FDA Issues Two Draft Guidances on Nanotechnology

On April 20, the U.S. Food and Drug Administration (FDA) released two draft guidance documents primarily focused on the use of nanotechnology by the food and cosmetics industries. The two guidance documents are “Guidance for Industry: Assessing the Effects of Significant Manufacturing Process Changes, including Emerging Technologies, on the Safety and Regulatory Status of Food Ingredients and Food Contact Substances, Including Food Ingredients that are Color Additives” (available here) and “Guidance for Industry: Safety of Nanomaterials in Cosmetic Products” (available at here). The draft guidance documents have been released for public comment, and FDA suggests that comments be submitted within 90 days to ensure that they are considered before FDA releases the final versions (comments should be submitted at www.regulations.gov, using docket no. FDA-2011-D-0490 and FDA-2011-D-0489 respectively).

Definition of Nanotechnology

Despite the Agency's increased focus on this area, FDA still has not formally defined what constitutes “nanotechnology.” Instead, FDA looks to certain parameters: (1) whether an engineered material or end product has at least one dimension in the nanoscale range (approximately 1 nm to 100 nm); or (2) whether an engineered material or end product exhibits properties or phenomena, including physical or chemical properties or biological effects, that are attributable to its dimension(s), even if these dimensions fall outside the nanoscale range, up to one micrometer.

Draft Food Guidance

Much of the food draft guidance will be familiar to those experienced with the regulation of food additives and food contact substances. The guidance reviews the existing regulatory framework for these substances, outlining the criteria for determining whether a substance requires premarket approval by FDA, whether the approval should take the form of a food or color additive petition (FAP/CAP), GRAS determination, or a food contact substance notification (FCN), and what information should be included in the submission. The guidance also describes the factors manufacturers should consider when determining whether changes in manufacturing processes for a cleared food/color additive or food contact substance, particularly changes involving nanotechnology, create a significant change that may affect the identity, safety, or regulatory status of the use of the food substance and whether the change warrants a regulatory submission to FDA.

Identity and Conditions of Use

Manufacturers should look to whether the manufacturing process change affects the identity or conditions of use of a food substance, thereby taking it out of the scope of its existing clearance. This should include a review of its physicochemical structure and properties, purity, and impurities. If the identity or conditions of use are sufficiently different to that previously described to FDA, or if new impurities make the substance no longer food grade, that would be considered a significant change.
Safety

FDA notes that products containing nanomaterials or otherwise involving application of nanotechnology are not intrinsically classified as harmful; rather, safety reviews for nanotechnology-derived products follow the same process as conventional foods. Nevertheless, nano-engineered food substances may have new properties, such as particle size, surface area, aggregation/agglomeration, or shape, which may impact the absorption, distribution, metabolism and excretion (ADME) of the substance and thus, potentially, its safety. These considerations may also merit additional or different testing methods to demonstrate safety. Thus, a manufacturer should consider the characteristic properties of the substance, such as its physicochemical structure and properties, purity, impurities, bioavailability, or toxicity, when determining whether a manufacturing process change is significant because it affects the safety of the substance.

Regulatory Status

There also may be cases where it simply is not clear whether the use of a food substance complies with an existing regulatory clearance. A manufacturing process change may be significant if it takes the substance outside of the requirements, limitations, or specifications provided in the clearance.

Consequences of a Significant Change

If a manufacturer determines that a significant change in the manufacturing process has occurred, or if it is not clear, the guidance recommends consulting with FDA. This consultation may result in FDA concluding that the intended use of the food substance continues to be safe and lawful after the change in manufacturing process. Alternatively, if the identity, conditions of use, or safety evaluation is significantly changed to take the substance outside the scope of its existing clearance, a new regulatory submission may be necessary. FDA particularly notes that a nano-engineered food substance likely would not be covered by an existing GRAS determination for a related food substance manufactured without using nanotechnology.

Draft Cosmetic Guidance

The cosmetic guidance reviews the existing regulatory framework for cosmetic substances, outlining that the Federal Food, Drug, and Cosmetic Act (FD&C Act 21 U.S.C. 362) does not subject cosmetics or cosmetic ingredients (aside from color additives) to FDA premarket approval. In fact, a cosmetic manufacturer may use any ingredient in its product that is not prohibited by statute or that does not otherwise cause the cosmetic to be adulterated (§ 601) or misbranded (§ 602) under the FD&C Act. To ensure the product is not adulterate or misbranaded, the manufacturer should have obtained all data and information needed to substantiate the product prior to marketing. The guidance is primarily focused on describing the factors manufacturers should consider in assessing the safety of nanomaterials in cosmetic products.

Safety Assessment

Similarly to FDA’s guidance on nanomaterials used in food ingredients and food contact substances (described above), FDA notes that cosmetics containing nanomaterials or otherwise involving application of nanotechnology are not intrinsically classified as harmful; rather, safety reviews for nanotechnology-derived products follow the
same process as conventional cosmetics. However, the manufacturing process of a nanomaterial may alter the purity, concentration of the starting materials, or changes in identity. Changes to the manufacturing process often include the use of different solvents, time/temperature conditions, starting chemicals, and additional agents. A manufacturer should consider these changes when assessing the overall safety of the end product.

Most cosmetic products are applied to or sprayed near the skin or mouth, and so traditional cosmetic safety evaluations may be limited to the consideration of dermal, inhalation, and oral exposures. But because nanomaterials may be systemically absorbed, exposure to secondary organs should be accounted for in the evaluation of their safety. Specifically, the safety assessment of a nanomaterial to be used in cosmetics should address whether the unique physicochemical properties of the compound will alter its absorption, distribution, metabolism, excretion, or toxicity. FDA notes that manufacturers should modify traditional toxicity testing methods, or develop new methods as needed, with respect to appropriate solvents and dosing formulations, methods to prevent agglomeration of particles, purity and stability conditions, and other variables to account for the nanoscale properties of the materials.

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