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OF THE
UNITED STATES OF AMERICA

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November 10, 2006

Dockets Management Branch
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane, Room 1061
Rockville, MD 20852
Docket Number 2006P-0210

Re: Comments on Petition to FDA to “Amend its Regulations for Products Composed of Engineered Nanoparticles Generally and Sunscreen Drug Products Composed of Engineered Nanoparticles Specifically”

The U.S. Chamber of Commerce, the world’s largest business federation representing more than three million businesses and organizations of every size, sector, and region, is pleased to submit the following comments on a petition, filed by the International Center for Technology Assessment and other entities (Petitioners), requesting the Food and Drug Administration (FDA) amend its regulations with regard to products containing nanomaterials.¹

Petitioners have called upon FDA to create an entirely new regulatory framework to address nanoscale particles, one that treats all nanoparticles as new substances subject to nano-specific paradigms of health and safety testing, and labeling requirements. The U.S. Chamber strongly disagrees with Petitioner’s position on nanotechnology—and particularly Petitioners’ request for a product recall and development moratorium for sunscreens and cosmetics—and urges FDA to reject the Petition on all counts.

¹ The petition can be accessed at:

<http://www.fda.gov/ohrms/DOCKETS/dockets/06p0210/06p-0210-cp00001-01-vol1.pdf>

The U.S. Chamber's interest in this Petition is based on the Chamber's recognition that nanotechnology will likely be the largest single driver of technological innovation and economic growth in the 21st century. Many of these innovations offer tremendous, and in some cases, transformational benefits to society, human health, the environment, and emerging and developed economies. Our members understand these facts and, as a result, are investing heavily in nanotechnology research and development (R&D). Last year alone, governments, corporations, and venture capitalists invested \$9.5 billion in nanotechnology R&D, with almost half that amount coming from private industry.²

NANOTECHNOLOGY PRODUCTS

There is little doubt that nanotechnology offers enormous economic and societal benefits through a wide variety of potential applications. Nanotechnology was incorporated into more than \$30 billion worth of manufactured goods last year, and this figure is projected to grow exponentially to more than \$2.6 trillion in global manufactured goods by 2014.³ Nanotechnology is an "enabling" technology, rather than its own industry, allowing for remarkable advancements across many diverse sectors, such as electronics, pharmaceutical and life sciences, manufacturing, energy, environmental remediation, and many more.

There are more than 300 nanotechnology products currently on the market⁴ aimed at improving consumers' lives, including sunscreens and personal care products containing two nanoscale ingredients, titanium dioxide⁵ and zinc oxide. In addition, there are about 130 nano-based drugs and delivery systems and 125 devices or diagnostic tests in preclinical, clinical, or commercial development.⁶

² *The Nanotech Report, 4th Edition*, by Lux Research, Inc., 2006.

³ *Id.*

⁴ See the Project on Emerging Technologies, which maintains a database of nanotechnology products on the market. That database can be accessed at: <http://www.nanotechproject.org/44>.

⁵ In this comment, "titanium dioxide" refers to ultrafine TiO₂, not pigmentary TiO₂, which is not an ingredient in sunscreens.

Thus, many FDA-regulated products are expected to be impacted by nanotechnology, including drugs, medical devices, biotechnology products, tissue engineering products, vaccines, cosmetics, and combination products. As these products are developed, FDA works to ensure that the drugs, drug delivery systems, cosmetics, medical devices, vaccines, and food products reaching the marketplace are safe and effective. It does this through a rigorous “risk management” regulatory paradigm based on sound scientific principles and testing that operates to identify, analyze, and control risks.

PETITIONERS’ REQUEST

Despite the existing regulatory system, and its many rigorous procedures and requirements to demonstrate safety and efficacy of all regulated materials and products, Petitioners have called on FDA to develop an entirely new regulatory framework specifically designed for nanotechnology. Furthermore, as this redundant framework is developed—and despite any credible evidence to support such a need—Petitioner’s also have demanded that FDA order a product recall and future moratorium on any cosmetics or sunscreens containing nanotechnology.

RESPONSE 1: EXISTING SCIENCE DOES NOT SUPPORT PETITIONERS’ CLAIMS

Toxicological research has not identified any toxicological risks that are unique to nanomaterials. Indeed, nearly all drugs go through a nanosize stage prior to absorption into the body. Yet, on the basis of concerns about potential adverse health impacts from products for which no adverse health impacts have been identified, petitioners seek to unnecessarily stifle the development and sale of a technology that is increasingly used to make medicines, foods, and cosmetics safer, more effective, and more affordable.

The Petition singles out two sunscreen ingredients—titanium dioxide and zinc oxide—as evidence that nanoscale particles are unsafe. Petitioners argue

6 Dow Jones *Market Watch*, October 5, 2006. Accessible at:
<http://www.marketwatch.com/News/Story/Story.aspx?dist=newsfinder&siteid=google&guid=%7BA851EFF7-72C7-4941-ADA1-DAC9A958ADEFB%7D&keyword=>

that these ingredients are dermally applied and absorbed, and therefore penetrate cells, tissue, and organs, presumably with ill effects. Yet the fact is that these two ingredients enjoy a protracted safety record, they have been extensively researched, studied and found safe, and they provide a clear public health benefit by protecting people from harmful UV radiation. (Gasparro *et al.*, 1998; Nash, 2006). More importantly, the scientific evidence does not support Petitioners claim that these ingredients are absorbed through the skin. To the contrary, both *in vitro* and *in vivo* studies provide compelling evidence that titanium dioxide and zinc oxide do not penetrate the skin (SCC-NFP, 2000; Gamer *et al.* 2006, Nohynek *et al.* 2006).⁷

⁷ Gasparro, F.P., Mitchnick, M., Nash, J.F.: A review of sunscreen safety and efficacy. *Photochemistry and Photobiology* **68**(3): 243-256, 1998; Nash, J.F.: Human safety and efficacy of ultraviolet filters and sunscreen products. *Dermatol Clin* **24**: 35-51, 2006; Gamer, A.O., Leibold, E., van Ravenzwaay, B.: The *in vitro* absorption of microfine zinc oxide and titanium dioxide through porcine skin. *Toxicology in vitro* **20**:301-307; Opinion concerning Titanium Dioxide, Colipa n S75 adopted by the SCCNFP during the 14th plenary meeting of 24 October 2000. Accessible at: http://ec.europa.eu/health/ph_risk/committees/sccp/sccp_opinions_en.htm. Nohynek, G.J., Lademann, J., Ribaud, C., Roberts, M.S.: Grey Goo on the skin? Nanotechnology, cosmetic and sunscreen safety. *Critical Reviews in Toxicology*, submitted 2006.

See also, Dussert, A.-S., E. Gooris, and J. Hemmerle. 1997. Characterization of the mineral content of a physical sunscreen emulsion and its distribution onto human stratum corneum. *Intl. J. Cosmet. Sci.* 19:119-129; Bennat, C., and C.C. Müller-Goymann. 2000. Skin penetration and stabilization of formulations containing microfine titanium dioxide as physical UV filter. *Intl. J. Cosmetic Sci.* 22:271-283; Pflücker F et al. 1999. The outermost stratum corneum is an effective barrier against dermal uptake of topically applied micronized titanium dioxide. *Int. J. Cos. Sci.* 21:399-411; Menzel, F., T. Reinert, J. Vogt, and T. Butz. 2004. Investigations of percutaneous uptake of ultrafine Titanium dioxide particles at the high energy ion nanoprobe LIPSION. *Nuclear Instru. Meth. Phys. Res. B* 219-220:82-86; Lademann, J., H. Weigmann, C. Rickmeyer, H. Barthelmes, H. Schaefer, G. Mueller, and W. Sterry. 1999. Penetration of titanium dioxide microparticles in a sunscreen formulation into the horny layer and the follicular orifice. *Skin Pharmacol. Appl. Skin Physiol.* 12(5):247-256; Gamer A, Leibold E, and B. van Ravenzway. 2006. The *in vitro* absorption of microfine zinc oxide and titanium dioxide through porcine skin. *Toxicology In Vitro* 20, 301-307; Schulz, J., H. Hohenberg, F. Pflucker, E. Gartner, T. Will, S. Pfeiffer, R. Wepf, V. Wendel, H. Gers-Barlag, and K.P. Wittern. 2002. Distribution of sunscreens on skin. *Adv. Drug Deliv. Rev.* 54 Suppl 1:S157-163; Tan, M.H., Commens, C.A., Burnett, L., and P.J. Snitch. 1996. A pilot study on the percutaneous absorption of microfine titanium dioxide from sunscreens. *Australia. J. Dermatol.* 37(4):185-187; Pflücker, F., V. Wendel, H. Hohenberg, E. Gartner, T. Will, S. Pfeiffer, R. Wepf, and H. Gers-Barlag. 2001. The human stratum corneum layer: An effective barrier against dermal uptake

RESPONSE 2: FDA HAS EXTENSIVE EXPERIENCE REGULATING PRODUCTS CONTAINING NOVEL TECHNOLOGIES

It is important to note that FDA has successfully regulated products containing other novel and evolving technologies, like biotechnology and genetic engineering, by utilizing existing authorities and statutory tools to incorporate its understanding of science into its regulation of specific products, such as genetically modified food and new treatments for cancer and hepatitis. For nanotechnology, FDA recently formed a Nanotechnology Task Force to ensure that it remains current and fully engaged on this emerging science as it relates to the regulation of products under its jurisdiction. The Task Force held its first meeting on October 10, 2006, to gather input from industry, academics, and interested members of the public concerning the use of nanotechnology in FDA-regulated products.

RESPONSE 3: FDA REGULATES PRODUCTS, NOT TECHNOLOGY

A basic premise of FDA's congressionally mandated authority set forth under the Federal Food, Drug, and Cosmetic Act (FFDCA) is that the agency regulates products, not technology.⁸ FDA does not regulate products based on the type of technology a product contains but rather evaluates all products according to consistent proven safety standards. It has no authority to impose different safety standards on—much less a separate regulatory framework for—products, such as cosmetics, simply because the product contains a particular technology.

Indeed, in contrast to Petitioners' views, the FDA has indicated a commitment to facilitating commercialization of the safety and health benefits promised by nanotechnology. While working to ensure rigorous testing of all nanotechnology products, the agency has adopted nanotechnology as an element under evaluation in FDA's Critical Path Initiative, which aims to reduce existing

of different forms of topically applied micronised titanium dioxide. *Skin Pharmacol. Appl. Skin Physiol.* 14(Suppl 1):92-97.

8 21 U.S.C. 301, *et seq.*

hurdles to medical product design and development and to encourage innovative science and technologies.⁹ Under the Critical Path Initiative, the FDA has encouraged public-private collaborations to explore the physical and chemical characteristics of nanoparticles and to develop new test methods, protocols and standards to help move nanoproducts from preclinical testing to commercialization.

CONCLUSION

By all accounts, nanotechnology innovations will bring forth innumerable advances that will benefit the public, support a growing U.S. economy, create thousands of new jobs, and assure the acquisition of a strong competitive position in the global nanotechnology marketplace. As such, it is vital that the federal government encourage the development of commercial applications for nanotechnology.

While continued vigilance is needed to ensure that products containing nanotechnology are safe for consumers, FDA has the authority, the demonstrated experience, and the ability to do just that. And as FDA (as well as other federal agencies) continues to refine its approach to nanotechnology, the U.S. Chamber of Commerce will work closely with FDA to ensure that any regulatory policies are consistent, adequate, and based on the best available science.

FDA has in place a comprehensive regulatory system for products and ingredients, and decades of experience in ensuring individual and public health. FDA has already proven it can use this system to regulate products containing other novel technologies, such as biotechnology and genetic engineering, which has resulted in the availability of safe new foods and life-saving new medicines. FDA oversight of cosmetics and sunscreens—in conjunction with rigorous industry self-regulation—has resulted in some of the safest products on the market today. More importantly, the availability and marketing of those products in conjunction with industry, non-profit, and government-led education about skin cancer prevention has combined to deliver a clear public health benefit. As such, the U.S. Chamber urges FDA to continue to regulate

⁹ FDA maintains a webpage devoted to its Critical Path Initiative, accessible at <http://www.fda.gov/oc/initiatives/criticalpath/>.

Docket Number 2006P-0210

November 10, 2006

Page 7 of 7

nano-containing products according to the same guiding principles based on sound science that have allowed it to foster developments that protect and improve public health.

The U.S. Chamber is grateful for this opportunity to present its comments on the petition.

Sincerely,

A handwritten signature in black ink, appearing to read "William L. Kovacs". The signature is written in a cursive style with a prominent initial "W".

William L. Kovacs