EMBO reports

A little hard to swallow?

The use of nanotechnology in the food industry might be both boon and bane to human health

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Eating a 'grey goo' of nanoparticles may seem unpalatable, but the food industry believes that nanotechnology could deliver commercial benefits for the processing and preservation of food (Fig 1). However, as with all new technologies, the question arises as to whether ingesting such particles—some of which are being used to kill microorganisms in food—might also have potential negative effects on human health. Because of major food-producers' increasing interest in nanotechnology, the question is becoming relevant to researchers as well as regulators.

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Nanotechnology involves the use of extremely small particles that range from a few nanometres in size—roughly half the diameter of a DNA strand—to 100s of nanometres—about the size of cell organelles and viruses. Nanoparticles per se are not man-made, as they occur naturally in various forms such as oceanic spray and fine sand. Human-engineered particles have been around for years in cosmetics, sunscreens and cleaning products. Now, however, the food industry wants to use nanotechnology to extend the freshness of products, detect spoilage and inhibit the growth of microorganisms. Given this, the US Food and Drug Administration (FDA) has issued a non-regulatory 'guidance' asserting the critical need to better understand the reactivity of engineered nanoparticles. The agency is specifically concerned about the 'deliberate manipulation and control of particle size' as such materials might have an impact on public health and safety (http://www.fda.gov/regulatoryinformation/guidances/ucm257698.htm).

Many critics of the food industry's use of nanotechnology think the guidance document is not sufficient and that the US government should take regulatory action. Among them is J. Clarence Davies, who chaired the US National Academy of Sciences' Committee on Decision Making for Regulating Chemicals in the Environment and who was involved in creating the US Environmental Protection Agency. "The guidance did not say much and Margaret Hamburg [the FDA commissioner] stated that the purpose of the guidance was to narrow the discussion [...] and work with the industry to determine if this focus is an appropriate starting place," he said. As a senior advisor to the Project on Emerging Nanotechnologies, Davies authored a report in 2006 titled 'Managing the Effects of Nanotechnology' which recommended more government regulation of engineered nanomaterials (http://www.nanotechproject.org/process/assets/files/2708/30_pen2_mngeffects.pdf). Since then, the US National Research Council has released additional authoritative reports calling for more research on the safety of nanoparticles.

Meanwhile, food companies are exploring the application of nanotechnology to their products. Plastic wraps made of silicate nanoparticles, for example, help keep food fresh longer by keeping oxygen out and retaining moisture. Bottles made of plastic containing special nanoparticles decrease carbon dioxide seepage and are stronger and lighter than regular bottles. Perhaps most impressive, though, is the work to develop nanosensors that detect foodborne toxins or harmful bacteria such as *Salmonella* and *E. coli,* and other nanomaterials that can help consumers identify spoiled or contaminated food by changing the packaging colour. "I strongly believe that an application in which nanosensors measure [...] certain spoilage processes in the package is a much better proposition than the use of sell-by or use-by dates," commented Frans Kampers, the coordinator of the Innovative Technologies group at Wageningen University and Research Centre in the Netherlands, which conducts research into the application of nanotechnology to food. He added that such package sensors would not only inform consumers when to discard spoiled products, but would also tell them whether a product is still edible, regardless of estimated use-by dates. Given that the US Centers for Disease Control and Prevention (CDC; Atlanta, GA, USA) reports that approximately 48 million Americans a year become sick from foodborne diseases, including 128,000 hospitalizations and 3,000 deaths, such measures could have a serious impact on public health.

Kampers, who also co-founded the International Society of Food Applications of Nanoscale Science (ISFANS; Ontario, Canada), thinks that nanotechnology can also add nutritional and palatable benefits. "Some of the ingredients [used] to improve the nutritional quality of a food product taste bad," he said. "By encapsulating them in a nanostructure it is possible to eat them without experiencing the taste."

Despite these potential benefits, not all major food-companies are jumping on the nanotech bandwagon. "We

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DOI 10.15252/embr.201438925 | Published online 19 May 2014

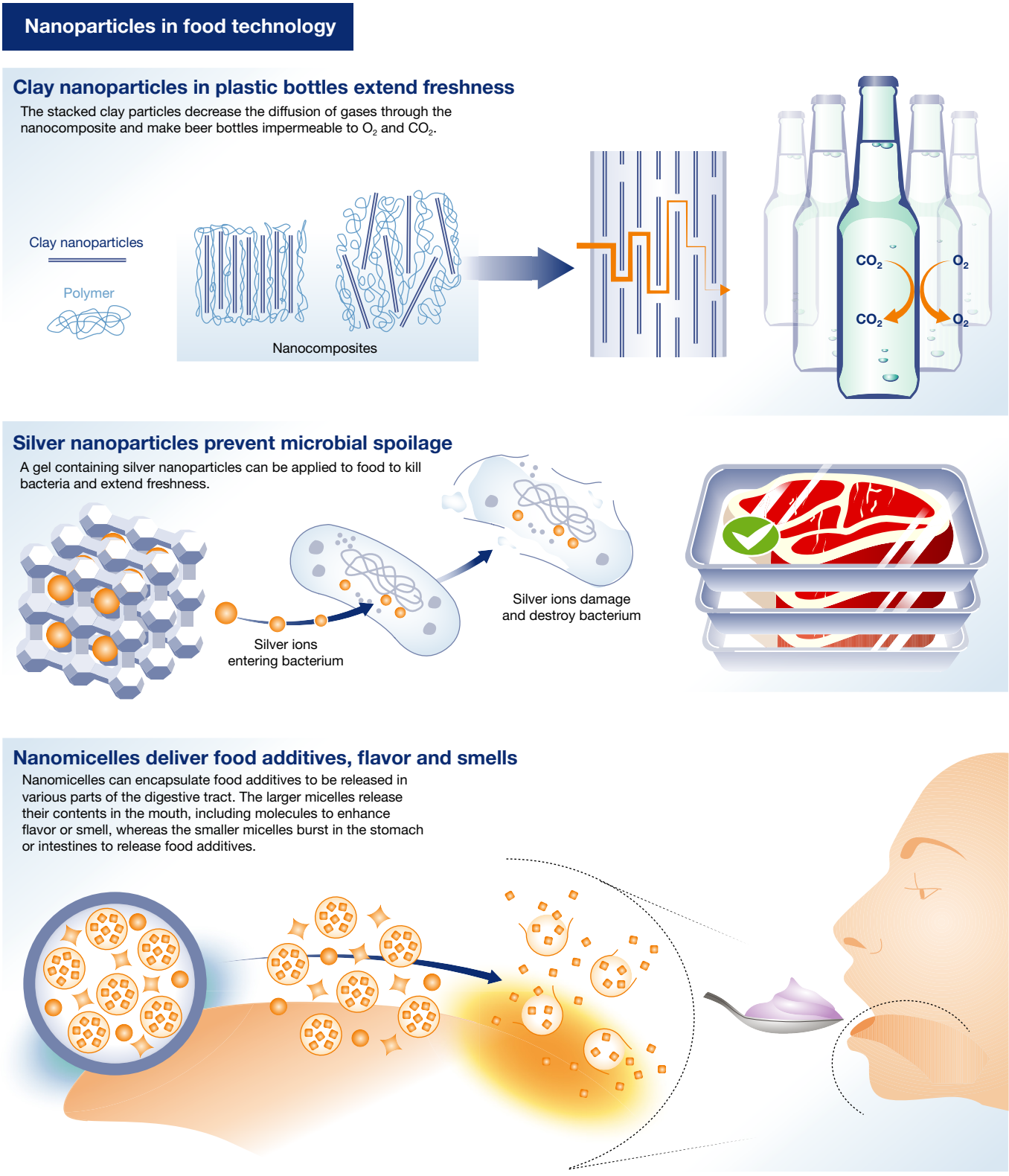

Figure 1. Potential benefits of using nanotechnology in the food industry.

have not, nor are we currently using nanotechnology in our products or packaging," said Richard Buino, a spokesman for Mondelēz International (Deerfield, IL, USA), formerly known as Kraft Foods. In 2000, Kraft created a consortium to collaborate with researchers studying the risks of nanomaterials used in food processing. Originally called the Nanotek Consortium, Kraft renamed it the Interdisciplinary Network of Emerging Science and Technologies. It is unclear whether the name change was to protect intellectual property or was a result of public concerns about nanotechnology.

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Mondelēz International is not the only company to harbour reservations about the use of nanotechnology in food. Some scientists believe there is already enough evidence to worry about the health effects of ingesting nanoparticles. Dora Pereira, a scientist at the UK Medical Research Council Human Nutrition Research [sic] (MRC HNR; Cambridge, UK), acknowledged that the use of nanotechnology in packaging might sometimes be better than existing alternatives. "Using soluble materials [in packaging] would be more detrimental [than nanomaterials], as [soluble materials] have the potential to migrate to foods more readily than nanomaterials," she explained. However, she also noted that some engineered nanoparticles are not easily digestible, which is especially relevant if they are being used to encapsulate food additives. "During risk assessment[s], it should be taken into consideration that some gut diseases may [result in] an increased permeability with respect to nanoparticle uptake," she said, adding that while many studies assess the effects of nanoparticles on the respiratory tract, there is considerably less research about how nanoparticles affect the digestive system. "Nanotechnology can make some nutrients such as iron safer in the gut than the soluble currently-used counterparts," she explained. "Nonetheless, other materials [such as] silver, titanium [and] gold, may accumulate more in the gut mucosa than the soluble counterparts, since these are not natural food constituents and our bodies have no metabolic use for them."

Davies pointed out that another potential detriment with nanoparticles is that their small size means they can travel to places in the body where other compounds physically cannot go. He said that some nanoparticles can even move across the blood-brain barrier, or find their way across a placenta and into a foetus. In addition to these risks, Davies also highlighted that the technology might pose environmental hazards. "To the extent that nanomaterials are used in food, they find their way into the ambient environment through wastes from manufacturing, human waste disposal, and disposal of other wastes," he said.

Deborah Koons Garcia, who produced and directed the documentary, *The Future of Food*, which contributed to a 2004 ordinance that outlawed the cultivation and distribution of genetically modified organisms (GMOs) in Mendocino County, CA, thinks that the chemicals used in food—including nanoparticles—that are added to kill unwanted bacteria, might destroy more than they were designed to. "The more chemicals you put in the food, the more the healthy benefits of the food begin to deteriorate," she said. Since researchers are unsure about the risks of ingesting engineered nanoparticles, Garcia commented that it is best to avoid potentially toxic material. "If we don't know what the consequences are, let's just not do it," she said. "Let's focus on something else that will make a safer food-system instead of [...] putting something in our food that may kill more than just the thing that you don't want in there."

While the US government appears to be on the fence concerning the use of nanotechnology in food, other countries have begun addressing the risks of nanoparticles by implementing the first steps towards safety regulations. After a number of Belgian non-governmental organizations (NGOs) expressed concern about the safety of nanomaterials—pointing out that despite the uncertainty of the technology's impact on the environment and human health, the number of consumer products containing nanomaterials is on the rise —Belgium mandated that the use of all nanomaterials and mixtures containing nanomaterials must be reported to a national registry that is yet to be created. The decree states that the registry will allow authorities to react if a type of nanomaterial proves dangerous to public health, and will also ensure transparency and strengthen public trust (http://nanotech.lawbc.com/2014/02/articles/international/eu-member-state/belgium-creates-register-of-nanomaterials/). To date, Belgium and France are the only two EU-member states that regulate consumer products containing nanomaterials. Norway and Denmark, however, are following suit and are in the process of creating similar registries.

Nevertheless, most EU-member states, and the EU itself, have no current plans to introduce nanotechnology-specific food regulations. The European Food Safety Agency (EFSA; Parma, Italy), however, published a guidance outlining a risk assessment of nanotechnology applications in food products (http://www.efsa.europa.eu/en/efsajournal/doc/2140.pdf). While the document provides some directions, it also acknowledges that "there are currently uncertainties related to the identification, characterization and detection of ENM [engineered nanomaterials] [...] similarly, there are a number of uncertainties related to the applicability of current standard biological and toxicological testing methods to ENM. For these reasons, this ENM Guidance will need to be updated based on experience and acquired knowledge." Similar to the FDA document, this European guidance was published in 2011 and has not led to legislation, although in December 2013, EFSA followed up with a report on nanomaterials used in the food industry (http://www.efsa.europa.eu/en/supporting/doc/531e.pdf).

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In the UK, a 2009 memorandum issued by the Economic and Social Research Council's (ESRC; Swindon, UK) Centre for Business Relationships, Accountability,

Sustainability and Society (also known as BRASS) stated that, "in principle, current uses of nanotechnologies and nanomaterials will fall within the scope of a range of existing regulatory provisions" (http://www.publications.parliament.uk/pa/ld200910/ldselect/ldsctech/22/22we04.htm). Kai Savolainen, Director of the Nanosafety Research Centre at the Finnish Institute of Occupational Health (FIOH; Helsinki, Finland), said that the lack of legislation may be because many officials believe that nanotechnology is not prevalent in the food supply. "If one asks the Finnish regulators, there are no nanomaterials in the food [...] in Finland, [but] according to some food producers, this is not the case, [since there are] nanocapsulated vitamins and micronutrients in some food items," he said. "In the EU, there is not —to my knowledge—horizontal legislation on engineered nanomaterials in food items, even though EFSA is preparing such for the EU Commission."

Like the UK and Finland, Germany has not issued any specific legislation, but the German government did commission health and environmental risk assessments of nanotechnology, which resulted in a report on the 'First Evaluation on the Joint Research Strategy of German Governmental Research Institutions: Nanotechnology—Risks related to Nanomaterials for Humans and the Environment' (http://www.bfr.bund.de/cm/349/first-evaluation-on-the-joint-research-strategy-nanotechnology-risk-related-to-nanomaterials-for-humans-and-the-environment.pdf). The report states that the "use of the nanoscale form of an already authorised substance requires a new assessment and new authorisation. The Food Information Regulation, which came into force in 2011, prescribes labelling [sic] of foods that have additives in nanoscale form from 2014." The German Federal Institute for Risk Assessment (Bundesinstitut für Risikobewertung; BfR), a contributor to the report, also noted that there are "reasons which suggest that nanomaterial could conceal risks [due to] the special (physical-chemical) properties of a nanomaterial, e.g. large, highly reactive (reaction-promoting) surfaces [...], special behaviour inside the body, e.g. a long retention time and the overcoming of natural biological barriers [and] the increased contamination that is to be expected by their release" (http://www.bfr.bund.de/en/health_assessment_of_nanotechnology-30439.html).

Despite these risk assessments, there still are not enough scientific studies on the potential health hazards of nanotechnology. Of those that have been conducted, various studies found that certain nanomaterials—including zinc-oxide nanoparticles, which are commonly found in sunscreens—are poisonous to lung cells; a 2009 study found that "nanoparticles transferred from pregnant mice to their offspring can damage genital and cranial nerve systems [1]; and a third in 2013 concluded that some nanoparticles cause cancerous characteristics in stomach cells *in vitro*" [2]. However, Mark Ratner, a professor of chemistry and the associate director of the Institute of Nanotechnology and Nanofabrication at Northwestern University (Evanston, IL, USA), pointed out that, "there is [a] vast store of information out there about toxicity of semiconductor nanoparticles [...] The general conclusion is that most size ranges are not harmful. But there still is a lot to do before we can be totally secure that toxicity can be controlled."

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While not discounting the potential health risks of engineered nanomaterials, Kampers believes that ultimately, the benefits outweigh the risks. "Very few innovations, including the ones that involve an innovative technology like nanotechnology, reach the market and [as a result] important benefits are not available for consumers," he said. "By focusing on very small risks and letting that influence our opinion about new food products, we cut ourselves short of these benefits." Kampers added that many popular products—such as beer, wine and even salt—would not be approved by regulatory agencies today.

Lynn Bergeson, the chair of the Nano-Business Commercialization Association's Environment, Health and Safety Committee (Shelton, CT, USA), said that public reservations about using nanotechnology stem mostly from fears of the unknown. "There is a legitimate reason to be concerned with the commercialization of any new technology," she said. "We certainly don't know everything there is to know about an engineered nanoparticle." Rather than creating blanket regulations, however, Pereira thinks that nanoparticles should be assessed and regulated on a case-by-case. "We must move away from trying to label nanotechnology in foods as a whole as safe or unsafe," she said.

For now, most governments seem hesitant to introduce binding legislation to regulate the use of engineered nanoparticles in food. Because of this, and owing to the lack of scientific studies examining nanomaterial use in food to pinpoint and quantify the exact risks, a cloud of uncertainty continues to loom over the fusion of nutrition and nanotechnology.

Conflict of interest

The author declares that she has no conflict of interest.

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