed on the market. Briefly, a safe product is one that, under normal and reasonably foreseeable conditions of use, does not present any risk (or only the minimum acceptable risk), taking into account the characteristics, effects, presentation of the products, and the categories of persons at risks. Owing to its broad and horizontal scope, the Directive applies to risks that are not covered by other specific European Union

1) For the purposes of this chapter, other relevant legislative instruments include the Dietary Supplement Health and Education Act of 1994, the Food Additive Amendment Act of 1958, and the Code of Federal Regulations.

2) Available at: http://www.foodstandards.gov.au/foodstandards/foodstandardscode/.

provisions on products. Thus it applies to products containing engineered nanomaterials, with the onus of ensuring the safety of such products resting with the person who places them on the market. Another notable regulation relevant to nanotechnology applications for food packaging is the EU's chemicals regulation (EC 1907/2006, in effect from 1 June 2007) REACH (Registration, Evaluation, Authorization, and Restriction of Chemicals), which requires registration of all substances that are produced and/or marketed in the European Union above $1\,t\,yr^{-1}$ – as such, in preparations, or in articles.

A number of studies have assessed the relevance and adequacy of existing regulatory frameworks in relation to the increasing applications of nanotechnologies for the food sector [55, 58–61]. Findings of these reviews suggest that the current regulatory frameworks for food and food contact materials in different jurisdictions, such as the European Union, the USA, and Australia, are broad enough to "catch" nano-enabled food and food contact materials. A few uncertainties in regulatory frameworks, however, appear to arise from the current lack of understanding in relation to, for example, a clear definition that encompasses the distinctive properties of nano-ingredients and additives, a clearly defined responsibility and liability for relevant products and applications, appropriate permissible limits that relate to the (potential) effects of nano-substances in food, and an exclusive pre-market approval system for nano-enabled food products. Nevertheless, a case-by-case assessment of the safety of intended applications by the manufacturers (as recommended in the recent EFSA opinion [5]) should ensure that only safe applications of the new technology are placed on the market.

In this regard, there are also some recent developments in the regulatory area. These include recasting of key European regulatory instruments, such as Regulation 258/97 (the Novel Foods Regulation), which requires safety assessment of any food product that does not have a significant history of use in the European Union, or that is produced using a new production process, or that gives rise to significant changes in the nutritional value, metabolism or level of undesirable substances of the foods or food ingredients. The legislation is currently being reviewed in Europe, and is expected to include a specific reference to foods modified by new production processes "such as nanotechnology and nanoscience, which may have an impact on food".

The use of food additives in the European Union is currently controlled by the Food Additives Framework Directive) and the subordinate legislation. Subject to adoption by the European Community, the Food Additives Framework Directive will be replaced by a common authorization system in 2010, which will provide for a common basis of controls on food additives (EC Regulation No. 1333/2008), food enzymes (EC Regulation No. 1332/2008), and food flavorings (EC Regulation No. 1334/2008). The adoption of the common authorization procedure will also bring together all of the existing food additive regulations, and will introduce comitology[3] for the approval of the three categories of substances. The most relevant aspect in relation to the use of nano-sized food additives in the new

3) Comitology in the European Union refers to the committee system that oversees the delegated acts implemented by the European Commission.

Regulation is the re-evaluation of safety assessment, which will ensure that food additives, once permitted, are kept under continuous observation and re-evaluation. Therefore, under the new Regulation, producers or users of food additives that are “significantly different from those included in the risk assessment of the Authority or different from those covered by the specifications laid down” will be obliged to inform the Commission of any new information that may affect their safety assessment. Also, under the new Regulation, the EFSA will be invested with the power to re-evaluate a food additive on the basis of “new scientific information”.

The commercial exploitation of nanotechnology is almost concurrent to that of the start of online marketing of consumer products via the Internet. Virtually all of the currently available nanotechnology-derived consumer products in the areas of food and health food can be bought via the Internet anywhere in the world. The global boundaries of online marketing have also raised questions over the applicability and effectiveness of national food laws to control risks from products that may be produced abroad but are bought by a consumer through the Internet for personal consumption. This results in the regulation of nanotechnology products to be applied at the global scale, together with establishing liabilities, which poses a challenge in that food laws in many countries may not conform to each other. As research clears some of the main scientific uncertainties in the coming years, issues like these will need resolving at the international level through the development of frameworks that relate to global trade agreements.

11.6 Conclusions

The overview of nanotechnology applications presented in this chapter shows a variety of benefits for the whole of the food chain – from new or improved tastes, textures, and mouth sensations, through potential reduction in the dietary intake of fat and various food additives, to enhanced absorption of nutrients, preservation of quality and freshness, better traceability, and security of food products. It is also clear that currently there are major knowledge gaps in our understanding of the properties, behavior, and effects of the engineered nanomaterials that may be used in food applications. While these knowledge gaps make it difficult to assess the risk of such applications to a consumer, a careful consideration of the materials and applications can provide a basis for a conceptual risk assessment.

For example, the use of “soft” nanomaterials may not require as detailed evaluations as the “hard” nanomaterials. As more research uncovers the basic rules that drive the properties, behavior, and effects of engineered nanomaterials, even some “hard” nanomaterials may not prove to be as harmful as feared. This does not, however, mean that an unexpected hazard or risk of some engineered nanomaterials will not come to surface in the future, but this applies equally to other (conventional) materials, processes, and products. The existence of stringent regulatory controls provides some reassurance that only safe products and applications of nanotechnologies will be permitted on the market. However, the industry needs to adopt a pragmatic approach – especially where intended applications relate to the use of "hard" engineered nanomaterials and carry a likelihood of consumer exposure – and perform a case-by-case safety evaluation of the intended products (as recommended in the recent EFSA opinion [5]) before placing them on the market.

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