INSTITUTE FOR AGRICULTURE AND TRADE POLICY

Racing Ahead

U.S. Agri-Nanotechnology in the Absence of Regulation

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Executive summary

On June 9, the U.S. Environmental Protection Agency (EPA) and the Food and Drug Administration (FDA) separately released ground-breaking, albeit voluntary, draft guidance to industry, the first, long-overdue step toward regulating products that incorporate nanomaterials. The White House issued an executive memorandum the same day, on principles of regulation and oversight of nanotechnology and nanomaterials. The memo noted that, "[c]ompanies are already offering nanotechnology-enabled products with break-through capabilities in areas such as disease detection, lighter and stronger materials, and next-generation batteries."

But none of these products are regulated by U.S. federal agencies. Research and development for agricultural and food applications of nanotechnology has expanded rapidly in recent years, with over $50 billion in global public investment and at least as much in privately funded research. At least 1,300 products with Engineered Nanotechnology Materials (ENMs) have been commercialized, despite myriad uncertainties about the public health and environmental effects of ENMs.

These uncertainties result, in part, from novel physical, chemical and biological properties that are due to the extremely small size of these particles, which may range from 1 to 300 nanometers (the diameter of a human hair is about 80,000 nanometers). The exponentially greater surface-to-mass ratio of nanoscale materials results in different properties and uses than what is possible for the macro-scale counterparts of those materials. It is not yet clear what human health hazards may be created when nanoparticles are ingested, or the extent to which ENMs might migrate from food packaging to the food and hence through the entire human body.

Several steps are needed to arrive at an operative and mandatory regulatory structure for nanotechnology products and processes. There is no agreed legal definition of what constitutes an ENM. Regulators do not have an official registry needed to regulate products already in the market nor an inventory of products in development. As of March 2011, the nongovernmental Project on Emerging Nanotechnologies (PEN) had registered more than 1,300 products whose manufacturers claim to include ENMs, and estimates that the number could grow to 3,400 by 2020.

The lack of definition is not just a technical issue, but also a political challenge. The decision to commit to binding legal definitions would be predicated on related decisions to regulate and a commitment to ensure the human, technical and financial resources to implement and enforce regulations. Even if, after the June EPA guidance on submitting ENMs for EPA review, definitions could be determined, and adequate resources provided, it will be difficult to require product data from commercialization applicants. A research project to estimate ENM production levels found that most companies surveyed regarded production levels as confidential business information (CBI) that they refused to disclose, even after the researchers guaranteed company confidentiality.

There are EHS risks that regulators could begin to assess, if they had nanotech product data, on the basis of current peer-reviewed scientific literature. Chinese researchers, for example, have discovered in animal testing that absorption of nano-silver may interfere with the replication of DNA molecules and can reroute molecular networks that could create genetic mutations. Nano-silver, among myriad other uses, is incorporated into food packaging materials to kill pathogenic bacteria and thereby extend a food's shelf life.

Estimates of the global cost of testing even just the toxicological effects of known ENMs range from $265 million to $1.8 billion. In the United States, the government bears the legal burden of collecting and analyzing data for risk assessments, but there is strong congressional opposition to providing the budget necessary to carry out that legal mandate. A report from the first (and thus far only) expert consultation on agri-nanotechnology under the auspices of the World Health Organization (WHO) and the United Nations Food and Agriculture Organization (FAO) suggests a "tiered approach" to ENM risk assessments. Such a tiered approach is characteristic of the European Union's "Registration, Evaluation, Authorization and Restriction of Chemicals" (REACH) legislation for regulation of chemical substances, products and wastes. Where the scientific literature indicates higher likely risks to public, worker and environmental health, regulators informed by such literature should obtain product data and perform risk assessments, leaving low-risk applications further down the priority list.

The range of food and agricultural nanotechnology applications includes making toxins more bio-available in pesticides, targeting nutrients in smaller doses, improving the texture of ice cream and detecting bacteria in packaged foods. Under current rules, companies have the discretion to determine whether a macro-substance already considered by the company to be safe and therefore not reportable to the FDA, deemed to be likewise safe and hence non-reportable in its nano-scale form. In addition, the

exponentially larger surface-to-mass ratio of ENMs, compared to that of macro-versions of the "same" materials, will make the determination of Acceptable Daily Intakes impossible if companies are not required to submit data to regulators for their independent assessment.

In 2008, the Project on Emerging Nanotechnologies (PEN) and the Grocery Manufacturer's Association (GMA) brought together industry representatives, government regulators and NGOs to consider how EPA and FDA might regulate generic and hypothetical food packaging incorporating ENMs. The project revealed challenges to FDA's present regulatory process for food packaging materials, including: 1.) validating methodologies to characterize ENM properties to determine whether ENMs might migrate into food; 2.) validating migration study protocols that would determine consumer exposure to ENMs; 3.) evaluating whether current FDA set dietary concentration triggers for toxicity testing are adequate for ENMs; and 4.) determining whether toxicological data for the macro-scale counterparts of ENMs have any utility for predictive toxicology and safety assessment.

But these challenges are not just theoretical. The Pulitzer Prize–winning journalist Andrew Schneider has reported that some fruits and vegetables exported from Latin America are coated with nano-particles to extend their shelf life. Based on a review of patent filings, regulators have some knowledge of the ingredients of food nano-coatings. These ingredients include nano-silver and nano-zinc oxide as anti-microbials to combat bacteria; nano-silica to prevent water content loss and to ensure the film's transparency; and nano-titanium dioxide to prevent deterioration due to ultraviolet rays. The macro forms of these ingredients are permitted food additives, but testing has not yet been done to assess their safety at nano-scale. Administrative, technical and resources constraints create enormous hurdles to effective import inspection of food nano-coatings and food packaging using ENMs.

Because of, or perhaps despite, the scientific, budgetary and infrastructural difficulties of developing methods to simply and reliably measure the presence of ENMs in food, feed and food packaging materials, the Codex Alimentarius Commission, the international food standards body, may consider in July whether or not to include nanotechnology in its strategic plan for 2013–2018. Codex standards are presumed to be authoritative by the World Trade Organization Agreement on the Application of Sanitary and Phytosanitary Measures for the purpose of trade facilitation. There are many reasons why the commission should undertake work on agri-nanotechnology, not the least of which is that such products are already being traded without regulation or risk assessment on which to base regulations. At the same time, Codex standards require the scientific advice of FAO/WHO expert meetings and/or standing committees, such as the Joint FAO/WHO Committee on Food Additives. However, FAO and WHO member governments have not made the funding of such scientific advice a Codex priority. There is a risk, however, that if standards are developed before member countries have effective rules and resources to do mandatory pre-market safety assessments and post-market surveillance of foods with ENMs, Codex standards would only facilitate greater trade without adequate regulatory enforcement capacity.

There is a serious imbalance between optimistic public assessment of potential benefits and the potential risks of nanotechnology applications. Efforts to determine appropriate safety regulations should begin with a framework of comparative technology assessment to assess whether a nanotechnology application is the optimal means for achieving a specific technological or public interest goal. It appears that investors hope that products will become ubiquitous and "accepted" before risk research reveals harms so prevalent and/or severe as to force withdrawal of the product from commerce.

The June 9 announcement by EPA and FDA of their intent to issue voluntary guidance to industry on nanotechnology products under their respective authority is a small, but encouraging first step toward regulation. Minimizing the budgets and mandate for environmental, health and safety research into agri-nanotechnology and trusting that agri-nanotechnology hazards, if they appear as public health and environmental harms, will be untraceable and beyond the reach of liability plaintiffs, is not a viable technology or commercialization policy. Surely, a policy that relies on non-regulation and paltry investments in risk research cannot enable the so-called "New Industrial Revolution" for the 21st century that nanotechnology promoters promise.

Overview

Seldom, if ever, has a U.S. federal agency request for comment on a draft, voluntary and legally non-binding guidance to industry come with a White House memo; a new guidance on nanotechnology is a rare exception. On June 9, the U.S. Environmental Protection Agency (EPA) and the Food and Drug Administration (FDA) separately released draft guidance.[1] The FDA guidance cites a White House "Memorandum for the Heads of Executive Departments and Agencies: Policy Principles for the U.S. Decision-Making Concerning Regulation and Oversight of Applications of Nanotechnology and Nanomaterials" released the same day.

The memo notes that "[c]ompanies are already offering nanotechnology-enabled products with breakthrough capabilities in areas such as disease detection, lighter and stronger materials, and next-generation batteries."[2] Remarkably, none of these products are currently regulated by U.S. federal agencies.

After at least a $50 billion in global public investment in nanotechnology research and development through 2009, including a $16 billion U.S. taxpayer investment during the past decade, the U.S. government has begun to take the first baby steps towards regulating Engineered Nanoscale Materials (ENMs).[3] The memo, from the presidential Office of Science and Technology Policy, and the Office of Management and Budget and the Office of the U.S. Trade Representative, is to remind all high-ranked officials that they are to "protect public health, safety and the environment while promoting economic growth, innovation, competitiveness, exports and job-creation." This mission impossible weighs most heavily on the officials charged by law with protecting public health, safety and the environment.

DEFINING NANOTECHNOLOGY

Although the regulatory definition of ENMs is far from agreed, according to the website of the U.S. National Nanotechnology Initiative, "Nanotechnology is the understanding and control of matter at the nanoscale, at dimensions between approximately 1 and 100 nanometers, where unique phenomena enable novel applications [...] there are 25,400,000 nanometers in one inch."[4] The size, surface reactivity and configuration of ENMs results in properties of and uses different from those of their macro-scale counterparts.

For EPA, to issue voluntary guidance has been a struggle. At a 2010 Organization for Economic Cooperation and Development (OECD) meeting, an EPA official stated, "The U.S. is now looking at a regulatory approach, requiring reporting on all nanomaterials and the testing of some. The hope is to have proposed rules by the end of the calendar year."[5] This hope had been announced by EPA administrator Lisa Jackson in a December 2009 U.S. Senate hearing, but was opposed fiercely by anonymous clients of the Washington law firm of Wilmer Hale,[6] and has yet to be realized since voluntary guidance does not compel industry to do anything. The voluntary guidance is only a step towards a regulation that would require the submission of ENM data used in products under EPA authority, e.g., pesticides.

This essay first reviews the general nanotechnology regulatory paralysis and a few risks that could result in public health and environmental harm if that paralysis continues. Then we give an overview of the state of U.S. agri-nanotechnology regulation, including how the U.S. Food and Drug Administration might apply existing law to the regulation of hypothetical products incorporating ENMs in food-packaging materials. Thirdly, a specific application, the nano-coating of fruits and vegetables to retain moisture and retard spoilage, is analyzed from the viewpoint of generic risks that nano-sized ingredients of proprietary food coatings present and of the capacity of FDA to inspect and test produce imports for such risks at ports of entry. Finally, we consider briefly how the Codex Alimentarius Commission, the international food standards organization, might develop standards for ENMs in nano-coatings. Codex standards can be used to facilitate international trade in food nanotechnology products, regardless of governments' capacity to implement and enforce such standards.

Despite the research and development to promote the use of nanotechnology in food and agriculture, knowledge gaps and uncertainties about how to fill the gaps are more prevalent than scientific certainties about the public health and environmental effects of ENMs in food packaging. A presentation to a June 2010 conference co-sponsored by the United Nations Food and Agriculture Organization (FAO) and the Brazilian Agribusiness Research Corporation outlined some major scientific challenges to regulating nano-enabled food packaging and agri-nanotechnology more generally. Two challenges stand out: "First, there is a lack of understanding on how to evaluate hazard of nanomaterials by the oral (food) route. This is not a unique knowledge-gap for any migration from food packaging because it applies to all applications of nanotechnology in the food sector. [...] Second, there is a lack of tools to estimate exposure. [...] Currently, based on theoretical considerations and the fixed or embedded nature of nano-particles in food packaging, the expectation is that they are not likely to migrate and pose any significant risk to the consumer. But we do not have the analytical measuring tools to confirm this no-migration prediction by actually testing packaged foods."[14] Given the lack of such tools and knowledge, the unregulated commercialization of food packaging and coatings with ENMs should be scandalous for anyone who believes that governments are obligated to protect public, worker and environmental health.

Lack of progress in establishing regulatory structure

Despite several years of hard work by governments, intergovernmental organizations and nongovernmental organizations, there is not yet an operative and mandatory regulatory structure for nanotechnology products and processes. (We cannot and should not assume that the June 9 beginning of voluntary guidance will lead rapidly to mandatory rules.) Rather, there are risks to the environment and public health from ongoing regulatory paralysis in the midst of unregulated commercialization of products that incorporate ENMs to make them lighter, stronger, harder, transparent and/or more bio-available, etc.

This is not to say that there are no rules pertaining to nanotechnology, but such rules that exist are wholly inadequate to ensure consumer, worker and environmental safety. For example, the U.S. Environmental Protection Agency (EPA) requires that manufacturers of carbon nano-tubes notify the EPA of the laboratory testing it has done and occupational safety measures taken 90 days before nano-tubes are produced. The EPA rule allows the manufacturers to maintain testing results as confidential business information.[15] Because carbon nano-tubes are ten times as strong as steel, harder than diamond, lightweight and have unique electrical conductivity, they have a wide range of industrial applications. Just as chronic human exposure to asbestos fibers induces a number of lung diseases in humans, there are more than a few laboratory animal studies in which exposure to the fibrous nano-tubes result in asbestos like pathologies.[16]

The Project on Emerging Nanotechnologies (PEN), a partnership between the Pew Charitable Trusts and the Woodrow Wilson International Center for Scholars, a nonpartisan U.S. government research center, has registered, as of March 2011, more than 1,300 products whose manufacturers claim to include ENMs. PEN Director David Rejeski stated, "When we launched the inventory in March 2006, it contained 212

BABY STEPS: THE EPA AND FDA VOLUNTARY GUIDANCE

IATP will respond and urge others to respond to EPA and FDA requests for comments on these documents to determine whether they offer a pathway towards regulating ENMs to protect public health, the environment and those who work with ENMs, including those in the food and agriculture industries. The EPA and FDA draft guidance documents are of a very distinct origin, about which it is worth commenting here.

The EPA's 43-page draft guidance[7] is, at least in part, a response to a May 2008 petition by the International Center for Technology Assessment (ICTA) to regulate nano-silver under the law governing pesticides (Federal Insecticide, Fungicide and Rodenticide Act (FIFRA)). IATP, as a co-petitioner, joins ICTA in welcoming this draft guidance and request for comments on questions EPA poses on its proposed alternative pathways for industry to submit product data on ENMs in pesticides.[8] The draft guidance states EPA's preference for requesting information on all ENMs used in already registered and commercialized products, as well as ENMs in products under development. Evaluation of this information will be used to determine whether the ENMs pose new hazards that require risk assessments, and subsequent decisions about whether or not to register the nano-pesticides for commercial use. EPA states its preference for a broad request for ENMs in pesticides, adding "that merely filing an additional report under FIFRA section 6(a)(2) does not stigmatize any nanomaterials in pesticides, since such reports are quite common. On average, EPA receives 200 studies and 56,000 incident reports per year under this authority."[9]

However, some industry stakeholders have proposed submitting information under another section of FIFRA on a case-by-case basis and with the possibility that the pesticide could be withdrawn from commerce if the pesticide product developer failed to respond to the request for information about the ENMs used in the registered pesticide. EPA believes that requesting ENM information under this authority would be more resource intensive for both industry and for EPA. The industry proposed submission authority might require new (and time consuming) data-gathering regulations and might require industry to develop new ENM information, rather than to report just what it already knows, as under section 6(a)(2).[10] The regulatory pathway chosen will determine both the efficiency and comprehensiveness of the EPA's guidance for submitting information about ENMs in pesticides. Therefore, the EPA poses a number of questions for comment about the alternative pathways it outlines, as well as eliciting commenter ideas about issues not framed by the questions.

It would be an idle pursuit to speculate about the timing of the release of the draft 2-page FDA guidance, "Considering Whether an FDA-Regulated Product Involves the Application of Nanotechnology," on the same day as the draft EPA guidance. However, the simultaneous release of the draft FDA guidance and a White House statement on overarching principles for the regulation of nanotechnologies, plus the referencing of the White House statement within the draft FDA guidance leaves little room for speculation. The FDA draft guidance is far from requesting information that could lead to regulation. Rather the draft guidance poses very general questions about whether FDA-regulated products incorporate ENMs on the basis of the size of the materials incorporated and whether "an engineered material or end product exhibits properties or phenomena" outside a nano-scale range of 1nm to 100 nm up to one micrometer (1000 nms).

However, it is not so difficult to imagine that the very general scope of these questions is a cautious response to the firm warning to all agency and department heads in the White House memo. According to the Office of Management and Budget, the Office of Science and Technology Policy, and the Office of the U.S. Trade Representative, regulatory decisions to protect consumer health and the environment must be based on "sound science" (itself a public relations term from a campaign against regulation of second-hand smoke's health effects) since "uncertainty and speculation about potential risks threaten to undermine consumer and business confidence" in nanotechnology.[11] Furthermore, regulators are enjoined to protect "human health, safety and the environment without prejudging new technologies or creating unnecessary barriers to trade or hampering innovation."[12] Finally, the memo states, "Federal agencies should avoid making scientifically unfounded generalizations that categorically judge all applications of nanotechnology as intrinsically benign or harmful."[13] The terms of the draft EPA guidance do nothing to violate the injunctions of this memo, but the EPA draft guidance is an important step towards regulating ENMs, while the scope of the FDA guidance seems constrained to not offend the trade-related "sound science" language of the White House memo.

products. If the current trend continues, the number of products could reach 3,400 by 2020."[18] PEN believes this to be a very conservative number. Rejeski testified in 2009, "These products are available in shopping malls or over the Internet, and we have purchased many of them online. Thanks to business-to-consumer (B2C) e-commerce, nanotechnology products easily flow across international borders, raising control, trade, and oversight issues."[19] There are no official government registries of products with ENMs, since official registration would be part of regulation. Unfortunately, PEN's 2006 database review of U.S. federally funded food and agriculture applications of nanotechnologies, comprising some 160 projects, has not yet been updated.[20] PEN has developed an iPhone application to help consumers identify products with ENMs.[21] It is critical to note, however, that there is neither an official or unofficial registry of nano-scale ingredients and materials that are either incorporated into consumer products or into industrial products and processes. Establishing such a registry, as well as consumer products registry, would be necessary components of the eventual regulation of nanotechnology.

As a consequence of their small size, nanoparticles may migrate easier in biological systems like the human body, and be able to cross biological barriers in the lung, gut or brain, and therefore cause unexpected and unusual exposure.

European Commission Joint Research Centre, 2010[17]

Despite the growth in commercially available, nano-enabled products, basic pre-requisites still are lacking to regulate products incorporating ENMs. First, there is no agreed legal definition of what constitutes an ENM. Unofficial working definitions generally concern a substance having a least one dimension of 1–100 nanometers (one nm = a billion of a meter) and exhibiting properties distinct from those of the macro form of the material, such as greater strength, reactivity, water retention, nutrient delivery, or toxicity. (A human hair is about 80,000 nm wide.) On the other hand, the multiplicity of provisional definitions suggests that consistent characterization of the physical, chemical and biological properties of specific ENMs incorporated in products may provide a sounder basis for regulation than the canonic, uni-dimensional legal definition.[22]

Governmental failure to provide the most rudimentary features of oversight and regulation, despite burgeoning commercialization, has prompted the ETC Group to write:

> Ten years, $50 billion, and a couple of thousand products since the nanotech boom began in 2000, the 60+ governments with national [nanotechnology] programs still lack an agreed definition for nano; an accepted measurement standard; replicable research models; public health and environmental safety regulations; and the remotest understanding of the potential social-economic, intellectual property or competition issues involved in the several hundred nanomaterials under research or manufacture. Barring catastrophe, it is increasingly unlikely that OECD-country regulators will have the courage or the clout to provide the governance nanotechnology requires.[23]

Given the lack of such governance to ensure consumer, worker and environmental safety of commercialized nano-enabled products, the ETC Group recently reiterated its 2002 call for a moratorium on the commercialization of nanotechnology products. Although there is more than sufficient evidence of regulatory failure and peer-reviewed evidence of potential ENM harms to justify a moratorium on commercialization, no government has adopted the moratorium proposal. In 2007, IATP played a small role in developing "Principles for the Oversight of Nanotechnologies and Nanomaterials" and is one of over 70 signatories to those principles.[24] This paper is guided by those principles, including application of the precautionary principle to make regulatory decisions about the many uncertainties of nanotechnologies.

Two causes of regulatory paralysis: no agreed definitions and no product data to review

It is not for lack of interest that there is not yet a legally applicable ENM definition. A European Commission report that summarizes numerous national and international efforts states that the definition should be broad enough to be adaptable "for specific regulations or directives. It should therefore be emphasized that adoption of a definition will also involve policy choices, and accordingly will entail political decisions."[25] Even if legislators delegated to regulators the authority to define ENMs and other nanotechnology terms for regulatory purposes, the definitions would entail more than descriptions of particle size and material properties that would trigger regulatory concern.

The decision to commit to binding legal definitions would be predicated on related decisions that would collectively signal to industry and to consumers that there was political will to regulate and a commitment to ensure the human, technical and financial resources to implement and enforce regulations. However, during the past 30 years, writes former EPA official J. Clarence Davies, in the United States, "most of the EHS [environmental, health and safety] regulatory agencies have been deprived of the resources needed to perform their basic functions."[26] This deprivation, driven by well-financed initiatives against so-called "over-regulation," is dangerous, given the many and difficult regulatory challenges posed by nanotechnologies in the United States, to say nothing of those pertaining to imported products with ENMs. Despite the well-researched and comprehensive proposals of Davies and others to create a nanotechnology-specific regulatory regime, the fear of the economic impact of mandatory pre-market EHS research on the anticipated nanotechnology market has blocked the realization of those proposals.

Consumer groups have called on U.S. and EU officials not to delay regulation through failure to agree on a definition of ENMs and other nanotechnology-related terms.[27] U.S. nanotech product developers want regulatory definitions and a predictable regulatory approval process that will enhance investor confidence, and ensure the commercialization of their products, or they may move their production facilities to more industry-compliant regulatory jurisdictions.[28] But if definitions could be agreed and political will to support regulation of nanotechnology products could be secured, what categories of problems would regulators face in assessing which products required which degree of regulatory scrutiny?

One problem will be to secure product data from commercialization applicants. According to assistant EPA administrator Steve Owens' presentation to an international regulatory conference, "about 90 percent of the various nanoscale materials already being used commercially, or thought to be used, were never reported to the government."[29] Since a broad range of nanoscale materials are reported to the United States Patents and Trademarks Office (USPTO), Dr. Owens probably meant that those materials had not been reported directly to EPA, and EPA did not have an agreement with USPTO to use patent information for pre-regulatory or regulatory purposes.

However, it is not just the kinds of ENMs and their uses that are not reported, or at least not reported directly, by industry to regulatory agencies. In order to set limits concerning permitted toxicological exposure of the environment and workers to ENMs, and to do life-cycle analyses of ENMs, it would be useful to know how many ENMs are produced annually and to where they are distributed for subsequent incorporation into consumer and industrial products. However, the surface-to-weight relation of ENMs is exponentially greater than that of macro-sized materials and this exponentially greater ratio makes them commercially useful. So a simple reporting of volume or weight of materials will not suffice as a guide to potential EHS consequences of exposure to a specific ENM.

A research project to estimate ENM production levels found that most companies surveyed regarded production levels as confidential business information that they refused to disclose, even after the researchers guaranteed company confidentiality. (For at least some ENMs, such as nano-copper, even the names of producing firms is classified by regulatory agencies as confidential business information.) Hence the degree of uncertainty about ENM production levels was a key finding of this study that estimated annual U.S. production of nano- titanium dioxide at somewhere between 7,800 and 38,000 tons per year. Nano titanium dioxide, like its conventional counterpart, is used in paints, varnishes and coatings, but because it is even more refractive than its conventional counterpart, the nano version is also used in sunscreen, cosmetics, self-cleaning windows and water treatment.[30]

Can consumers be protected with an austerity budget for regulation?

There are EHS risks that regulators could begin to assess, if they had nanotech product data, on the basis of current peer-reviewed scientific literature. In 2007, Consumer Reports published a study challenging the claim that sunscreen with nano-titanium dioxide provided better protection against ultraviolet rays than sunscreen without ENMs. Some scientific studies with laboratory animals have shown that nano-titanium dioxide in sunscreen increases cell toxicity, which can damage skin over time.[31] Nano-silver, one of the most commonly used ENMs, continues to be commercialized as a biocidal in a wide array of consumer goods, from hand sanitizers to mattress covers to underwear without pre-market safety assessment.[32] Annual U.S. nano-silver production, for antimicrobial applications, is estimated between 2.8 and 20 tons.[33]

Chinese researchers have discovered in animal testing that absorption of nano-silver may interfere with the replication of DNA molecules and can reroute molecular networks that could create genetic mutations.[34] Nano-silver, among myriad other uses, is incorporated into food packaging materials to kill pathogenic bacteria and thereby extend a food's shelf life.[35] However, nano-silver particles may migrate from the packaging material into the nano-wrapped food. The Chinese researchers said that the long-term effects of DNA interference from nano-silver are unknown and should be a priority for environmental health and safety (EHS) research.

The global cost of testing ENMs for just toxicological effects, to say nothing of genetic effects, would not be cheap. One study on the toxicological testing of the 265 known ENMs estimates "costs for testing existing nano-particles ranges from $249 million for optimistic assumptions about nano-particle hazards (i.e., they are primarily safe and mainly require simpler screening assays) to $1.18 billion for a more comprehensive cautionary approach (i.e., all nanomaterials require long-term in vivo testing)."[36] The study extrapolates these cost estimates from research and product development databases of current ENM firms, the portion of ENM research devoted to hazard testing, and testing models for reported cost of toxicology assays for conventional chemicals as proxies for ENMs. Relative to the multi-billion dollar government and corporate investments in nanotechnologies, and the trillions of dollars in anticipated sales of products with ENMs, even the higher figure seems nano-tiny to secure both retail consumer and industrial consumer markets.

In the United States, the government bears the legal burden of collecting and analyzing data for risk assessments, but there is strong congressional opposition to providing the budget necessary to carry out that legal mandate. The authors of the aforementioned study estimate it would take 34 to 53 years for the government to do toxicological testing of existing ENMs under a precautionary testing regime and under an ongoing austerity budget for the Environmental Protection Agency and the Occupational Health and Safety Agency. Corporations are unlikely to do long-term safety assessments of ENMs because "virtually no market benefits accrue to actors who produce research on the long-term safety of products."[37] Given the frequency of news releases about new applications for ENMs, particularly for medical applications of nano-silver, one might assume that the nanotech product developers must be passing on some data from their internal testing to FDA.[38] However, if there is no economic incentive for the private sector to do long-term safety research and government fiscal crises, triggered in part by bailouts of the private sector, limit the abilities of governments to conduct such research, how are consumers to be protected from hazards in products with ENMs?

The existing U.S. federal oversight agencies have generally been too small to have much flexibility. All their resources are devoted to survival and to the performance of the minimal required functions; they have limited ability to anticipate and respond to new problems or to consider new ways of doing things.

J. Clarence Davies, "Oversight of Next Generation Nanotechnology"[43]

One conclusion, according to an analysis of EU nanotechnology regulations, is that it may already be too late to fully protect consumers: "the unprecedented rate at which nanotechnology is now infiltrating all market sectors has already rendered the adoption of any considered and generalized EU-wide program of proactive regulatory interventions an impossibility."[39] There are, of course, good grounds for this pessimism, particularly insofar as "EU trade in nanotech products is underpinned by a strong presumption in favor of free trade"[40] that puts the burden of proof on governments to show that a new technology is not safe. Alternatively, if a free trade approach to regulation results in wide-scale and severe harm that can be traced back to still unregulated nanotechnology products, governments will be confronted with the problem of how to regulate to protect consumers in the midst of what promises to be highly straitened budgets for regulatory agencies in the near to medium term.

A report from the first (and thus far only) expert consultation on agri-nanotechnology under the auspices of the World Health Organization (WHO) and the United Nations Food and Agriculture Organization (FAO) stated, "[a] tiered approach to ENM risk assessments may prove useful to prioritize the use of resources for generation of new data and risk methodologies."[41] Such a tiered approach is characteristic of the European Union's "Registration, Evaluation, Authorization and Restriction of Chemicals" (REACH) legislation for regulation of chemical substances, products and wastes. Where the scientific literature indicates higher likely risks to public, worker and environmental health, regulators informed by such literature obtain product data and perform risk assessments, leaving low-risk applications further down the priority list. J. Clarence Davies has argued convincingly that adequate nanotechnology oversight will require a legislative framework that has some elements of REACH but a much stronger government scientific platform than exists in U.S. (or EU) regulatory agencies.[42]

Not all ENMs will require the same degree of EHS testing and regulatory scrutiny. Northwestern University researchers in the course of other nanotechnology research inadvertently

discovered how to make edible nanostructures "for virtually any sort of encapsulation," e.g., of medicines, flavorings or nutrients. One of the researchers was certain that because the components of the nanostructure were food grade ingredients, there would be no need for regulatory approvals of the nanostructure.[44] Having patented the product and process, the researchers let The New York Times publish the recipe for edible nanostructures.[45] To read the recipe in its off-the-shelf simplicity, you could believe that regulation would just get in the way of a safe and beneficial application—but it's not so simple.

Prior to the June 9 EPA announcement of a voluntary first step towards required data submission, Richard Denison of the Environmental Defense Fund wrote, "in 2011, we are essentially no closer to achieving it [obtaining basic ENM product data for regulatory review] than we were in 2004."[46] EDF has worked with the DuPont Corporation to agree on a model risk assessment framework for voluntary use by nanotechnology product developers.[47] Thus far we are aware of only two ENMs that have been reviewed using this framework. Other NGOs have petitioned the U.S. government to regulate ENMs under existing U.S. law, e.g., the petition of the International Center for Technology Assessment et al to the Environmental Protection Agency to regulate nano-silver under laws governing pesticides (IATP is a co-petitioner).[48]

Neither working with industry on a voluntary code of practice, as a confidence building measure towards regulation, nor a legal petition to compel regulation has moved the U.S. government to regulate ENMs and products containing them. Perhaps, as Denison proposed in 2007 U.S Senate testimony, U.S. federal agency investments in nanotechnologies, $16.5 billion since 2001,[49] have resulted in a paralyzing conflict of interest between the government as investor/promoter and as regulator. Denison's proposal that a new and independent agency be created to do EHS research into nanotechnology, which could provide a scientific basis for rule-making, has fallen on deaf congressional ears.[50]

A March 11, 2011 memo, under the executive order authority of President Barack Obama, on "Principles for Regulation and Oversight of Emerging Technologies," including nanotechnology, reveals the federal government's tension between U.S. federal investments to promote technology innovation and obligations to enforce statutory EHS protections: "Where possible, regulatory approaches should promote innovation while also advancing regulatory objectives, such as protection of health, the environment and safety."[51] One of the authors of the memo, to all federal agency heads, Islam Siddiqui, is the chief agricultural trade negotiator, an official with no EHS regulatory responsibilities. Presumably, the regulatory promotion of innovation involves rules to expedite the commercialization of products with ENMs, rather than a regulatory framework that would prioritize EHS protection over commercialization.

Instead of regulating products with ENMs on the basis of the best public and peer-reviewed scientific literature and mandatory product data submission for EHS assessment, U.S. regulators provide draft voluntary guidance to industry on how regulators might apply rules and laws for macro-materials to ENM data. If regulators had such data, they could not be shared with other agencies if the commercial applicant declared the data to be confidential business information. Individual rules concerning non-nano EHS issues sometimes take several years to finalize. In that context, Denison's aforementioned lament about the time lapse of seven years with no mandatory product data submission (since he began to work on nanotechnology regulation) may appear to be unremarkable. But since 2004, the volume and heterogeneity of nanotechnology products commercialized has grown, but government capacity to regulate nanotechnology has not, despite the growing scientific literature on nanomaterial harms.

A multi-billion dollar unregulated nanotechnology market: testing, testing?

Nano forms of silver, carbon, titanium dioxide and silica are the most common ENMs incorporated into a broad array of consumer and industrial products, including cosmetics, dietary supplements, computers, clothing, and sports equipment, as well as in food packaging materials and other agricultural and food applications. As of July 2010, there were about 2,100 companies worldwide, with an estimated 1,100 in the United States, which produce ENMs and/or incorporate them into products.[52] Although companies may claim to incorporate ENMs in products without them to enhance their marketing prospects, only a couple firms have been fined by FDA for having made false product claims, despite the lack of formal regulation of ENMs. Already in 2007, the market for products with ENMs was estimated to be worth $147 billion, although many of those products do not advertise their nanotechnology component and are not required to do so. Another consultancy estimate projects a $3.1 trillion market by 2015, with half that value coming from nano-electronic applications in semi-conductors.[53]

Given the heterogeneity of products incorporating ENMs and of nanotechnology enabled manufacturing, targets for new U.S. legislation, as well as broad regulatory reforms, have been identified. One proposed change to the Federal Food Drugs and Cosmetics Act is to give the Food and Drug Administration "authority to review safety tests on food and cosmetic ingredients and to require post-market monitoring

and surveillance of many types of products."[54] The present congressional campaign to defund regulatory agencies and remove regulations that businesses identify as impediments to commercialization may make such legislative objectives seem utopian.[55] However, anti-regulatory ideology and budget cutting notwithstanding, there could be a consumer backlash to some food and food packaging products incorporating ENMs, if there is no post-marketing surveillance of them, to say nothing of the pre-market safety assessments that consumer groups have demanded.[56]

The need for agri-nanotechnology regulation is urgent. FDA policy is to deny that there are any foods commercialized with ENMs, but FDA scientists, speaking off the record, said there are at least a few foods commercialized that incorporate ENMs.[57] The nano-enabled foods likely include fortified juices and nutritional drinks for young children, according to a Friends of the Earth paper.[58] The PEN list includes several more food products with ENMs. Given the presence or imminence of commercialization and the extent of what is not known about ENMs, one would think that their incorporation into food packaging materials, food contact surfaces and consumable foods, would have already resulted in studies published on the effects of ENMs on the gastro-intestinal tracts of laboratory animals. However, despite the lack of research undertaken on the "fate of nanomaterials in the gut," when investigators for the United Kingdom's House of Lords asked the UK's Food Safety Authority (FSA) how many applications it had received in response to an FSA funding announcement to undertake such research, the FSA refused to report the number, much less disclose the content, of the applications. The House of Lords report characterized the FSA response as "unnecessary and inappropriate secrecy."[59]

The extent of what the FDA does not wish the public to know about ENMs is perhaps even greater than that of the FSA. According to the House of Lords investigators interviewing FDA officials in 2009, "There was no centralized source of information on nanotechnologies used in the food sector, and the FDA ***was not convinced that such information needed to be made available*** [emphasis mine]. There were no lists or formal monitoring by the FDA of the nanotechnologies being researched by companies working in the food sector."[60] Nevertheless, the House of Lords investigators reported that, according to one informant, "There was a good relationship between government and the food industry, with a frequent flow of information in both directions. However, in many cases the information sharing was informal and on a confidential basis."[61] Industry lawyers discourage nanotechnology product developers from publicizing their work or submitting data to regulators for review out of concern over legal liability that companies might face if ENMs resulted in adverse public health effects.[62]

There is just one FDA recommendation that could prompt to agri-nanotech product developers to submit data: "If the particle size is important for the additive to achieve its intended technical effect, such that the additive is produced or processed using techniques or tools that manipulate the particle size and may contain altered particles that are formed as manufacturing by-products, data on the size (average and distribution), shape, surface area (average and distribution), surface charge (zeta potential), and morphology of the particles, as well as any other size-dependent properties (e.g., agglomeration, aggregation, dispersion) should be included, as appropriate."[63] Particle size and shape are among the attributes that distinguish the chemical and toxicological properties of ENMs from their macro-size counterparts. Product developers are not compelled to submit particle size data but under a binding FDA rule, they are required to explain why they haven't submitted the data.

The near dearth of ENM data submitted to FDA has a further troubling consequence: the discretion given to companies to determine whether a macro-substance already considered by the company to be safe and therefore not reportable to the FDA is then deemed by the company to be likewise safe and hence non-reportable in its nano-scale form. The General Accountability Office concluded that "Despite the challenges inherent in assessing the safety of food ingredients containing engineered nanomaterials, under the Food, Drug, and Cosmetic Act and FDA regulations, a company may market such an ingredient without informing FDA as long as the company has concluded that the substance is GRAS [Generally Recognized As Safe]."[64] Furthermore, "FDA reviews those GRAS determinations that companies choose to submit. However, FDA in general does not have information about other GRAS determinations because companies are not required to inform the agency of their GRAS determinations."[65] So, in the absence of nanotechnology=specific rules, in theory a company could decide that the nano version of a macro-material it had determined to be GRAS was also GRAS, without informing the FDA.

In 2006, a coalition of nongovernmental organizations petitioned FDA to regulate ENMs, particularly titanium dioxide and zinc oxide used in sunscreens to decrease the likelihood of developing skin cancer from over-exposure to solar rays.[66] After nearly five years, the FDA still has not responded to the petition. One property of nano-titanium dioxide is to refract the ultra-violet rays that would hasten food spoilage. Retarding spoilage is a commercially valuable trait for the nano-coating of fruits and vegetables.

Test marketing regulation: food packaging materials with ENMs

The range of food and agricultural nanotechnology applications includes making toxins more bio-available in pesticides, targeting nutrients in smaller doses, improving the texture of ice cream and detecting bacteria in packaged foods. Regardless of the application, companies are concerned about a consumer backlash, and hence are prioritizing development of those products for which they can most readily demonstrate consumer benefits. Incorporating ENMs into food packaging, e.g., nano-clays into polymers to reduce moisture promoting bacteria, is a priority for many companies.[67] However, companies that are brand-sensitive, such as McDonald's, express an interest in ENMs research for their products but disavow any current use of them.[68]

The United Kingdom, having invested in agri-nanotechnology research and product development, has conducted citizen forums to assess the "acceptability" of one agri-nanotechnological application compared to another. At one such forum, once the forum leader explained the benefits of food packaging with ENMs, that application was seen as acceptable.[69] In effect, governments are focus-group testing consumers to discover how their investments in nanotechnology research and investments in public-private partnerships can best be recouped. Therefore, when U.S. government officials and the agri-nanotechology industry undertook to hypothesize how risk assessment of ENMs might be done, without first requiring companies to submit actual product data to regulatory scientists for assessment of EHS risks, it is not surprising that they settled on ENMs applied to hypothetical food packaging products.

"With the right partner, we could be less than a year from commercialization [...]. All proof of concept is complete with regard to properties and continuous—roll-to-roll—processing. I am very interested in finding partners for food packaging."

Dr. Jaime Grulan, inventor of nano-brick coating, March 2011[73]

In 2008, the Project on Emerging Nanotechnologies (PEN) and the Grocery Manufacturer's Association (GMA) brought together about 40 industry representatives, 15 government regulators and a handful of NGOs to consider how EPA and FDA might regulate generic and hypothetical food packaging incorporating ENMs. For GMA, the largest association of food retailers, which claims aggregate sales of $2.1 trillion annually, the market for nano-enabled packaging materials in the next decade will amount to 25 percent of the total $100 billion annual food packaging market.[70] By 2008, there were an estimated 400–500 food packaging materials that had been commercialized with ENMs,[71] so it may seem strange that PEN and GMA would rehearse regulation of nano-enabled food packaging with hypothetical products, rather than with a few of the already commercialized products. However, such is the concern about being held liable for any EHS harms from ENMs that both FDA and industry maintain the legally protective fiction that unregulated products have not been commercialized.

PEN and GMA's sophisticated exercise in pre-commercial communication between industry and government identified possible issues that might arise if regulators attempted to apply existing law and FDA and EPA policies to review three generic nano-enabled food packaging products: 1) 'active packaging' that prevents contamination of the packaging itself by inhibiting microbial growth; 2) "'smart packaging' that detects harmful bacteria in packaged food" by incorporating nano-biosensors into the packaging material, which could "read" the bacterial status of a microbe according to its fluorescent spectrum and "report" to a discerning consumer whether the bacteria were pathogenic; and 3) incorporating nano-clays into plastic carbonated beverage bottles to enable their resulting impermeability to conserve flavors, carbonation and liquids as well as heavier and breakable glass containers.[72] (At the risk of oversimplification, Taylor's summary of EPA's chemical and toxicological analysis and standards for food packaging are left out of the following account.) These generic nano–food packaging applications are similar to applications that have been patented and whose developers are in search of commercial partners.

The PEN/GMA project, as interpreted by then Professor, now FDA Deputy Commissioner for Food, Michael Taylor, outlines FDA's regulatory process for non-nano food packaging materials and contact surfaces (e.g., food conveyor belts) and then considers how that process might be applied to nano. Among the challenges that ENMs present to FDA's present regulatory process for food packaging materials are: 1.) validating methodologies to characterize ENM properties to determine whether ENMs might migrate into food; 2.) validating migration study protocols that would determine consumer exposure to ENMs; 3.) evaluating whether current FDA-set dietary concentrations triggers for toxicity testing are adequate for

ENMs, given the greater bio-availability of ENMs due to their exponentially greater surface to mass ratio; and 4) determining whether toxicological data for the macro-scale counterparts of ENMs have any utility for predictive toxicology and safety assessment.[74]

Meeting these challenges are made all the greater by Taylor's assumption that no categorical judgments should be made about testing results from one ENM that might be applied to another whose data would be submitted for regulatory review: "assuring the safety of any ENM requires a careful, case-by-case assessment. Each ENM should be approached, in other words, as if it were an untested new material with unfamiliar properties or a significant new use of a material."[75] Such an approach is both resource intensive and time intensive. Unfortunately, currently and in the near-term budget-cutting future, FDA has neither the resources nor the time for such an approach to be effective in safeguarding public health, workers and the environment. (The aforementioned dearth of resources, relative to the increase in volume and value of product lines overseen by FDA, is illustrated below in the case of import inspection and testing.)

Nevertheless, Taylor's study is well worth reading, both for its succinct presentation of the U.S. regulation of conventional food packaging and as an example of industry/government policy dialogue otherwise usually inaccessible to the public. As described by Taylor, an important regulatory decision made about food packaging material applications for commercialization is whether the scientific safety review of data presented by the applicant results in a daily dietary concentration of toxins "migrated" to the packaged food that is sufficient to trigger a formal regulation.

If the dietary concentration of the "food-contact substance" (FCS) is deemed by FDA to be insufficient to trigger a more extensive regulatory review, then the substance is allowed into commerce after FDA review of an applicant submitted Food Contact Notification (FCN). FDA provides extensive guidance on how companies should conduct migration studies and oral feeding studies of rodents to determine acceptable FCS daily intake for humans. If the FCS is designed to be toxic, such as a biocide incorporated into a food packaging material, then the parts per billion trigger for undertaking the more extensive regulatory review for a formal rule is set at a fifth of the trigger for an FCS not designed to be toxic.[76]

If the daily dietary concentration is sufficient to trigger regulatory concern and/or if the data submitted raises new or unresolved questions about the cancer-causing potential of the substance, then the applicant has to submit a food additive petition. While the FCN process is the "presumptive regulatory pathway for market entry of new packaging materials"[77] for conventional scale substances, the traditional setting of and evaluation of daily dietary concentrations may be irrelevant, or of very limited relevance, for ENMs in food packaging materials and other food contact surfaces. Taylor recognizes this possibility and cautiously allows that reducing the toxicological trigger for starting a formal regulation process might become a "general rule for ENMs" and not just a case-by-case determination.[78]

The rule of thumb that the dose of a toxic substance determines exposure to a toxin will be difficult to apply to an ENM compound of small volume but exponentially larger bio-availability. Fortunately, toxicologists have begun to develop nano-appropriate metrics to measure the toxicity of both low and high bio-persistent ENMs: "In general, toxicologists express doses by mass. However, given the extremely low mass of nano-particles and increasing doubts about the usefulness of mass as a metric, other metrics have been proposed, i.e., [nano-] particle number and particle surface area" to measure dose response.[79]

The exponentially larger surface-to-mass ration of ENMs, compared to that of macro-versions of the "same" materials, will make the determination of Acceptable Daily Intakes impossible, if companies are not required to submit data to regulators for their independent assessment. Assuming that companies submit relevant product data for regulatory review, the properties of ENMs may confound predictive toxicology studies on enough occasions so that a formal and more resource and time intensive regulation, rather than an expedited FCN, will become the most frequent regulatory pathway to commercialization.

When Taylor considers how the hypothetical products with ENMs might be regulated under current FDA rules, there is often a high degree of uncertainty: "FDA has not specifically addressed how the principles, rules, and guidance outlined here would apply to nanoscale versions of previously cleared substances. Thus, there is potential for uncertainty about whether and under what circumstances nanoscale food contact surfaces could come to market without any FDA review."[80] Previously cleared substances include those macro-scale versions which FDA has characterized as Generally Recognized As Safe (GRAS) upon industry petition. The possibility that all GRAS substances in macro forms could be subject to regulatory review in specific applications as ENMs would pose very large regulatory challenges for the evaluation of the estimated 400–500 FCSs with ENMs that have already been commercialized. Presumably FDA would have to develop some kind of post-market surveillance plan that would target the ENMs used in the food packaging materials traced back from the foods to which the ENMs had migrated.

Eat your fruits and vegetables—and ENM protective coatings!

How might FDA inspect and test for nano-coatings on imported fruits and vegetables? An answer to this question assumes hypothetically that: 1.) industry would submit product data for regulatory review according to a regulation developed by FDA; 2.) nano-specific risk assessments are developed with agreed metrics and assessment protocols to ensure the safety of consumers; 3.) a post-market surveillance program organized and evaluated data from both domestic and imported food and agriculture products with ENMs; 4.) the aforementioned programs will become adequately resourced to carry out statutory and regulatory obligations; and 5) FDA would work internationally to ensure robust pre-market safety assessment and post-market surveillance of nano-coated produce in other countries. These steps would assume in common recognition that only a comprehensive regulatory structure can both ensure an orderly market for products with ENMs and protect public health, worker health and the environment. Absent such a comprehensive and well-resourced regulatory structure, commercialization should not be allowed.

However rigorous and transparent the pre-commercialization regulatory process, robust product inspection and testing should verify that other food safety programs are working to protect public health and fulfill regulatory requirements. The following scenario assumes that nanotechnology applications to inform consumers of the bacterial status of a product, i.e., Taylor's hypothetical product No. 2, should not replace inspection and testing. However, at present, there is not an affordable and reliable inspection technology that FDA or any other regulatory agency could use in a port-of-entry situation. According to Dr. Stefan Weigel, leader of a European Commission financed food nanotechnology project, "there are no suitable methods for detecting the presence of nano-particles in food reliably and simply,"[81] methods that would be required for inspection and testing. Contra-factually, we assume that such methods will be developed and that they can be deployed at ports of entry, if there is the political will and budget to do so.

Further scientific and regulatory challenges occur when considering that nano-coatings of produce already commercialized may allow ENMs to migrate to the foods they coat. Nano-silica has been commercialized for food applications, but how it is used is only partly known from laboratory experiments, not from the evaluation of proprietary nano-coatings.[82] "At least one study suggests that silica migrates into vegetables from biodegradable nano-composite films."[83] ENM residues that could not be washed away by consumers in nano-coated produce are already reportedly being exported from Latin America to the U.S., without pre-market safety assessment or regulation. Pulitzer Prize winning health reporter Andrew Schneider writes:

> According to the USDA [U.S. Department of Agriculture] researcher—who asked that his name not be used because he's not authorized to speak for the agency—apples, pears, cucumbers and other fruits and vegetables are being coated with a thin, wax-like nanocoating to extend shelf-life. The edible nanomaterial skins will also protect the color and flavor of the fruit longer. "We found no indication that the nanocoating, which is manufactured in Asia, has ever been tested for health effects," said the researcher.[84]

Based on a review of patent filings, regulators have some knowledge of the ingredients of food nano-coatings. These ingredients include nano-silver and nano-zinc oxide as anti-microbials to combat bacteria; nano-silica to prevent water content loss and to ensure the film's transparency; and nano-titanium dioxide to prevent deterioration due to ultra-violet rays.[85] The macro forms of these nanocoating ingredients are permitted food additives. We assume, in the best of all possible regulatory worlds, that the nano-forms of these ingredients will go through a formal risk assessment and rule-making process.

However, based on the first attempt to fully risk assess just nano-silica alone, a pre-market safety evaluation of the other most likely components in a nano-coating will not be easy. A full risk assessment of nano-silica "is generally hampered by a lack of information on oral exposure to specific nanomaterials and any subsequent toxicity."[86] Developing such information should be an urgent priority, but will take time and money. In the meantime, if nano-coated produce is imported to the United States without regulatory review, what capacity does the FDA, the responsible regulatory agency for produce, have to inspect and test whether produce is coated with a permitted non-nano transparent coating vs. a transparent coating with ENMs?

FDA and industry solution: Don't test the product, certify the export process

Converting risk-assessment knowledge into an inspection protocol involves aggregating the inspection and testing requirements and tools (when they are developed) for ENMs to the existing inspection system. As indicated above, 30 years of budgetary and anti-regulatory attacks have left the U.S. federal agencies with import inspection and testing responsibilities in survival mode. U.S. congressional testimony concerning the FDA inspection and testing capacity at ports of entry is instructive for evaluating FDA

nanotechnology regulatory capacity, insofar as FDA import inspectors are required to re-inspect all products under FDA authority, not just food.

According to former FDA administrator Benjamin England, in 2007, FDA had about 200 inspectors for about 300 ports of entry. They inspect the paperwork for everything from fish and produce to cosmetics, medical devices and pharmaceuticals.[87] FDA Commissioner of Food and Drugs Margaret Hamburg stated in a 2010 report, "the estimated 20 million shipments of FDA-regulated imports that will come into the country this year will be handled by fewer than 500 inspectors."[88] In 2007, about 22 percent of U.S. fruit consumption and 24 percent of vegetable consumption was imported.[89] By 2010, imported produce comprised 35 percent of U.S. fresh fruit and vegetable consumption,[90] as U.S. food retailers contracted with foreign suppliers, rather than sourcing from more expensive U.S. fruit and vegetable growers.

Not surprisingly, current FDA inspection and testing frequency of imported fruits and vegetables is minimal, and consumer exposure to agents of foodborne illness is greater than from domestic produce. Food and Water Watch reported that "[l]ess than one percent of imported fresh produce shipments were inspected at the border in recent years. In 2007, the FDA performed only 11,000 border inspections on 33 billion pounds of imported fresh produce."[91] However, even this minimal inspection frequency and testing of produce for pesticide residues and pathogens showed, according to a 2006 FDA study, the imported produce to have three times greater likelihood of having Salmonella or Shigella and that imported fruit was four times as likely to have illegal pesticide residue levels than domestically produced fruit.[92] In light of this pre-nano inspection rate and incidence of pathogens and pesticide residue levels, some producer exporters are looking to nano-coating as a way to extend produce shelf life and reduce the incidence of imported produce food safety violations.

Evidently, there is an overall pre-nano capacity deficit for inspection and testing that has not been significantly reduced since England's testimony to Congress in 2007. Insufficient paperwork or past exporter import rule violations, rather than testing results, are the most frequent reasons for shipment refusal by import inspectors.[93] FDA's Science Board reported in 2008, a 78-percent decline over 35 years in inspection of FDA-regulated products and production facilities, "an appallingly low inspection rate."[94] Part of the reason for this low inspection rate is a resource deficit, combined with an ever-greater reliance on imports.

However, that deficit reflects industry pressure to avoid verifying the efficacy of pre-commercialization food safety programs by means of a robust inspection and testing program. A comment by John Allan of the American Frozen Food Institute on the implementation of the "FDA Food Safety Modernization Act of 2010," is perhaps typical of the animus against inspection and testing: "industry and FDA effort should focus mainly on ensuring that preventative measures are properly designated and effective, rather than utilizing valuable resources to try to detect the rare positive [i.e., contaminated] food sample coming off a production chain."[95] Unfortunately, contaminated fresh produce is not rare,[96] and the estimated public health cost of hospitalizations, loss of life and lost work productivity from foodborne illness is over $100 billion annually in the United States alone.[97]

In 2007, FDA published the results of a task force on nanotechnology that included comments from a 2006 public consultation. The comments concerned a wide array of FDA capacities relative to the challenges presented by nanotechnology applications to products under FDA authority. Among other topics, the comments concerned inspection and testing capacity. For example, "[a]nother comment emphasized that FDA's ability to inspect products is also significantly limited with regard to products that may contain nanoscale materials. Other comments noted that detection of nanoscale materials requires expensive and sophisticated equipment, and it is often unclear which parameters are relevant to toxicity."[98] In light of the aforementioned capacity deficit, this summary of comments surely is a gross understatement. As a result of FDA's nanotechnology task force activities, FDA told an industry conference in June 2009 that it would produce nanotechnology guidance to industry by the end of 2010.[99] Therefore, it is not possible to know at this time whether there will be any specific guidance on import inspection and testing. In May, the European Food Safety Authority released its guidance for risk assessing food and feed applications of nanotechnologies.[100]

Responding to the contamination of U.S.-imported pet food that killed about 39,000 pets, in November 2007, the Bush administration created an interagency task force to develop a plan for import product safety. The task force proposed to apply the Hazard Analysis Critical Control Point (HACCP) food safety management program to all exporting facilities and products. Third parties would certify that exporting facilities were operating in compliance with company designed HACCP plans. Regulatory officials would conduct onsite audits of a very small number of those facilities to verify compliance.[101] Since then FDA has further moved to implement the interagency report with the aid of computer software that models information concerning specific product risks.

U.S. food importers have complained that FDA is not implementing quickly enough the problem ridden PREDICT, the Predictive Risk-Based Evaluation for Dynamic Import Compliance Targeting, a computer program to expedite

imports deemed by PREDICT not to pose risks that require inspection and testing.[102] PREDICT is part of a broader import plan that minimizes port-of-entry inspection and testing and relies instead on 30 bilateral agreements of exporting governments with FDA to certify that export facilities meet FDA requirements.[103]

IATP evaluated the first of these agreements, in 2008 with China. We found it difficult to imagine how the agreement could be implemented, given the complexity of Chinese export supply chains, the differing objectives of Chinese national and provincial authorities, the reluctance of U.S. importers to pay for produce food safety programs, and the difficulty of applying the problematic HACCP program to design food safety management programs for a vast heterogeneity of foreign government certified food export facilities.[104] Unfortunately, production of unsafe food continues to prevail in China.[105] Since 2008, the FDA has established a total of ten permanent offices, in China, India, Mexico, Costa Rica, Chile and Jordan, as regional bases from which to implement its import safety program.[106] We assume that PREDICT and the import safety program would put fruits and vegetables with nano-coatings in the high-risk, to-be-inspected and tested category, if the FDA has the technology to do so and can identify the exporting nano-coated produce facilities.

However, on the basis of a report on U.S. food facilities inspection, inspection of foreign food facilities producing and exporting high risk products is likely to be difficult. The first Office of the Inspector General report in at least a decade on FDA food safety management gives some idea of the resource and training deficit that would be exacerbated by the additional requirements to inspect ENMs in products under FDA authority.[107] The report reviews FDA domestic inspection, not of food products, but of food processing and warehousing facilities, since facilities inspection is a pre-requisite to inspecting products to ensure that food is safe and wholesome, as required by the Federal Food Drug and Cosmetics Act.

The Inspector General reported that of 51,229 U.S. food facilities identified by FDA in Fiscal Years 2004–2008, about 56 percent had gone five years or more without inspection, making it impossible to know whether they were complying with FDA regulations.[108] Of more than 8,667 facilities identified by FDA as "high risk," just 63 percent were inspected in Fiscal Year 2007.[109] FDA acted to correct violations discovered in 36 percent of the facilities inspected. As the number of facilities inspected fell, so did the number found to violate FDA rules, from 614 in FY 2004 to 283 in FY 2008.[110] Furthermore, the full-time equivalents of personnel responsible for facilities inspection declined from 3,167 in FY 2003 to 2,569 in FY 2007,[111] i.e., during the time when produce imports began to increase dramatically.

The decline in resources dedicated to domestic facilities inspection would be presumably reversed for those exporting facilities that incorporate ENMs into food contact surfaces or into foods themselves, if FDA could determine the location of those facilities, be able to interview plant employees, review facility documents, and do other tasks of the audits required by the bilateral food safety agreements. Importers who want nano-coated produce with an extended shelf life will either have to consent to not just export facilities inspection, but to product inspection and testing. Or they will have to successfully lobby to have their nano-coated produce classified as a low-risk product and then hope that any resulting public health problems cannot be traced back to them because of the generally weak traceability capacity of the food processing industry, as noted in another Inspector General's report.[112]

International trade in food and agri-nanotechnology products

Because of, or perhaps despite, the scientific, budgetary and infrastructural difficulties of developing methods to simply and reliably measure the presence of ENMs in food, feed and food packaging materials, the Codex Alimentarius Commission, the international food standards body, may consider in July whether or not to include nanotechnology in its strategic plan for 2013–2018. Codex standards are presumed to be authoritative for the purpose of trade facilitation by the World Trade Organization Agreement on the Application of Sanitary and Phytosanitary Measures (Annex A, paragraph 3). At the 2010 meeting of the Commission, Egypt proposed the creation of a nanotechnology task force, in view of the extent of commercialization of agri-nanotechnology without risk assessment, standards or regulation.[113] However, the majority of the commission's members viewed the aforementioned June 2009 FAO/WHO expert meeting on the food safety issues in agri-nanotechnology to be sufficient grounds to delay any decision on whether Codex should form such a task force: "The Commission therefore agreed that there was no need to establish a dedicated Task Force for the time being and encouraged Egypt to work closely with FAO/WHO on this matter."[114] Since a second FAO/WHO expert meeting has not been announced, it is not clear how Egypt or any other Codex member should collaborate with FAO/WHO.

There are many reasons why Codex should undertake work on agri-nanotechnology, not the least of which is because, as the Egyptian delegate pointed out, agri-nanotechnology products already are being traded without regulation or risk assessment on which to base regulations. Furthermore, there are good reasons to take up that work in a task force, rather than within a Codex committee, such as the Committee on Food Additives, where the nano-coating of fruits and vegetables would be considered an additive. A task force is better

able to consider the many cross-cutting EHS issues of nanotechnology that Codex committee mandates would exclude from standard setting or have to refer to another committee.

At the same time, there are many reasons why Codex cannot readily add agri-nanotechnology to its strategic plan, whether via a task force or in committees. Codex standards, such as Acceptable Daily Intakes or Maximum Residue Levels for nano-pesticides, require the scientific advice of FAO/WHO expert meetings and/or standing committees, such as the Joint FAO/WHO Committee on Food Additives. However FAO and WHO member governments have not made the funding of such scientific advice a Codex priority, assigning only $500,000 to pay for all expert meetings in 2011, probably less than the cost of one food industry meeting.[115] There is at least one other reason not to take up agri-nanotechnology until Codex members have effective rules and resources to do mandatory pre-market safety assessments and post-market surveillance of foods with ENMs: Once Codex standards are agreed for nanotechnological applications, as a matter of trade law, international commercialization could take place even in the absence of WTO-member statutes, regulations, implementation measures, infrastructural and training investment, and enforcement of domestic law applied to agri-nanotechnology.

Conclusion

Governments, companies and university researchers are, for the most part, far more active in promoting nanotechnologies as sources of investments, job creation and "potential benefits," than they are in EHS risk research. The story to investors and legislators of "potential benefits" is far more attractive than the story of risks and the costs of regulation. Much less attractive to investors, whether public or private, is the very real possibility that research into those risks could result in regulatory delays and even prohibitions against commercialization, with consequent loss of research and development costs. There is an imbalance between assessment of potential benefits and potential risks of nanotechnology applications: "Contrary to the lax evidentiary standards applied to claims of benefits, risk must be definitely proven and quantified before regulation will be enacted to protect public health and safety, and even before nano-specific safety assessment of new products will be required."[116] From this inconsistent, and indeed, self-interested inequity in the application of evidentiary standards comes the constant promotion of "potential benefits" that may be unrealized for years, while research into EHS risk is a budgetary and policy orphan.

Part and parcel of a rigorous analysis of purported "potential benefits" is a framework of comparative technology assessment to assess whether a nanotechnology application is the optimal means for achieving a specific technological or public interest goal. In the U.S. government, robust comparative technology assessment died with the congressional decision in 1995 to shut down the Office of Technology Assessment, "a decision that one journalist at the time characterized as 'driving into the future with the headlights off.'"[117] In the case of the promotion of unregulated agri-nanotechnology, the investment driver not only has the lights off, but the foot on the pedal in the hope that products will become ubiquitous and "accepted" before risk research reveals EHS harms so prevalent and/or severe as to force withdrawal of the product from commerce.

The June 9 announcement by EPA and FDA of their intent to issue voluntary guidance to industry on nanotechnology products under their respective authority is a small, but encouraging first step towards regulation. However, such is the hope for myriad benefits from nanotechnologies, that promoters fear a loss of investment and public confidence in nanotechnology if "too much precaution" is applied in adopting regulations to manage poorly understood, as well as known, nanotechnology risks.[118] Surely, minimizing the budgets and mandate for EHS research into agri-nanotechnology and trusting that agri-nanotechnology hazards, if they appear as public health and environmental harms, will be untraceable and beyond the reach of liability plaintiffs, is not a viable technology policy. A policy that relies on non-regulation and paltry investments in EHS risk research cannot enable the so-called "New Industrial Revolution" for the 21st century that nanotechnology promoters promise.

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