Food-Related Applications of Nanotechnology: Regulatory Issues

Statement of
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at the
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Introduction

I welcome this opportunity to provide input as FDA considers next steps in developing its approaches to regulatory oversight of nanotechnology, including the technology's food-related applications.

My interest and views concerning the regulation of nanotechnology stem primarily from work I have done for the Project on Emerging Nanotechnologies at the Woodrow Wilson International Center for Scholars. This includes an October 2006 report analyzing FDA's readiness to oversee the wide range of potential drug, medical device, cosmetic, dietary supplement, and food-related products that could be derived from nanotechnology.[1] In that report, I made a number of recommendations for actions FDA and Congress could take to help ensure FDA's readiness to regulate this important new technology, not the least of which is to ensure that FDA has the resources it needs to do what needs to be done.

I stand by my previous recommendations. I want to emphasize that the recommendations made in that report, like the comments I will make today, are mine alone and do not necessarily represent the views of the Wilson Center.

In this statement, I will focus on issues related to FDA's oversight of nanotechnology-derived substances purposefully added to food or used in its processing. I thus find it noteworthy that this meeting is being held on the 50th anniversary of the law that governs FDA's regulation of new food technologies, including nanotechnology. I'm referring of course to the Food Additives Amendment of 1958, which was enacted on September 6, 1958.

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[1] Taylor, M.R., *Regulating the Products of Nanotechnology: Does FDA Have the Tools it Needs?* (October 2006) (http://www.nanotechproject.org/publications/archive/regulating_products_nanotechnology_does/).

Nanotechnology is all about the future, and Congress certainly did not have nanotechnology in mind in 1958 when it passed the new food additive law, but in discerning the path forward it is crucial to look back and to review the key goals and concepts underlying the 1958 law. For me, this review reveals the fundamental and enduring strengths of the food additive law, as well as some challenges with respect to nanotechnology that FDA and the regulated community need to address.

Key Goals and Concepts Underlying the Food Additives Amendment

When Congress enacted the FAA in 1958, the chemical revolution was well under way, with food companies making increasing use of chemical technologies to produce the convenient and low-cost packaged foods consumers were demanding. Congress passed the new law with two broad goals in mind: ensuring the safety of food for consumers and fostering continued innovation in food technology.

To ensure safety, Congress established a strong "reasonable certainty of no harm" safety standard for new substances added intentionally to food and placed on the industry the burden to prove scientifically that the standard had been met. For substances falling within the FAA's legal definition of "food additive," the law requires formal pre-market review and approval by FDA through a food additive petition process that results in a regulation specifying the conditions under which the additive may be safely and lawfully used.

The goal of fostering innovation is embodied in several features of the 1958 law. First, Congress and the industry saw the assurance of safety provided by FDA's new regulatory oversight to be important to the public acceptance and confidence that are required for innovative food technologies to succeed in the marketplace. The food industry supported, and even urged, passage of the FAA.

Second, Congress established a safety standard that is rigorous but scientifically realistic in that it requires a "reasonable" but not absolute "certainty" that no harm will result from the use of the additive.

Finally, Congress constructed the law so that substances or uses of substances whose safety was already well established and well recognized among scientists were excluded from the legal definition of "food additive" and thus would not have to go through the FDA approval process. The resulting GRAS concept – the idea that substances "generally recognized as safe" could be used without FDA pre-market approval – has been an important feature of the FAA's implementation over the years and raises important questions for the law's application to nanotechnology.

As the GRAS concept has been interpreted and applied over the years, companies wishing to market or use a substance based on its GRAS status are free to do so based on their independent determination that the substance is "generally recognized as safe," subject to the risk that FDA will subsequently object and seek to halt marketing or use by showing that the substance is not GRAS. However, in making an independent GRAS

determination for a substance that does not have a history of use in food prior to 1958, a company must be able to marshal the same quantity and quality of scientific evidence on safety that would be required to gain approval by FDA as a food additive. Furthermore, that evidence must be widely available to the community of qualified experts and the safety of the substance for its intended use must be common knowledge among those experts.

In keeping with the innovation goal of the FAA, as well as the aim of providing public assurances of safety without undue expenditure of FDA resources, FDA has created a voluntary GRAS notification program. Under this program, sponsors can submit to FDA pre-market notification of the basis for their independent GRAS determinations, which FDA reviews and lists publicly with notations about whether the agency objects to the determination or "has no questions." FDA does not, however, make its own safety evaluation or GRAS determination on substances of which it is notified under this program.

Regulatory Challenges for FDA and the Industry

Marshaling the Science to Satisfy the Safety Standard

The appeal of nanotechnology is that it enables the manipulation and use of familiar substances at dramatically reduced particle sizes that give the substances new and potentially very beneficial functional properties as a result of their changed physical properties. Small particle size does not by itself change the safety profile of a substance. To the extent the nano-scale version of a familiar substance has different properties, however, the safety of the nanomaterial cannot be assumed or demonstrated solely on the basis of the evidence supporting the safety of the conventional scale version of the substance. A case-by-case scientific assessment is required using methods that are suitable to the evaluation of nano-scale materials.

This scientific reality has important implications for the FDA regulatory process and for the developers and potential users of nano-derived foods and food packaging due to scientific uncertainties concerning the suitability for nano-scale particles of established safety assessment methods. These include uncertainties about how to characterize nano-scale particles for purposes of measuring potential exposure resulting from a particular use and uncertainties about whether standard toxicity tests need to be supplemented or modified to be suitable for evaluating the safety of nanomaterials. Some of these uncertainties are described in a recent report addressing issues associated with nano-scale food packaging, on which I worked under the auspices of the Wilson Center.[2]

In the FDA regulatory process for new food technologies, in which the sponsor bears the burden of proof on safety, uncertainty at this methodological level is a fundamental impediment to FDA's safety evaluation and to making the "reasonable certainty of no harm" finding required for FDA approval. If the methods for generating safety data have

[2] Taylor, M.R., *Assuring the Safety of Nanomaterials in Food Packaging: The Regulatory Process and Key Issues* (July 2008) (http://www.nanotechproject.org/publications/archive/nano_food_packaging/).

not been validated as suitable for evaluating nano-scale particles, FDA is not in a position to make a finding of "reasonable certainty of no harm." For products going through the pre-market approval process, consumers remain protected, but innovation is stymied.

It is thus incumbent on FDA and the industry to identify the methodological issues and develop the methods that are needed to support a scientific assessment of the safety of nano-scale substances for food-related uses. The safety testing itself is the responsibility of the sponsor, but FDA has an essential role to play in ensuring that suitable test methods exist and are used.

Clarifying the Applicability of the GRAS Concept

The central purpose of the FAA was to ensure the proper testing and the safety of substances whose safety had not already been established prior to 1958 through experience based on common use in food. To this end, Congress required that, as a general rule, substances that had not previously been used in food or were being put to new uses would have to go through an FDA pre-market approval process.

Congress created the GRAS concept to build some flexibility into the system by exempting GRAS substances from the pre-market approval requirement, and FDA and the industry have used this authority creatively over the years to avoid the food additive approval process for well-tested substances whose safety is recognized by experts. For FDA, this conserves scarce scientific review and administrative resources. For industry, avoiding the time-consuming food additive approval process means saving time and money in getting products to market.

From a consumer protection and public acceptance perspective, however, the GRAS concept, if not applied in the rigorous way intended by Congress, opens the door to independent decisionmaking by technology providers and food companies to market truly new food technologies without a pre-market safety evaluation and approval by FDA. This may be unlikely to happen with respect to nanotechnology, given the high standard for GRAS status set by Congress and the state of the science regarding safety evaluation of nanotechnology. In fact, from my perspective, it is very difficult to imagine how GRAS status could be justified for a nano-scale particle with novel physical properties, and food companies are generally conservative in adopting new technologies that have not received FDA's blessing.

I can understand why FDA may not want to prematurely rule out the applicability of the GRAS concept to nano-scale particles. Indeed the time may come, when the science is better settled, that a nano-derived substance will meet the GRAS standard by virtue of having been tested in a manner that has produced the same quantity and quality of evidence demonstrating safety as would be needed to be approved by FDA as a food additive, such evidence has been published in a widely available form, and the safety of the particular use of the substance is widely recognized by experts. When that is the case, FDA has no basis to object to a GRAS determination, and the GRAS notification system

may provide adequate assurance to the public that the basis for the determination has been reviewed by FDA.

In the meantime, however, I am concerned that the public credibility of the regulatory process, in the case of nanotechnology or any major new food technology, is jeopardized by the fact that the system includes, at least theoretically, the opportunity for technology developers and users to make independent GRAS determinations and go to market without even notifying FDA. One way to reduce this vulnerability would be for FDA to make clear through guidance to the industry its position on the applicability of the GRAS concept to food-related uses of nanotechnology.

Nature of the Food Additive Rulemaking Process

One reason FDA's GRAS notification procedure is appealing to industry is that it avoids the often very lengthy food additive approval process while providing the marketplace and public acceptance that comes with FDA having reviewed the basis for the GRAS determination and implicitly blessing it.

For the foreseeable future, however, the food additive rulemaking process is likely to be the channel through which nano-scale particles with novel properties will have to go, and the challenge this will present is a good reminder that this process has features that may merit review and reform. The formal rulemaking process used for food additive approvals can be legalistic and can bog down over issues that have more to do with preparing the administrative record for possible review before an administrative law judge and federal appeals court and less to do with the quality of the scientific safety evaluation. Moreover, the food additive approval process has very little public transparency, which can be especially important for novel new technologies.

Perhaps nanotechnology is an appropriate springboard for FDA and its stakeholders to consider options for making the food additive approval process as fully science-driven, transparent and timely as possible.

Conclusion

I applaud FDA for convening this public meeting. I hope it succeeds in surfacing and helping FDA prioritize issues that need to be addressed to ensure proper oversight of products made possible by nanotechnology. I also hope is helps Congress and the agency's stakeholders appreciate the challenge nanotechnology poses for FDA and encourages them to be sure FDA has the resources and policy tools it needs to meet that challenge.