

Reporting on Nanotech

An FDA task force faces the challenge of very, very small products.



**BY MARC J. SCHEINESON
AND JULIE K. TIBBETS**

As tiny molecule nanotechnologies begin to infiltrate the American consumer marketplace, the Food and Drug Administration must grapple with how to regulate the safety and effectiveness of these products under its existing regulatory framework.

With a consumer climate increasingly sensitive to safety issues and with products containing nanotechnology, such as sunscreens, already on the market, the FDA established an intra-agency Nanotechnology Task Force. The main objective of the task force was to assess the regulatory issues associated with these products and offer recommendations to the agency.

On July 25, the FDA released the long-anticipated task force report, which offers a glimpse at the agency's current thinking concerning these products. It recommended that the agency gather more safety information and data about nanoscale materials; issue a series of guidance for researchers, sponsors, and manufacturers of these products to promote transparent and predictable approval pathways; and use its existing regulatory authority to ensure product safety and efficacy.

Although the FDA Task Force declined to define nanomaterials or nanotechnology, the intergovernmental National Nanotechnology Initiative has defined "nanomaterials" as technology developed at the atomic, molecular, and macromolecular levels on the scale of 1 to 100 nanometers. One nanometer equals one-billionth of a meter. For reference, a sheet of paper is about 100,000 nanometers thick, and a human hair is about 80,000 nanometers wide.

According to FDA consumer health information, examples of nanocomponents include microscopic, man-made chips, vessels, and pumps. These nanocomponents have, among others, the following applications: extending the

shelf life of foods or packaging; improving product formulations; delivering life-saving medicines precisely to the cells and tissues that need them; and detecting disease with sensors or images.

ACROSS CATEGORIES

Nanotechnology challenges the traditional product categories established by the Federal Food, Drug, and Cosmetic Act. The vexing issue for regulators interested in removing entry barriers to the development of this new technology is its universal application across and among the FDA's jurisdictional product categories: over-the-counter and prescription drugs, medical devices, biologics; foods (including packaging, color additives, and indirect food additives), animal feeds and animal drugs, and even cosmetics.

As such, the Nanotechnology Task Force, co-chaired by FDA Associate Commissioner for Science Norris Alderson and Associate Commissioner for Policy and Planning Randall Lutter, focused its efforts on examining whether the agency's existing regulatory mechanisms adequately address the unique features of nanotechnology products and the safety of nanoscale materials.

In particular, the task force closely examined the FDA's regulatory reach over nanomaterials added to cosmetics and dietary supplements, which are subject to only light pre-market regulation without the level of pre-market review to which drugs, devices, biologics, and food and color additives are subject. The task force concluded that the FDA's existing regulatory authority includes sufficient mechanisms for requesting, and in many cases requiring, data from manufacturers and sponsors concerning their nanoscale materials.

Specifically, the task force found that nanoscale materials in drugs, devices, biologics, food and color additives, "generally recognized as safe" (known as GRAS) food

substances, and certain dietary supplements would be subject to the FDA's existing regulatory review processes. These processes include investigational new drug applications, new drug applications, biologics license applications, device pre-market approval applications, device pre-market notifications, food and color additive petitions, notifications for GRAS substances, and new dietary-ingredient notifications. These pre-market mechanisms provide a platform for the FDA to request additional data and information from applicants and from those filing notifications should the agency find that the submissions include insufficient or no data on the nanoscale materials in their products.

In addition, the report suggested that the agency could issue a call for data to identify over-the-counter drugs and food and color additives already on the market that contain nanoscale materials. In particular, the task force focused its data concerns on evaluating the interactions of nanoscale materials with biological systems and on ensuring the safety of these materials and their finished products.

Given the agency's many pre-market review mechanisms, the task force concluded that only cosmetics and dietary supplements not subject to new dietary ingredient notifications lack the regulatory pre-market mechanisms for sufficient FDA review of the nanoscale materials in those products. In lieu of pre-market authority over these products, the report noted that the agency can utilize its enforcement mechanisms, including its authority over adulterated products, to ensure post-market product safety.

In addition, the task force identified a call for information and data through notices in the Federal Register as a means for collecting and reviewing pertinent safety information for the nanoscale materials in these products.

Moreover, the report recommended that the FDA issue guidance for manufacturers that identifies potential safety issues for cosmetics containing nanoscale materials and that addresses whether nanoscale versions of "old" ingredients trigger the notification requirement for dietary ingredients in supplement products. The report also recommended the development of guidance on the effect of nanoscale materials on the manufacturing process as a whole.

PRODUCT LABELING

The task force considered whether potential safety concerns associated with nanomaterials could be allayed by using the agency's authority over product labeling.

For example, the FDA requires foods treated with irradiation to include in product labeling the statement "treated with radiation" or "treated by irradiation," along with an international symbol for irradiation. Manufacturers and producers irradiate foods to delay product maturation and control insects and microorganisms in foods. The FDA instituted irradiation labeling after reviewing several decades of irradiation safety information and data.

Although irradiation labeling could be a model for the agency to employ in proposing nanotechnology labeling in the future, the Nanotechnology Task Force rejected the need

for universal labeling in its report. It reasoned that there is a lack of scientific knowledge about the safety concerns, if any, that nanoscale materials present.

The task force noted, however, that the FDA's enforcement authority over false or misleading labeling permits a case-by-case review by the agency concerning whether companies must include nanotechnology-related information in product labeling.

According to a 2004 article in *Nanotechnology Law and Business*, there were more than 22,000 scientific publications related to nanotechnology in 2002 alone.

Despite this body of science, the FDA and the National Science and Technology Council Working Group on Nanotechnology Environmental and Health Implications, which is made up of 18 federal government agencies including the FDA, reported on Aug. 16 that basic scientific research was absent about the metabolism and movement of nanomaterials in the human body.

All agreed that the government should strengthen efforts to increase scientific understanding and facilitate assessment of data needs for regulated products. Likewise, the Nanotechnology Task Force report concluded that the agency needs more information about the effects of nanotechnology properties on product performance and safety.

The NEHI Working Group recently identified the following five major research needs involving nanomaterials: instrumentation, measurement, and analytical methods; nanomaterial exposure and human health; environmental impact; environmental exposure from industrial processes; and risk-management methods. Next, the working group will identify those needs not addressed by current research.

In addition, the FDA currently participates on the American National Standards Institute's Nanotechnology Standards Panel. The panel is working with industry, university, and other governmental authorities to develop test methodologies and characterization standards, among other things.

FUTURE GUIDANCE

Based on the recommendations from the task force, companies should expect the FDA to issue guidance addressing product-specific issues and considerations related to nanoscale materials as the agency learns more about this technology.

In addition, it is likely that the agency will issue notices in the Federal Register calling for manufacturers and sponsors to submit information and data about their nanoscale materials as the FDA builds expertise in this emerging area. Congressional activity over the FDA's regulation of nanotechnology is unlikely because of the available regulatory mechanisms in the existing statutory framework of the act.

Companies and researchers should expect that the FDA and the working groups to which it belongs will continue to narrow their list of research needs and priorities for studies identifying the impact of nanoscale materials on people, workplaces, and the environment. To minimize any regulatory obstacles in bringing nanotechnology products to mar-

ket, companies and sponsors would be wise to consult with the FDA early in their development processes, even where no formal requirement to do so exists.

Given the limitations of the agency's pre-market authority over their products, makers of cosmetics and dietary supplements that incorporate nanoscale materials should also prepare for the possibility of increased agency enforcement activity for these products.

As with any emerging technology, there is still much to learn about the effects of nanotechnology on product safety and efficacy. The versatility of product applications for nanoscale materials across the full spectrum of FDA-regu-

lated product categories promises to redefine product innovation. Through its Nanotechnology Task Force and various other working group and panel memberships, the FDA is actively working to keep regulatory pace with the possibilities that nanotechnology offers.

Marc J. Scheineson heads the food and drug practice in the D.C. office of Alston & Bird. He is a former associate FDA commissioner for legislative affairs. Julie K. Tibbets is a food and drug associate in the firm's D.C. office. They can be contacted at marc.scheineson@alston.com and julie.tibbets@alston.com.