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Division of Dockets Management (HFA-305)

Food and Drug Administration

5630 Fishers Lane

Room 1061

Rockville, MD 20852

**RE: Draft Guidance for Industry: Considering Whether an FDA-Regulated Product Involves the Application of Nanotechnology (Docket Number: FDA-2010-D-0530)**

On behalf of the Consumer Healthcare Products Association (CHPA), we are pleased to submit the following comments in response to the June 14, 2011 Federal Register notice (FR 76(114): 34715-34715) on the draft guidance “Considering Whether an FDA-Regulated Product Involves the Application of Nanotechnology.”

The Consumer Healthcare Products Association and its members, the U.S. manufacturers and distributors of Over-the-Counter (OTC) medicines and nutritional supplements, recognize the efforts of the U.S. Food and Drug Administration to further develop regulatory strategies and guidance on nanomaterials for drug applications. In addition, CHPA applauds the approach for creating a public forum to collect current research and comments to advance the science of engineered nanomaterials.

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Our consumers rely on these safe and effective OTC medicines which are currently the most cost-effective preparations in the healthcare environment. The consumer healthcare industry is continuously striving to improve the science to develop new innovative medicines and to enhance the efficacy of existing products. Although presently, engineered nanomaterials do not appear to be widely used in our industry, CHPA does feel it is a promising and important technology that has the potential to deliver innovative products with increased benefit to the consumer.

Nanotechnology is not a separate drug category, but a technology used to generate nanometer-sized ingredients and excipients. Inclusion of nanometer-sized active ingredients or excipients in a drug product does not determine a product's safety and efficacy (i.e. size alone is not itself an indicator of toxicity); the drug product should be held to the same stringent standards as any other drug product to prove both safety and efficacy.

CHPA agrees with the FDA that proposing a "definition" for nanotechnology is not straight forward; applying a strict, universal definition of nanotechnology to the fields of drug research, drug product development and drug manufacturing is not, in our view, an appropriate science-based approach. Defining a nanomaterial as a structure between 1 and 100 nm and using this definition to establish new regulations on products containing nano-sized materials will erroneously group drug products together to form a new category based on size of ingredients. Additional guidance is necessary for particles between 100 nm and 1 micron; there exist common pharmaceutical ingredients with a long history of use that should not be considered as "engineered nanomaterials" or as agglomerates of nanomaterials but may have particles whose size falls within this range. NIOSH accurately refers to "nanotechnology (as) the manipulation of matter on a near-atomic scale to produce new structures, materials, and devices" and here, does not limit the classification to a specific size range. Nanomaterials are mainly engineered for their novel chemical, physical, and quantum mechanical properties; at the nanometer size, many materials exhibit such unique beneficial properties that may not exist when at the micron size.

CHPA members agree that the agency should distinguish between engineered nanomaterials and those naturally occurring at the nanoscale. We feel it may be appropriate to include in the description of engineered nanomaterials, materials whose particles are deliberately manipulated and controlled at the nanoscale which also exhibit changes in physical, chemical, or electromagnetic properties that differ at the nanoscale from that of the bulk. It is imperative that the description for “nanomaterial” include both the nano-size requirement *and* the existence of unique phenomena to enable novel applications. If both of these factors are not met, then the material, drug substance or drug product should not merit additional scrutiny and investigation by the FDA. For example, milling, a beneficial process for the manufacturing of many individual pharmaceutical ingredients, may create particles with average particle sizes or a portion of the particle size distribution under 1 micron; however, the chemical properties of the milled ingredient usually do not differ drastically from that of the bulk ingredient. Current robust regulatory processes ensure drug products with milled ingredients are safe and effective.

On that note, all materials should not be considered equal under a single guidance for “nanotechnology” of drug products, and each material must be evaluated on a case-by-case basis. There exist many categories under the main umbrella of engineered nanomaterials; for example, soluble nanomaterials should not be treated the same as insoluble ones. In addition, properties of “soft” nanomaterials differ greatly from that of “hard” nanomaterials. Criteria that are considered important include: shape and size (how many dimensions are on the nanoscale), surface area, agglomeration/aggregation, distribution of particles, functional properties such as mobility, flow, hydration, desiccation, surface charge (hydrophobicity/hydrophilicity), and zeta potential.

The agency should take a risk-based approach when developing its regulatory strategies and should continue to base decisions and guidance on science. The agency should reach out to scientific organizations such as the Product Quality & Research Institute (PQRI), and other domestic and global academic and technical institutes for their data, established criteria and other scientific information on nanomaterial characterization techniques, toxicology and structure-function relationships. For example, PQRI, of which FDA is a member, has just completed the first phase of its project reviewing the currently

used and soon to be used nanoparticles and nano-enabled devices in pharmaceutical and other biomedical industries. This document could prove to be extremely useful to the FDA when creating risk- and science-based regulatory decisions and in developing this guidance.

In addition to reaching out to these organizations, CHPA feels that it is important to coordinate FDA's activities with other major regulatory bodies (including Europe and other nations outside the United States) so that there is a harmonized approach to how these issues are handled.

The agency should also consider including additional clarity in the Guidance or drafting of additional guidance that is consistent with the Memorandum for the Heads of Executive Departments and Agencies. This department clearly states that the framework developed by the U.S. government for "oversight and regulation for nanomaterials and applications of nanotechnology build on existing laws and individual authorities, such as risk-based approaches... (and) strive to provide their stakeholders with clear information that delineates the specific risks identified and the content in which they arise."

CHPA member companies feel the agency should consider providing additional clarity and guidance around the following:

- **The term "unique phenomena"**

CHPA agrees that this is an important term to understand when categorizing a material as an "engineered nanomaterial;" however, the agency should provide examples or provide clarity around the types of unique chemical, physical, or quantum mechanical property changes that exist when the material is less than 1 micron in at least one dimension. It must be clear that these unique properties do not exist for the same material when it exists in the bulk form.

- **Size Distribution of Particles**

The agency should add language to describe the treatment of materials whose average particle size is greater than 1 micron but has a portion of its particles with measurements below 1 micron.

- **Agglomerates and Aggregates**

The agency should consider providing guidance on how to treat agglomerates and aggregates.

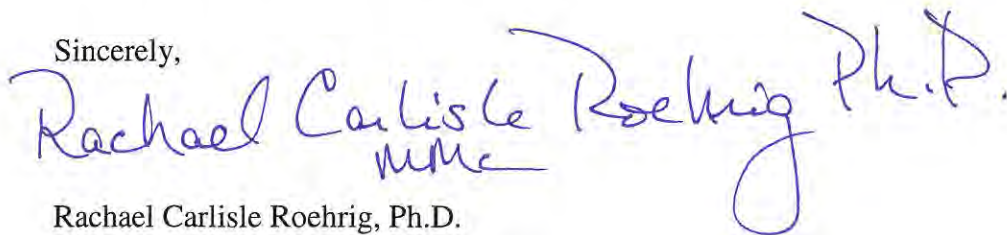
- **Nano-size on One-Dimension**

Additional clarity is needed as to why a material with only one dimension on the nanoscale is considered a nanomaterial. Once again, size alone should not determine safety; the material must also exhibit unique chemical, physical, or quantum mechanical properties that differ from that of the bulk.

Furthermore, CHPA understands the current demand on the agency's staff and resources and has been a longtime advocate for additional FDA funding. We believe that unnecessary communications and data collection on the application of nanomaterials could also constrain the agency's time and resources. The agency should prioritize the areas of concern through adding clarity to its draft guidance, "Considering Whether an FDA-Regulated Product Involves the Application of Nanotechnology." Not all nano-sized materials or drug components should be evaluated more extensively solely because of their size; pharmaceuticals with components exhibiting unique properties or product attributes due to their nano-size may need to be tested accordingly to determine if the drug's efficacy or safety profile was altered. A clear evaluation and decision process should be described by the agency in its final guidance to help determine the categorization of a material as an "engineered nanomaterial."

Again, we appreciate the opportunity to comment. Please feel free to contact me if any questions arise regarding this issue or the comments in this letter.

Sincerely,



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Director, Technical & Scientific Affairs

Consumer Healthcare Products Association