August 29, 2011

Division of Dockets Management (HFA-305)
U.S. Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: EWG Comments on FDA's Draft Guidance on Nanotechnology

Docket No. FDA-2010-D-0530

The Environmental Working Group submits this letter in response to the U.S. Food and Drug Administration's request for comments on its June 2011 draft guidance on whether products contain nanomaterials or involve the application of nanotechnology.[1] EWG is a non-partisan, non-profit organization dedicated to using the power of information to protect public health and the environment. As part of that mission, EWG conducts original research and monitors the latest science on health effects linked to chemical exposures.

EWG is particularly interested in the proliferation of nanomaterials in consumer products, many of which fall under FDA's jurisdiction. EWG acknowledges the utility of nanomaterials but remains concerned by how little scientists understand their potential risks. Despite substantial data gaps on the safety, fate, transport, and structural properties of nanomaterials, it is clear from the literature that these particles can have unique chemical and/or physical properties and the potential for toxicity characteristics not indicated by studies of their non-nano forms.[2]

In view of that, EWG believes FDA must begin to give meaningful attention to these properties when assessing the safety and effectiveness of products containing nanomaterials or produced using nanotechnology. EWG praises FDA for proposing broad definitional criteria to identify such products going forward.[3] By thinking holistically about how to identify nanomaterials, FDA will be better suited to evaluate those that present unique toxicological concerns, thus meeting its public health objectives.

In its notice, FDA states that for identification purposes it will consider: (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 . . . that are attributable to its dimension(s), even if these dimensions fall

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[1] Considering Whether an FDA-Regulated Product Involves the Application of Nanotechnology, 76 Fed. Reg. 34,715 (June 14, 2011); see also U.S. Food & Drug Admin., Guidance for Industry: Considering Whether an FDA-Regulated Product Involves the Application of Nanotechnology (Draft Guidance) 1 (2011), http://www.fda.gov/RegulatoryInformation/Guidances/ucm257698.htm [FDA Nanotechnology Guidance].

[2] E.g., Memorandum from Joseph E. Bailey, Designated Federal Official, FIFRA Sci. Advisory Panel, to Steven Bradbury, Acting Director, EPA Off. Pesticide of Programs (Jan. 26, 2010), http://www.epa.gov/scipoly/sap/meetings/2009/november/110309ameetingminutes.pdf (meeting minutes from Nov. 3-5, 2009, on "evaluation of nanosilver and other nanometal pesticide products").

[3] FDA Nanotechnology Guidance, supra note 1, at 6.

outside of the nanoscale range, up to one micrometer."[4]

With regard to FDA's draft criteria, EWG offers the following comments:

1. EWG supports FDA's proposal to consider size-dependent properties of particles larger than 100 nm, a measure frequently used as an outer parameter for identifying nanomaterials.[5] EWG's review of mineral sunscreens reveals that nearly every zinc oxide- or titanium dioxide-based sunscreen on the market utilizes nano-scale materials to increase product transparency on the skin.[6] Some mineral sunscreens are marketed as "non-nano," but manufacturers may be basing this claim on the size of aggregated particles or may be using particles only slightly larger than the 100 nm cut-point.[7] Yet scientific data indicates that products slightly larger than 100 nm pose similar risks to those falling within FDA's proposed range.[8] Accordingly, EWG believes that FDA should account for properties attributable to a particle's dimensions even when they exceed 100 nm.

2. EWG is concerned with FDA's proposal to use 1 micrometer (μm) as an absolute upper boundary when considering particles that exhibit properties attributable to their dimensions. EWG believes this is an arbitrary cut-point and would prevent FDA from fully identifying all of the ingredients used in products that rely on nanotechnology. EWG has identified several sunscreen products that utilize nanomaterials greater than 1 μm to boost their transparency features.

   One example is ZinClear-IM, a product made by Antaria Limited and sold in the United States by Dow Chemical as a "transparent micron-sized nanostructured zinc oxide powder."[9] ZinClear-IM particles have features that are 5 nm to 50 nm in size, which provide transparent UV protection on skin.[10] However, the surface area of ZinClear-IM particles is similar to that of nanoscale zinc oxide particles currently used in sunscreens (20 to 70 m^2/gram compared to 20 to 30 m^2/gram for most nano zinc oxide products).[11] The increased surface area of nanoparticles leads to toxicological concern because it generally translates into greater photo-reactivity relative to larger-sized particles.[12]

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[4] Id.
[5] E.g., Nat'l Nanotechnology Initiative, Nanotechnology 101, http://www.nano.gov/nanotech-101 (last visited Aug. 26, 2011).
[6] E.g., Lauren K. Wolf, Scrutinizing Sunscreen, 89 Chem. & Eng'g News 44 (2011).
[7] E.g., BASF, Z-Cote Grade: Statement on Particle Size Distribution and Safety 1-2 (Mar. 30, 2010) (on file with EWG).
[8] See U.S. Envtl. Prot. Agency, Nanomaterial Case Studies: Nanoscale Titanium Dioxide in Water Treatment and in Topical Sunscreen (External Review Draft) 1-5 (2009), oaspub.epa.gov/eims/eimscomm.getfile?p_download_id=490825 [hereinafter EPA Nanomaterial Case Studies].
[9] Advanced Nanotechnology Ltd., Advanced Nanotechnology Limited Concise Financial Report 8 (2007), http://www.antaria.com/financials/ano_cfr_replacement_210907.pdf (Advanced Nanotechnology Limited subsequently changed name to Antaria Limited).
[10] Antaria, Ltd., U.S. Patent Application No. 2010/0310871 (published Dec. 9, 2010) ("Mesoporous zinc oxide powder and method for production thereof").
[11] Id.
[12] EPA Nanomaterial Case Studies, supra note 8, at 1-5-6.

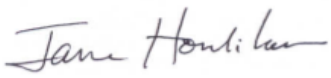
A sunscreen product by Kobo Products, Inc., contains particles that exhibit properties attributable to their dimensions even though they exceed 1 μm. Kobo sunscreens contain Nylon-12 "microspheres" that are 6 μm in diameter, sold under the trade name DAIAMID MSP.[13] These spheres contain individual zinc oxide particles 35 nm in size or titanium dioxide particles 15 nm in size, which are desirable for their transparency features.[14] EWG is unsure as to whether FDA would label these particles as nanomaterials according to its draft guidelines. However, EWG believes that Kobo sunscreens and similar products should be subject to further review for safety and effectiveness purposes in FDA's evaluations of nanomaterials.

As evidenced by these examples, the unique properties of nano-sized particles may be observed in materials that exceed FDA's upper boundary of 1 μm. In view of that, FDA should avoid stating an upper-size range and use a definition similar to one proposed by Health Canada, which in addition to a 1 nm to 100 nm criteria includes particles that are "smaller or larger than the nanoscale in all spatial dimensions and exhibits one or more nanoscale phenomena."[15] Specifically, FDA might consider whether engineered materials and/or their end products have "physical or chemical properties or biological effects, that are attributable to [their] dimension(s), even if these dimensions fall outside the nanoscale range."

Despite the increasing prevalence of nanomaterials in FDA-regulated products, scientists still have much to learn about their short- and long-term effects on public health and the environment. That is why EWG praises FDA for taking a "first," yet important "step toward developing [a] framework" for identifying these ingredients, which will allow FDA to evaluate the "impact of such products."[16] In doing so, FDA will be in a better position to stay on the cutting edge of regulatory science and protect public health.

Sincerely,

Thomas Cluderay
Assistant General Counsel



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[13] Kobo Products, Inc., Spherical Non-Nano UV Filters 1 (2011), http://www.koboproductsinc.com/Downloads/Kobo-NonUVFilters.pdf.
[14] Id.
[15] Health Can., Interim Policy Statement on Health Canada's Working Definition for Nanomaterials 2 (2010), http://www.hc-sc.gc.ca/sr-sr/alt_formats/pdf/consult/_2010/nanomater/draft-ebauche-eng.pdf.
[16] FDA Nanotechnology Guidance, supra note 1, at 5.