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The Growing Consumer Exposure to Nanotechnology in Everyday Products: Regulating Innovative Technologies in Light of Lessons from the Past

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Nanoparticles are very small particles that are engineered using innovative technologies to be one to one hundred nanometers in size. Just how small is small? In comparison, a human hair is 80,000 nanometers wide. There are currently hundreds of unregulated and unlabeled consumer products on the market that contain engineered nanotech particles, with more on the way. A growing number of these nanotech products are being marketed for human consumption, including food, dietary supplements, cosmetics, and sunscreens. This expanding market ignores the growing scientific understanding that these unique substances can create unintended human health and environmental risks. This Article discusses the public health, regulatory, legal, and ethical issues raised by the developing appreciation of the health risks associated with nanotech products. This Article proposes a method for regulating nanotech products that protects public health while encouraging technical innovation. This proposal is based on lessons learned from past introductions of new chemicals and innovative technologies such as asbestos, PCBs, DES, Thalidomide, medical X-rays, and Benzene which all had serious, long-term public health consequences.

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The Growing Consumer Exposure to Nanotechnology in Everyday Products: Regulating Innovative Technologies in Light of Lessons from the Past

KATHARINE A. VAN TASSEL* & ROSE H. GOLDMAN**

I. INTRODUCTION

Consumers in the United States are being exposed to steadily increasing levels of novel, engineered nanoparticles as a result of their contact with everyday consumer products. Engineered nanoparticles are very small particles that are engineered using innovative technologies to be 1 to 100 nanometers in size.[1] Just how small is small? In comparison, a human hair is about 80,000 nanometers wide.[2] Nanoscale materials are

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[1] "Nanotechnology is the art and science of manipulating matter at the nanoscale to create new and unique materials and products." WILLIAM B. SCHULTZ & LISA BARCLAY, WOODROW WILSON INT'L CENTER FOR SCHOLARS, A HARD PILL TO SWALLOW: BARRIERS TO EFFECTIVE FDA REGULATION OF NANOTECHNOLOGY-BASED DIETARY SUPPLEMENTS 8 (2009), *available at* http://www.nanotechproject.org/process/assets/files/7056/pen17_final.pdf. The National Nanotechnology Initiative, the federal research and development program that coordinates the nanoscale research and technology activities of twenty-five different government agencies, including the FDA, defines nanotechnology as activities that include the following characteristics:

> (1) research and technology development at the atomic, molecular or macromolecular level, in the length scale of 1–100 nanometers; (2) creating and using structures, devices and systems that have novel properties and functions because of their small or intermediate size; and (3) ability to control or manipulate on the atomic scale.

Id.

[2] ROYAL SOC'Y & ROYAL ACAD. OF ENG'G, NANOSCIENCE AND NANOTECHNOLOGIES: OPPORTUNITIES AND UNCERTAINTIES, at vii (2004), *available at* http://www.nanotec.org.uk/report/Nano%20report%202004%20fin.pdf. A nanometer is one billionth of a meter. *What is Nanotechnology?*, NAT'L NANOTECH. INITIATIVE, http://www.nano.gov/nanotech-101/what/definition (last visited Sept. 15, 2011). To attempt to conceptualize just how small a nanoparticle is, compare

increasingly being used in a wide variety of areas, including electronic, magnetic, medical imaging, drug delivery, catalytic, materials applications, and cosmetic products.[3] According to the National Institute of Occupational Safety and Health ("NIOSH"), new nanotechnology consumer products are coming on the market at the rate of three to four per week.[4] Thus, consumers in the United States are being exposed to increasing levels of these novel and relatively untested engineered nanoparticles as a result of their contact with everyday consumer products. There are currently hundreds of unregulated and unlabeled consumer products on the market that contain engineered nanotech particles ("nanotech products"),[5] with more on the way.[6] Thousands of tons of engineered nanomaterials are currently being produced each year.[7] One-hundred-forty-seven billion dollars in manufactured goods using engineered nanotech materials were produced in 2007 and the global market in nanotechnology research and development is predicted to reach $3.1 trillion by 2015.[8] The financial resources put into the development, applications, and production of nanoparticle technology have far outpaced funding to explore health and safety issues.[9] In addition, the expanding market often ignores, or does not seek out, information about the scientific findings that are becoming available concerning the potential unintended human and environmental health risks posed by emerging nanotechnology.[10]

Products that contain nanoparticles include, among many others, sporting goods, cell phones, digital cameras, coatings for eyeglasses, paints, stain resistant clothing, and light emitting diodes used in

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nanoparticles to the size of a human hair, which is approximately 80,000 nanometers wide or the thickness of a sheet of paper, which is roughly 100,000 nanometers wide. *Size of the Nanoscale*, NAT'L NANOTECH. INITIATIVE, http://www.nano.gov/nanotech-101/what/nano-size (last visited on Sept. 15, 2011).

[3] *See, e.g.*, *Nanotechnology: Frequently Asked Questions*, CENTERS FOR DISEASE CONTROL & PREVENTION, http://www.cdc.gov/niosh/topics/nanotech/faq.html (last updated Sept. 22, 2010) (acknowledging the broad array of different categories of products that contain nanoparticles).

[4] *Id.*

[5] *See* SCHULTZ & BARCLAY, *supra* note 1, at 20–23 (explaining that the increasing amounts of products integrating nanotechnology go unregulated, due to the dated FDA regulatory scheme).

[6] *Id.* at 9.

[7] ROYAL SOC'Y & ROYAL ACAD. OF ENG'G, *supra* note 2, at 26–27.

[8] SCHULTZ & BARCLAY, *supra* note 1, at 8; *see also Buyer Beware: Product List Highlights Both Nanotech and Nano-marketing*, ELECTRO IQ (Mar. 16, 2006), http://www.electroiq.com/articles/stm/2006/03/buyer-beware-product-list-highlights-both-nanotech-and-nano-marketing.html (detailing the growing number of products containing nanoparticles); *Nanotechnology: Frequently Asked Questions*, *supra* note 3.

[9] *See infra* note 85 and accompanying text.

[10] *See infra* Section II.D.2.

computers.[11] These products contain nanoparticles that are "fixed" inside a solid matrix which makes them less likely to move into the environment or the human body.[12] Engineered nanoparticles that are produced and then fixed in consumer products are of greatest concern to workers who face heavy exposure to these nanoparticles during the manufacturing process.[13] Of more concern to the general public are the growing numbers of products that contain predominantly "free" nanotech particles which are being used in liquid products. This use of free nanoparticles in drugs,[14] food,[15] dietary

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[11] *See* Hope Shand & Kathy Jo Wetter, *Shrinking Science: An Introduction to Nanotechnology*, *in* STATE OF THE WORLD 2006 78, 80–82 (Linda Starke ed., 2006) (listing various consumer products containing nanoparticles); *Nanotechnology Consumer Products Inventory*, PROJECT ON EMERGING NANOTECH., http://www.nanotechproject.org/inventories/consumer/browse/categories/ (last visited Mar. 3, 2011) (same).

[12] While industry takes the position that fixed nanoparticles are unlikely to migrate into the environment or the human body, this conclusion is still being studied and the jury is still out. *See, e.g.*, Natasha Singer, *New Products Bring Side Effect: Nanophobia*, N.Y. TIMES, Dec. 3, 2008, at E1 (stating that some cosmetics industry representatives said there was no evidence that personal care products that contain nano-size components are a health hazard). Dr. Andrew Maynard, the former chief science advisor to the Project on Emerging Nanotechnologies, states that: "I would be very surprised if [fixed carbon nanotubes are] dangerous to use, let us say, [in] a tennis racket or baseball bat[,] . . . [b]ut I do not think it is OK to tell people that we think it is safe—we've got to have evidence." Ann Fernholm, *Carbon Nanotubes May Be as Harmful as Asbestos*, S.F. CHRON., May 21, 2008, at C-1. Dr. Maynard goes on to explain that issues remain over what happens when these products containing engineered nanoparticles break or the surface of one of these products is rubbed against the ground. *Id.* Many recall the level of human exposure to asbestos as car brake pads containing asbestos wore down and roads paved with asbestos-containing materials deteriorated. *See generally* AGENCY FOR TOXIC SUBSTANCES & DISEASE REGISTRY, U.S. DEP'T OF HEALTH AND HUMAN SERV., ASBESTOS TOXICITY, *available at* http://www.atsdr.cdc.gov/csem/asbestos/docs/asbestos.pdf (last visited Mar. 3, 2011).

[13] NAT'L INST. FOR OCCUPATIONAL SAFETY AND HEALTH, DEP'T OF HEALTH & HUMAN SERV., CURRENT INTELLIGENCE BULLETIN: OCCUPATIONAL EXPOSURE TO CARBON NANOTUBES AND NANOFIBERS 19, 39 (draft, Nov. 2010) [hereinafter NIOSH BULLETIN], *available at* http://www.cdc.gov/niosh/docket/review/docket161a/pdfs/carbonNanotubeCIB_PublicReviewOfDraft.pdf.

[14] *See, e.g.*, Christopher Weldon et al., *Nanotechnology for Surgeons*, 3 WILEY INTERDISCIPLINARY REV.: NANOMED. & NANOBIOTECH. 223, 226 (2011) (explaining that nanotechnology may provide powerful new tools that could have a marked impact on the therapeutic and diagnostic measures available to surgeons); Kevin O'Donnell & Robert O. Williams, *Nanoparticulate Systems for Oral Drug Delivery to the Colon*, 8 INT'L J. NANOTECH. 4, 4–15 (2011) (explaining that encapsulating a drug molecule within nanoparticles offers a highly effective option for controlling drug delivery and targeting the colon, for example for the treatment of colon cancer); Dorothy Farrell et al., *Recent Advances from the National Cancer Institute Alliance for Nanotechnology in Cancer*, 4 ACS NANO 589 (2010) (describing a range of advances, including some showing significant promise in clinical trials, that are poised to make a big impact on cancer).

[15] *See, e.g.*, GEORGIA MILLER & RYE SENJEN, FRIENDS OF THE EARTH, OUT OF THE LABORATORY AND ON TO OUR PLATES: NANOTECHNOLOGY IN FOOD & AGRICULTURE 9 (2008), *available at* http://www.foeeurope.org/activities/nanotechnology/Documents/Nano_food_report.pdf (identifying nanoadditives found in some margarine, soft drinks, beer, dairy products, sausages, and other processed foods).

supplements,[16] cosmetics,[17] and sunscreens[18] creates a high level of consumer exposure to new and unique substances.[19]

In spite of a mounting scientific awareness of the adverse physical effects and potential health risks associated with the human consumption of engineered nanoparticles, consumers remain uninformed of their exposure to these effects and risks as nanotech ingredients are not commonly listed on product labels. Labeling of nanotech ingredients on product packaging is not required by the Food & Drug Administration ("FDA"). The FDA has only recently begun to acknowledge that nano materials can have chemical, physical, and biological properties that differ from those of their larger counterparts.[20] However, the FDA has not changed its position on the safety of nanoparticles. Thus, the FDA has not yet begun regulating nanotech ingredients differently from their normal size counterparts, although there are task forces to study the issue.[21] In other words, if the large particle version of a product is considered to be safe, the FDA currently presumes that the nanotech version is also safe. Thus, manufacturers of nanotech food, food additives, dietary supplements, cosmetics, and sunscreens are not required to test their products for safety, are not required to obtain premarket approval from the FDA, and are not required to list nanotech ingredients on product labels.[22]

The FDA's presumption of bioequivalence for purposes of safety is based on its position that "[p]article size is not an issue."[23] In fact, nanotech particles have fundamentally different properties than their larger counterparts. These differences manifest themselves on multiple levels as differences in optical, magnetic, bioaccumulation, toxicity, electrical,

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[16] *See, e.g.*, SCHULTZ & BARCLAY, *supra* note 1, at 8. The number of dietary supplements with nanoparticle content has jumped over a two year period from eleven in 2007 to forty-four in 2009. *Id.* at 9.

[17] GEORGIA MILLER ET AL., FRIENDS OF THE EARTH, NANOMATERIALS, SUNSCREENS AND COSMETICS: SMALL INGREDIENTS, BIG RISKS 2 (2006), *available at* http://www.foeeurope.org/activities/nanotechnology/nanocosmetics.pdf.

[18] *Id.*

[19] *See infra* Section II.D.1.

[20] *Nanotechnology*, FDA, http://www.fda.gov/ScienceResearch/SpecialTopics/Nanotechnology/default.htm (last updated Jul. 8, 2011) ("The U.S. Food and Drug Administration (FDA) regulates a wide range of products, including foods, cosmetics, drugs, devices, veterinary products, and tobacco products some of which may utilize nanotechnology or contain nanomaterials. Nanotechnology allows scientists to create, explore, and manipulate materials measured in nanometers (billionths of a meter). Such materials can have chemical, physical, and biological properties that differ from those of their larger counterparts.").

[21] *Nanotechnology Task Force*, FDA, http://www.fda.gov/ScienceResearch/SpecialTopics/Nanotechnology/NanotechnologyTaskForce/default.htm (last updated Apr. 9, 2010).

[22] *See infra* Part III.

[23] *FDA Regulation of Nanotechnology Products*, NANOPHARMACEUTICALS.ORG, http://www.nanopharmaceuticals.org/FDA.html (last visited Nov. 30, 2011).

chemical, explosiveness, and persistence characteristics.[24] Numerous scientific animal studies over the past several years reveal that these unique properties actually produce negative physical effects that may create unintended health risks in people, such as mesothelioma, the condition caused by asbestos,[25] or could contribute to neurodegenerative processes, such as Alzheimer's disease.[26] These studies establish that the FDA's presumption of bioequivalence is no longer scientifically supportable and that a new system for nanotech product regulation is required.

This Article discusses the public health, regulatory, legal, and ethical issues raised by the developing appreciation of the negative physical effects and potential health risks associated with nanotech products, and is arranged as follows. After this Introduction, this Article describes the present scientific understanding of the health risks associated with the consumption of nanoparticles. Next, a summary of the existing FDA regulatory structure that governs food, dietary supplements, cosmetics, and sunscreens is provided along with an explanation of why these regulations fail to protect public health when applied to regulate the nanotech versions of these products. The Article goes on to illustrate how the FDA's dated position on bioequivalence, coupled with preexisting regulations, lead to a lack of a labeling requirement which bars a consumer from engaging in self-protection. Compounding this situation is the tort system's inadequate response if a consumer is injured from this unavoidable exposure. This Article spells out how the insensitivity of the tort system to injuries from innovative technologies means that an injury from a nanotech product will be borne by the consumer and not the manufacturers who are profiting from product sales. This disconnect violates basic principles of distributive justice. Finally, this Article proposes alternative methods of regulating nanotech products that better protect public health while encouraging technical innovation. These proposals are based on lessons learned from past introductions of new chemicals and innovative technologies, such as asbestos, PCBs, DES, Thalidomide, medical X-rays, and Benzene which all had serious, long-term public health consequences.

It is important to note that, while the FDA has recently acknowledged in one paragraph on its website that nanoparticles "*can* have chemical, physical, and biological properties that differ from those of their larger counterparts,"[27] the acknowledgment of the possibility that 'nano can mean

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[24] Cristina Buzea et al., *Nanomaterials and Nanoparticles: Sources and Toxicity*, 2 BIOINTERPHASES MR17, MR23–25, MR47, MR59 (2007); *see also* Ernie Hood, *Nanotechnology: Looking as We Leap*, 112 ENVTL. HEALTH PERSP. A740, A741 (2004); ROYAL SOC'Y & ROYAL ACAD. OF ENG'G, *supra* note 2, at 5.

[25] Andre E. Nel et al., *Understanding Biophysicochemical Interactions at the Nano-Bio Interface*, 8 NATURE MATERIALS 543, 550 (2009).

[26] *Id.* at 546.

[27] *Nanotechnology*, *supra* note 20 (emphasis added).

different' has yet to be given voice in any of the FDA's regulatory positions on safety. This Article will focus on the FDA's current regulatory positions on safety in order to explain how the FDA is currently regulating nanotech products and to explain what regulatory changes are necessary to better protect public health.

II. NANOTECHNOLOGY: BENEFITS AND RISKS

A. *Benefits*

Nanotechnology has been touted as the potential solution to global challenges, such as a cure for cancer, a source for renewable energy, and the answer to the provision of clean water.[28] More generally, nanotechnology offers economic benefits, improved materials, reduced use of resources, and new medical treatments.[29] Less compelling are the benefits associated with the use of nanoparticles in consumer products for direct and indirect human consumption. Nanotech cosmetics offer the opportunity for a more attractive appearance.[30] Nanotech sunscreens apply more smoothly and are clear instead of white and pasty.[31] Some nanotech dietary supplement manufacturers are currently claiming, without substantiation, that their products are more bioavailable or can be absorbed by the body more quickly.[32] Nanotech food and dietary supplement manufacturers hope that their products will, in the future, deliver nutrients directly to cells and block allergens and cholesterol.[33] Nanotech foods offer the possibility of "more potent food colourings, flavourings and nutritional additives, antibacterial ingredients for food packaging, and

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[28] Fabio Salamanca-Buentello et al., *Nanotechnology and the Developing World*, 2 PLOS MED. 0383, 0385 (2005). According to a study by the Canadian Program on Genomics and Global Health at the University of Toronto Joint Centre for Bioethics, the top ten applications of nanotechnology most likely to benefit developing countries, and which may contribute to the attainment of the United Nations Millennium Development Goals (MDGs) are as follows: energy storage; production and conversion; agricultural productivity enhancement; water treatment and remediation; disease diagnosis and screening; drug delivery systems; food processing and storage; air pollution and remediation; construction; health monitoring; vector and pest detection; and control. *Id.* at 0383, 0385.

[29] ROYAL SOC'Y & ROYAL ACAD. OF ENG'G, *supra* note 2, at viii–x.

[30] *See* Buzea et al., *supra* note 24, at MR36 (discussing how engineered nanomaterials in cosmetic products regenerate skin cells, help maintain a youthful appearance of the skin, and hide wrinkles and creases).

[31] Singer, *supra* note 12, at E1.

[32] SCHULTZ & BARCLAY, *supra* note 1, at 9 ("Examples of product claims that tout special properties due to the use of nanotechnology include: increased effectiveness in a calcium/magnesium product; more rapid, uniform and complete absorption of nutrients in a spray form; increased absorption of a B_{12} vitamin spray; supplements that pass through membranes directly into human cells; and increased absorption of gel supplements by transforming fat-soluble nutrients into water-soluble ones.").

[33] *See* MILLER & SENJEN, *supra* note 15, at 9.

more potent agrochemicals and fertilisers."[34]

In spite of these less than compelling benefits, these products are being freely marketed without undergoing any form of risk analysis by the FDA because, as more fully discussed below, the FDA has taken the position that, for safety purposes, nanoscale materials are bioequivalent to their normal size counterparts and, therefore, regulation is not needed.[35]

B. *Risks*

The FDA's presumption of bioequivalence results in nanotech food, dietary supplements, cosmetics, and sunscreens being regulated the same way as their non-nanotech counterparts. According to the FDA, if the normal size version of a substance is safe, the nanoscale version is also safe.[36] However, contrary to the FDA's presumption of bioequivalence, "nano" does not just mean that a particle is tiny or smaller, it means that the particle is fundamentally different. These differences manifest themselves on multiple levels as differences in optical, magnetic, bioaccumulation, toxicity, electrical, chemical, explosiveness, and persistence characteristics.[37]

As fully discussed in the next sections, numerous scientific studies over the past several years reveal that these unique properties actually create negative physical effects that may create unintended health risks such as mesothelioma, the condition caused by asbestos,[38] or could contribute to neurodegenerative processes, such as Alzheimer's disease.[39] In addition to consumer exposure to these health risks, workers handling nanomaterials are likely to be exposed at much higher levels than consumers during the manufacture, packaging, transportation, and use of nanotech materials.[40] In addition, there may be higher exposure levels during cleaning and maintenance of research, production, and handling

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[34] *Id.* at 4. Scientists have "developed several delivery systems not only for colorants, but also for vitamins, antioxidants, antifungals . . . with the goal of incorporating nanostructures in food systems for improved food quality and to promote human health." Stephen Daniells, *Nano Beta-carotene Entrapment Offers Natural Colour Options*, FOODNAVIGATOR.COM (Aug. 11, 2009), http://www.foodnavigator.com/Science-Nutrition/Nano-beta-carotene-entrapment-offers-natural-colour-options; *see also* Carlos E. Astete et al., *Ca2+ Cross-Linked Alginic Acid Nanoparticles for Solubilization of Lipophilic Natural Colorants*, 57 J. AGRIC. & FOOD CHEMISTRY 7505, 7505 (2009).

[35] *See Nanotechnology Task Force*, *supra* note 21, at 11 (noting that there is no available information suggesting that nanoscale materials are more hazardous than non-nanoscale materials).

[36] *See infra* Part III.

[37] ROYAL SOC'Y & ROYAL ACAD. OF ENG'G, *supra* note 2, at ix, 5, 7–9.

[38] Nel et al., *supra* note 25, at 550.

[39] *Id.* at 546.

[40] NIOSH BULLETIN, *supra* note 13, at 5, 18–19; Arthur Miller et al., *Characterizing Exposures to Airborne Metals and Nanoparticle Emissions in a Refinery*, 54 ANNALS OF OCCUPATIONAL HYGIENE 504, 511–12 (2010); RJ AITKEN ET AL., INST. OF OCCUPATIONAL MED. FOR HEALTH & SAFETY EXEC., NANOPARTICLES: AN OCCUPATIONAL HYGIENE REVIEW 2–3 (2004), *available at* http://www.hse.gov.uk/research/rrpdf/rr274.pdf.

facilities.[41] Currently, the levels at which workers can safely be exposed to nanoparticles in the workplace is unknown as the science on safe exposure levels and protective equipment is still evolving.[42] By 2015, it is estimated that over two million workers world-wide will be directly employed by nanotech industries.[43] And the numbers of individuals working indirectly in the supply chain will be much higher.[44]

Additional risks may result from nanopollution from manufacturing waste streams and accidental discharges.[45] Other nanopollutants include nanoparticles from washing off cosmetics and sunscreens into sinks and showers that flow into waste water, nanoparticles that wash off of swimmers into streams, lakes, and oceans, as well as nano-waste created as a by-product of the consumption of nanotech food and dietary supplements.[46] The environmental impact of these nanoparticles include brain damage in fish, damage to ecosystems, the opportunity for long range and wide-spread transport of pollutants in ground water, and the ability to bioaccumulate along the food chain.[47]

C. *What Makes Nanoparticles Different?*

Engineered nanoparticles differ significantly from their bulk counterparts[48] for two main reasons. First, the laws of classical physics do

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[41] NIOSH BULLETIN, *supra* note 13, at 19–20; MILLER ET AL., *supra* note 17, at 10.

[42] NIOSH BULLETIN, *supra* note 13, at 6, 8.

[43] Mihail C. Roco, *Converging Science and Technology at the Nanoscale: Opportunities for Education and Training*, 21 NATURE BIOTECH. 1247, 1248 (2003); *see also* NIOSH BULLETIN, *supra* note 13, at 19 ("[I]t has been projected that nanotechnology will employ millions of workers worldwide within the next decade.").

[44] *See* Roco, *supra* note 43, at 1248 (explaining that nanotechnology has the potential to create five million related jobs by 2015).

[45] *Nanotechnology in the Environment: Making Sure Wonder Materials Don't Become Wonder Pollutants*, SCIENCEDAILY (Apr. 12, 2008), http://www.sciencedaily.com/releases/2008/04/080408132129.htm (exploring the potential harm to the environment of nanoparticles); *see also* MILLER ET AL., *supra* note 17, at 10–11.

[46] MILLER ET AL., *supra* note 17, at 10–11.

[47] *See infra* notes 85–95 and accompanying text.

[48] Consistent with the nomenclature adopted by the literature, this Article will refer to particles that manifest these different properties as "nanoparticles" or "nanoscale" materials or versions and will refer to larger scale particles of the same chemical that do not have these unique properties as normal size materials or bulk materials. Buzea et al., *supra* note 24, at MR23–25; ROYAL SOC'Y & ROYAL ACAD. OF ENG'G, *supra* note 2, at 7. For example, the list of FDA approved active ingredients for use in sunscreens includes titanium dioxide for use up to a twenty-five percent concentration. Sunscreen Drug Products for Over-The-Counter Human Use: Final Monograph, 64 Fed. Reg. 27666, 27672 (May 21, 1999) (to be codified at 21 C.F.R. pt. 352) [hereinafter Final Monograph]. The FDA reviewed the safety and effectiveness of titanium dioxide in sunscreens prior to industry use of the engineered nanoparticle form of titanium dioxide pursuant to the normal process for over-the-counter (OTC) approval. *Small Business Assistance: Frequently Asked Questions on the Regulatory Process of Over-the-Counter (OTC) Drugs*, FDA, http://www.fda.gov/Drugs/DevelopmentApprovalProcess/SmallBusinessAssistance/ucm069917.htm (last visited Sept 14, 2011) (describing the process for OTC

not apply to a particle that is smaller than approximately 100 nanometers (nm).[49] At this small size, the laws of quantum mechanics apply which affect the magnetic, optical, and electric behavior of materials.[50] Second, nanotech particles have an enormous surface to volume ratio resulting in a larger number of atoms found on the surface.[51] Compared to macro-particles, this provides a greater surface area per unit mass.

> In the size range of < 100 nm, the number of surface molecules (expressed as a % of the molecules in the particle) is inversely related to particle size. For instance, in a particle of 30 nm size, about 10% of its molecules are expressed on the surface, whereas at 10 and 3 nm size the ratios increase to 20% and 50%, respectively. Because the number of atoms or molecules on the surface of the particle may determine the material reactivity, this is key to defining the chemical and biological properties of nanoparticles.[52]

Thus, because chemical reactions occur at the particle surface, nanoparticles have a greater potential for biological interaction and are more reactive than larger particles.[53] As a consequence, the intrinsic toxicity of any given mass of nanoparticles is greater than the same mass of larger particles.[54]

Finally, it is important to point out that engineered nanoparticles are different from those found in nature.[55] People have always been exposed to "naturally" produced nanoparticles.[56] For example, nature produces some nanoparticles, such as ultrafine salt nanocrystals found in ocean air, and man has accidentally produced others, like carbon nanoparticles

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approval). The FDA stated that it is aware that sunscreen products use engineered nanoparticles but that it "does not consider micronized titanium dioxide to be a new ingredient but it considers it a specific grade of titanium dioxide originally reviewed by the Panel." Final Monograph, *supra*, at 27671–72.

[49] Buzea et al., *supra* note 24, at MR23; ROYAL SOC'Y & ROYAL ACAD. OF ENG'G, *supra* note 2, at 7.

[50] Buzea et al., *supra* note 24, at MR24–25; ROYAL SOC'Y & ROYAL ACAD. OF ENG'G, *supra* note 2, at 7.

[51] Andre Nel et al., *Toxic Potential of Materials at the Nanolevel*, 311 SCIENCE 622, 622 (2006).

[52] *Id.* at 623 fig.1.

[53] *Id.* at 622.

[54] *Id.*; SCI. COMM. ON EMERGING & NEWLY IDENTIFIED HEALTH RISKS (SCENIHR), EUR. COMM'N., MODIFIED OPINION ON THE APPROPRIATENESS OF EXISTING METHODOLOGIES TO ASSESS THE POTENTIAL RISKS ASSOCIATED WITH ENGINEERED AND ADVENTITIOUS PRODUCTS OF NANOTECHNOLOGIES 13 (2005) [hereinafter SCENIHR], *available at* http://ec.europa.eu/health/ph_risk/committees/04_scenihr/docs/scenihr_o_003b.pdf.

[55] Buzea et al., *supra* note 24, at MR21–43.

[56] *Id.* at MR17.

produced from fire.[57] However, the increased risk from exposure to intentionally engineered nanoparticles arises from the fact that engineered nanoparticles are being generated in larger and larger quantities with a uniform, monodispersed size compared to natural ultrafine particles that are more physically and chemically variable and polydispersed.[58]

Because of all of these different properties, an understanding of the characteristics of a substance at its normal size is not predictive of the behavior of that substance as it operates on a nanoscale.[59]

D. *The Unique Adverse Physical Effects and Human Health Risks Associated with Nanoparticles*

The unique features of nanoparticles—their size, high surface area to volume ratio, and high reactivity—are the same properties that give nanoparticles a higher possibility for risks to health.[60] Nanoparticles are more easily absorbed and have a higher level of interaction with biological tissues, giving them a greater potential for toxicity.[61]

1. *Routes of Exposure*

Products that contain "fixed" nanoparticles include sporting goods, cell phones, digital cameras, coatings for eyeglasses, paints, stain resistant clothing, and light emitting diodes used in computers.[62] Fixed nanoparticles are contained inside a solid matrix which makes them less likely to move into the environment or the human body from consumer products.[63] On the other hand, workers face heavy exposure to these engineered products during the manufacturing process.[64] Of much more concern to consumers are liquid products that contain "free" nanoparticles such as nanotech food, dietary supplements, cosmetics, and sunscreens. Free nanoparticles are highly mobile[65] and can be absorbed by the body

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[57] *Id.* at MR21–22.

[58] Hood, *supra* note 24, at A745; U.S. ENVTL. PROT. AGENCY, EPA 100/B-07/001, NANOTECHNOLOGY WHITE PAPER 52 (2007) [hereinafter NANOTECHNOLOGY WHITE PAPER], *available at* http://www.epa.gov/osa/pdfs/nanotech/epa-nanotechnology-whitepaper-0207.pdf.

[59] Kenneth Chang, *Tiny is Beautiful: Translating 'Nano' into Practical*, N.Y. TIMES, Feb. 22, 2005, at F1; Shand & Wetter, *supra* note 11, at 83–86.

[60] Nel et al., *supra* note 51, at 622–23.

[61] *Id.* at 622–25.

[62] Buzea et al., *supra* note 24, at MR36; Shand & Wetter, *supra* note 11, at 80–82.

[63] *See supra* note 12 (noting that there is a clear possibility that "fixed" nanoparticles may be able to migrate into the environment or human body).

[64] NIOSH BULLETIN, *supra* note 13, at 6.

[65] David Rotman, *Measuring the Risks of Nanotechnology*, TECH. REV., Apr. 2003, at 71–73, (interviewing Dr. Vicki Colvin, Director of the Center for Biological and Environmental Nanotechnology at Rice University, about possibly unique health and environmental risks associated with nanotechnology); Buzea et al., *supra* note 24, at MR44–48, MR50–57.

through multiple routes of exposure.[66] Nanoparticles can enter the blood stream through the lungs,[67] skin,[68] and GI tract.[69] If nanoparticles are inhaled, they can travel to all areas of the respiratory tract.[70] Studies suggest that nanoparticles can enter the brain through the olfactory nerves[71] and can also cross the blood brain barrier.[72] In contrast to macro-particles that are caught and eliminated by the body's protective mechanisms,[73] once in the blood stream, nanoparticles can slip unhindered into bone marrow, muscles, the liver, brain, and spleen, and into cells themselves.[74] These tiny particles can bind to cellular structures, move through the cytoplasm[75] and lodge in the mitochondria.[76] Finally, during pregnancy, nanoparticles are capable of crossing the placenta to enter the fetus.[77]

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[66] Günter Oberdörster et al., *Principles for Characterizing the Potential Human Health Effects from Exposure to Nanomaterials: Elements of a Screening Strategy*, 2 PARTICLE & FIBRE TOXICOLOGY 1, 2, 4 (2005).

[67] NIOSH BULLETIN, *supra* note 13, at 7.

[68] In the context of cosmetics, nanotech cosmetics that are rubbed onto the skin contain nanoparticles 1000 nm in size that are capable of absorption through intact skin. Jillian Rouse & Jianzhong Yang, *Repetitive Motion Speeds Nanoparticle Uptake: 'Bucky Amino Acid' Penetrates Faster, Deeper When Skin Is Flexed*, SCIENCEDAILY (Jan. 9, 2007), http://www.sciencedaily.com/releases/2007/01/070104144839.htm (discussing study by Rice University chemists and North Carolina State University toxicologists finding that repetitive movement can speed up the uptake of nanoparticles through the skin); Sally S. Tinkle et al., *Skin as a Route of Exposure and Sensitization in Chronic Beryllium Disease*, 111 ENVTL. HEALTH PERSP. 1202, 1204–05 (2003) (studying the penetration of nanoparticles into human skin). When the skin is damaged, for example through blemishes, sun burn, eczema, shaving cuts, or other trauma, nanoparticles up to 7000 nm can penetrate the skin. Günter Oberdörster et al., *Nanotoxicology: An Emerging Discipline Evolving from Studies of Ultrafine Particles*, 113 ENVTL. HEALTH PERSP. 823, 834 (2005). In fact, many nanotech cosmetics and sunscreens are especially formulated to be used on damaged skin. And an as-yet-unanswered question is what impact the "penetration enhancers" that many cosmetic products use will have on this analysis. *Nanotechnology & Sunscreens*, ENVTL. WORKING GRP., http://www.ewg.org/nanotechnology-suncreens (last visited Sept. 13, 2011).

[69] Oberdörster et al., *supra* note 68, at 833–37; Peter HM Hoet et al., *Nanoparticles—Known and Unknown Health Risks*, 2 J. NANOBIOTECH., Dec. 2004, at 1, 2–10.

[70] Oberdörster et al., *supra* note 68, at 837; Hoet et al., *supra* note 69, at 1–4.

[71] Buzea et al., *supra* note 24, at MR50–51; Alex Kirby, *Tiny Particles 'Threaten Brain,'* BBC NEWS (Jan. 8, 2004), http://news.bbc.co.uk/2/hi/science/nature/3379759.stm; ANNABELLE HETT, SWISS REINS. CO., NANOTECHNOLOGY: SMALL MATTER, MANY UNKNOWNS 17 (2004), *available at* http://media.swissre.com/documents/nanotechnology_small_matter_many_unknowns_en.pdf.

[72] Rotman, *supra* note 65, at 73; Buzea et al., *supra* note 24, at MR51; Kirby, *supra* note 71.

[73] HETT, *supra* note 71, at 21.

[74] *Id.* at 22–23.

[75] Karen Florini et al., *Nanotechnology: Getting It Right the First Time*, 3 NANOTECH. L. & BUS. 39, 42 (2006).

[76] D. Maysinger et al., *Nanoparticles in Medicine*, *in* 3 OXFORD HANDBOOK OF NANOSCIENCE AND TECHNOLOGY: APPLICATIONS 503, 519 (A.V. Narlikar et al. eds., 2010); Buzea et al., *supra* note 24, at MR48.

[77] Karin S. Hougaard et al., *Effects of Prenatal Exposure to Surface-Coated Nanosized Titanium Dioxide (UV-Titan): A Study in Mice*, 7 PARTICLE & FIBRE TOXICOLOGY 16 (2010).

2. *Adverse Physical Effects and Associated Health Risks*

There are two major adverse physical effects that have been identified that may lead to human health risks associated with exposure to nanoparticles.[78] First, living tissue can be harmed from the usual (or expected) effect of nanoparticle reactivity.[79] Inside cells, nanoparticles interfere with cell signaling, causing structural damage and damage to DNA.[80] The smaller the particle, the more likely the toxicity.[81] Even if a material, like titanium dioxide, is safe at a normal size, studies have demonstrated that pulmonary toxicity increases when the particle shrinks to the nanoscale size.[82] Second, the scavenger cells that normally remove foreign substances, phagocytes, can be damaged by becoming overloaded with nanotech particles and cease to function.[83] Any foreign particles, including bacteria, that enter the body after the phagocytes are neutralized, can invade with impunity.[84]

It is not surprising, based on the relative amounts of investment in product development and investment in safety testing,[85] that there are very

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[78] *See* Jelena Kolosnjaj et al., *Toxicity Studies of Carbon Nanotubes, in* BIO-APPLICATIONS OF NANOPARTICLES 181 (Warren C.W. Chan ed., 2007) (presenting an excellent survey of toxicity studies). For a comprehensive and up to date summary of the most prominent experimental mechanisms of nanomaterial toxicity, see Nel et al., *supra* note 25, at 551 tbl.4.

[79] Nel et al., *supra* note 25, at 543.

[80] Jirasak Wong-Ekkabut et al., *Computer Simulation Study of Fullerene Translocation Through Lipid Membranes*, 3 NATURE NANOTECH. 363, 363, 367 (2008); CL TRAN ET AL., INST. OF OCCUPATIONAL MED., A SCOPING STUDY TO IDENTIFY HAZARD DATA NEEDS FOR ADDRESSING THE RISKS PRESENTED BY NANOPARTICLES AND NANOTUBES 15 (2005); Hisao Hidaka et al., *In Vitro Photochemical Damage to DNA, RNA and Their Bases by an Inorganic Sunscreen Agent on Exposure to UVA and UVB Radiation*, 111 J. PHOTOCHEMISTRY & PHOTOBIOLOGY 205, 212 (1997); Rosemary Dunford et al., *Chemical Oxidation and DNA Damage Catalysed by Inorganic Sunscreen Ingredients*, 418 FEBS LETTERS 87, 87–90 (1997).

[81] Qamar Rahman et al., *Evidence That Ultrafine Titanium Dioxide Induces Micronuclei and Apoptosis in Syrian Hamster Embryo Fibroblasts*, 110 ENVTL. HEALTH PERSP. 797, 797, 799 (2002); T. Uchino et al., *Quantitative Determination of OH Radical Generation and its Cytotoxicity Induced by TiO_2-UVA Treatment*, 16 TOXICOLOGY IN VITRO 629, 634 (2002); Nel et al., *supra* note 51, at 622.

[82] TRAN ET AL., *supra* note 80, at 21–23; Nel et al., *supra* note 51, at 622.

[83] Nel et al., *supra* note 25, at 550–52; Margot Lundborg et al., *Human Alveolar Macrophage Phagocytic Function is Impaired by Aggregates of Ultrafine Carbon Particles*, 86 ENVTL. RES. SEC. A 244, 252 (2001); Peter G. Barlow et al., *Reduced Alveolar Macrophage Migration Induced by Acute Ambient Particle (PM_{10}) Exposure*, 24 CELL BIOLOGY & TOXICOLOGY 243, 248–51 (2008); Buzea et al., *supra* note 24, at MR45–46.

[84] Lundborg et al., *supra* note 83, at 252; Barlow et al., *supra* note 83, at 251; Buzea et al., *supra* note 24, at MR45–46.

[85] Compared to the amount of funding for nanotech commercial applications, the amount of money spent on health and environmental risks associated with nanotech products is very small. For example, only four percent of the NNI's budget is dedicated to the health and environmental implications of this new technology. Letter from Joseph Mendelson III, Legal Dir., Int'l Ctr. for Tech. Assessment, to a Senator (Feb. 15, 2006), *available at* http://www.icta.org/doc/nano%20approp%20letter_Feb_2006.pdf.

few animal studies of the physical effects of exposure to nanoparticles.[86] One well-known study examines the effects of one form of nanoparticles called buckyballs[87] on fish.[88] Buckyballs are spherical, soccer-ball-shaped molecules containing sixty carbon molecules and are the smallest of the fullerene family.[89] Fullerenes are molecules made entirely of carbon.[90] Buckyballs are commonly used in food packaging, dietary supplements,[91] and cosmetics.[92] The exposure of the fish, here largemouth bass, caused toxic effects on the brain in the form of significant lipid peroxidation.[93] The buckyballs also killed off all the water fleas and bacteria in the water habitat containing the fish, thus negatively affecting the natural habitat.[94] Similarly, in a separate study, nanoparticles in small amounts were found to be toxic to soil bacteria.[95]

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[86] *Id.*

[87] Buckminsterfullerene (C60), called "buckyballs," was named after Richard Buckminster Fuller, the famous engineer known for the creation of the geodesic dome. *Buckyballs Could Keep Water Systems Flowing*, SCIENCEDAILY (Mar. 12, 2009), http://www.sciencedaily.com/releases/2009/03/090305080139.htm.

[88] Eva Oberdörster, *Manufactured Nanomaterials (Fullerenes, C_{60}) Induce Oxidative Stress in the Brain of Juvenile Largemouth Bass*, 112 ENVTL. HEALTH PERSP. 1058, 1058 (2004).

[89] T. Csörgő et al., Letter to the Editor, *Buckyballs and Gluon Junction Networks on the Femtometre Scale*, 30 J. PHYSICS G: NUCLEAR & PARTICLE PHYSICS L17, L17–18 (2004); H.W. Kroto et al., Letters to Nature, *C_{60} Buckminsterfullerene*, 318 NATURE 162, 162–63 (1985).

[90] Csörgő et al., *supra* note 89, at L17.

[91] LESLIE PRAY & ANN YAKTINE, INST. OF MED., NANOTECHNOLOGY IN FOOD PRODUCTS: WORKSHOP SUMMARY 739 (2009), *available at* http://www.nap.edu/catalog.php?record_id=12633; SCHULTZ & BARCLAY, *supra* note 1, at 9; Walter Derzko, *Novel, Safe Natural Food Supplement, Hydrated Fullerenes (C60-HyFn) or Water-Soluble Buckyballs Could Make 50–60% of the Riskier Synthetic Drugs and Pharmaceuticals Obsolete by 2025–30*, SMART ECONOMY (May 17, 2010), http://smarteconomy.typepad.com/smart_economy/2010/05/novel-safe-natural-food-supplement-hydrated-fullerenes-c60hyfn-or-watersoluble-buckyballs-could-make.html; *Questioning Safety Of Nanotechnology in Your Vitamins*, SCIENCEDAILY (Jan. 15, 2009), http://www.sciencedaily.com/releases/2009/01/090114114936.htm; *Nanoparticles in Dietary Supplements Cause Health Concerns, Regulatory Challenges*, SCIENCEDAILY (Feb. 10, 2009), http://www.sciencedaily.com/releases/2009/02/090209075633.htm.

[92] Bethany Halford, *Fullerene for the Face: Cosmetics Containing C60 Nanoparticles are Entering the Market even if Their Safety is Unclear*, 84 CHEM. & ENG'G NEWS 47, 47 (2006); MILLER ET AL., *supra* note 17, at 7.

[93] Oberdörster, *supra* note 88, at 1060; *see also* Emil Venere, *'Buckyballs' Have a High Potential to Accumulate in Living Tissue*, PURDUE NEWS (Sept. 18, 2008), http://news.uns.purdue.edu/x/2008b/080918JafvertBuckyballs.html (interviewing author Chad T. Jafvert who states that his recent research indicates that buckyballs have a greater chance of partitioning into fatty tissue than the banned pesticide DDT and referring to Chad T. Jafvert & Pradnya P. Kulkarni, *Buckminsterfullerene's (C_{60}) Octanol—Water Partition Coefficient (K_{ow}) and Aqueous Solubility*, 42 ENVTL. SCI. & TECH. 5945, 5946–49 (2008)).

[94] Oberdörster, *supra* note 88, at 1059.

[95] J. D. Fortner et al., *C_{60} in Water: Nanocrystal Formation and Microbial Response*, 39 ENVTL. SCI. & TECH. 4307 (2005); *Buckyballs Could Keep Water Systems Flowing*, SCIENCEDAILY (Mar. 12, 2009), http://www.sciencedaily.com/releases/2009/03/090305080139.htm; *Silver Nanoparticles May Be Killing Beneficial Bacteria in Wastewater Treatment*, *supra* note 87.

Another set of very recent, major studies[96] suggests that another form of nanoparticles, called multi-walled carbon nanotubes,[97] could be as

> For years, scientists have known about silver's ability to kill harmful bacteria and, recently, have used this knowledge to create consumer products containing silver nanoparticles. Now, a University of Missouri researcher has found that silver nanoparticles also may destroy benign bacteria that are used to remove ammonia from wastewater treatment systems.
>
> Several products containing silver nanoparticles already are on the market, including socks containing silver nanoparticles designed to inhibit odor-causing bacteria and high-tech, energy-efficient washing machines that disinfect clothes by generating the tiny particles. The positive effects of that technology may be overshadowed by the potential negative environmental impact.
>
> "Because of the increasing use of silver nanoparticles in consumer products, the risk that this material will be released into sewage lines, wastewater treatment facilities, and, eventually, to rivers, streams and lakes is of concern," said Zhiqiang Hu, assistant professor of civil and environmental engineering in MU's College of Engineering.
>
> "We found that silver nanoparticles are extremely toxic. The nanoparticles destroy the benign species of bacteria that are used for wastewater treatment. It basically halts the reproduction activity of the good bacteria."
>
> Hu said silver nanoparticles generate more unique chemicals, known as highly reactive oxygen species, than do larger forms of silver. These oxygen species chemicals likely inhibit bacterial growth. For example, the use of wastewater treatment "sludge" as land-application fertilizer is a common practice, according to Hu. If high levels of silver nanoparticles are present in the sludge, soil used to grow food crops may be harmed.

Too Much Nanotechnology May Be Killing Beneficial Bacteria, PHYSORG.COM (Apr. 29, 2008), http://www.physorg.com/news128694288.html.

[96] Vincent Castranova et al., *Persistent Pulmonary Fibrosis, Migration to the Pleura, and Other Preliminary New Findings After Subchronic Exposure to Multi-Walled Carbon Nanotubes*, NIOSH SCIENCE BLOG (Mar. 19, 2009, 10:24 AM) [hereinafter NIOSH Study], http://www.cdc.gov/niosh/blog/nsb031909_mwcnt.html (abstract published in 108 TOXICOLOGIST 457 (2009)); Craig A. Poland et al., Letters, *Carbon Nanotubes Introduced into the Abdominal Cavity of Mice Show Asbestos-Like Pathogenicity in a Pilot Study*, 3 NATURE NANOTECH. 423, 423–28 (2008); *Carbon Nanotubes that Look like Asbestos, Behave like Asbestos, Could Lead to Asbestos-Related Disease*, SCIENCEDAILY (May 22, 2008) [hereinafter *Carbon Nanotubes that Look Like Asbestos*], http://www.sciencedaily.com/releases/2008/05/080520144004.htm.

[97] "Discovered nearly 20 years ago, carbon nanotubes have been described as the wonder material of the 21st Century. Light as plastic and stronger that [sic] steel, they are being developed for use in new drugs, energy-efficient batteries and futuristic electronics." *Carbon Nanotubes that Look Like Asbestos*, *supra* note 96.

> Carbon nanotubes are atom-thick sheets of graphite formed into cylinders. They may be formed from a single layer of graphite or they may consist of multiple concentric layers of graphite, resulting in multi-walled carbon nanotubes. While the diameter of a nanotube can vary from a few nanometers up to tens of nanometers, they can be hundreds or even thousands of nanometers long. Carbon nanotubes come in many forms, with different shapes, different atomic

harmful as asbestos.[98] Like buckyballs, nanotubes are also part of the fullerene family as they are made entirely of carbon molecules. However, instead of being shaped like a ball, nanotubes consist of carbon atoms bonded into a tube shape, sometimes with a single wall—called single-wall carbon nanotubes ("SWCN"), or multiple walls—called multi-wall carbon nanotubes ("MWCN"). In fact, carbon nanotubes are sometimes called "buckytubes" because their ends, when closed, take the form of buckyballs.[99]

This second set of studies focused on whether carbon nanotubes have the potential to cause mesothelioma—a cancer of the lung lining that can take thirty to forty years to appear following exposure.[100] In one of these studies, published in 2008, nanoparticle material was injected into the abdominal cavity of mice—a sensitive predictor of long fiber response in the lung lining. The results showed that long, thin, multi-walled carbon nanotubes that look like asbestos fibers, behave like asbestos fibers, creating the chance that people who breathe in nanotubes could develop cancer years after exposure.[101]

> arrangements, and varying amounts and types of added chemicals—all of which affect their properties and might influence their impact on human health and the environment.

Id.

[98]

> Asbestos fibers are harmful because they are thin enough to penetrate deep into the lungs, but sufficiently long to confound the lungs' built-in clearance mechanisms for getting rid of particles. Widespread exposure to asbestos has been described as the worst occupational health disaster in U.S. history and the cost of asbestos-related disease is expected to exceed $200 billion.

Id.

> The toll of asbestos-related cancer, first noticed in the 1950s and 1960s, is likely to continue for several more decades even though usage reduced rapidly some 25 years ago. While there are reasons to suppose that nanotubes can be used safely, this will depend on appropriate steps being taken to prevent them from being inhaled in the places they are manufactured, used and ultimately disposed of. Such steps should be based on research into exposure and risk prevention, leading to regulation of their use.

Id. (quoting Anthony Seaton, professor emeritus at the University of Aberdeen, UK).

[99] *Nanotubes and Buckyballs*, NANOTECHNOLOGYNOW.COM, http://www.nanotech-now.com/nanotube-buckyball-sites.htm (last visited Nov. 5, 2011).

[100] *Id.*

[101] Poland et al., *supra* note 96, at 426–27. The lead author of the study cautions that, if nanotubes get into the sensitive outer lining of the lungs "in sufficient quantity, there is a chance that some people will develop cancer—perhaps decades after breathing the stuff." *Carbon Nanotubes that Look Like Asbestos*, *supra* note 96 (quoting Ken Donaldson).

One year later, in 2009, NIOSH completed a ground-breaking study involving mice that inhaled a small drop of liquid containing the multi-walled carbon nanotubes in a manner that closely resembles inhalation of the same material suspended in the air—similar to the exposure that a worker might encounter.[102] This study was the first to demonstrate that multi-walled carbon nanotubes aspirated by laboratory mice can actually migrate from the tiny structures in the lung called alveoli (the air sacks), which are critical for gas exchange, through the lungs to the pleura (the membrane that goes around the lungs).[103] The lungs of the mice showed persistent inflammation and fibrosis (scarring).[104] These findings are important as mesothelioma (a form of cancer) develops in the pleura after asbestos exposure and multi-walled carbon nanotubes share many of the same characteristics as asbestos.[105] This study linked up prior studies in that it showed that multi-walled carbon nanotubes can migrate from workers' lungs to the pleura.[106] The question remains whether this type of nanotube, like asbestos, will cause mesothelioma.[107] The authors of the study concluded:

> This is of considerable importance, because research and business communities continue to invest heavily in carbon nanotubes for a wide range of products under the assumption that they are no more hazardous than graphite. Our results suggest the need for further research and great caution before introducing such products into the market if long-term harm is to be avoided.[108]

According to Dr. Andrew Maynard, who is a co-author of the NIOSH study:

> This study is exactly the kind of strategic, highly focused research needed to ensure the safe and responsible development of nanotechnology . . . . It looks at a specific

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[102] NIOSH Study, *supra* note 96.

[103] *Id.*; *see also* L.M. Sargent et al., *Induction of Aneuploidy by Single-Walled Carbon Nanotubes*, 50 ENVTL. MOLECULAR MUTAGENESIS 708, 713–15 (2009) (discussing *in vitro* cell studies showing that single-walled carbon nanotubes can cause genotoxicity and abnormal chromosome number due to interference with cell division (mitosis)); Atsuya Takagi et al., *Induction of Mesothelioma in p53+/- Mouse by Intraperitoneal Application of Multi-Walled Carbon Nanotube*, 33 J. TOXICOLOGY SCI. 105, 110–14 (2008) (finding mesothelial tumors in mice after intraperitoneal injection of multi-walled carbon nanotubes).

[104] NIOSH Study, *supra* note 96.

[105] *Id.*

[106] *Id.*

[107] *Id.*

[108] Poland et al., *supra* note 96, at 423 (footnote omitted).

> nanoscale material expected to have widespread commercial applications and asks specific questions about a specific health hazard. Even though scientists have been raising concerns about the safety of long, thin carbon nanotubes for over a decade, none of the research needs in the current U.S. federal nanotechnology environment, health and safety risk research strategy address this question.[109]

Although further research is required, results presented today clearly demonstrate that, under certain conditions, especially those involving chronic exposure, carbon nanotubes can pose a serious risk to human health.[110]

As manufacturers are not required to identify the use of nanoparticles on product labels, and as it appears that manufacturers are reluctant to reveal this use voluntarily,[111] it is unknown whether carbon nanotubes are currently being used in particular food, food packaging, cosmetics, dietary supplements, or other products that are marketed for direct or indirect human consumption. However, like the buckyball, the nanotube can carry

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[109] *Carbon Nanotubes that Look Like Asbestos*, *supra* note 96 (internal quotation marks omitted).

[110] *See, e.g.*, Kolosnjaj et al., *supra* note 78, at 181 (concluding that "available data clearly show that, under some conditions, nanotubes can cross the membrane barriers and suggests that if raw materials reach the organs they can induce harmful effects as inflammatory and fibrotic reactions"); Alexandra E. Porter et al., *Direct Imaging of Single-Walled Carbon Nanotubes in Cells*, 2 NATURE NANOTECH. 713, 713, 716 (2007) (demonstrating that nanotubes can enter into cell "cytoplasm and localize within the cell nucleus, causing cell mortality in a dose-dependent manner"); Chiu-Wing Lam et al., *A Review of Carbon Nanotube Toxicity and Assessment of Potential Occupational and Environmental Health Risks*, 36 CRITICAL REV. IN TOXICOLOGY 189, 207 (2006); *see also* A. Hubbs et al., *Persistent Pulmonary Inflammation, Airway Mucous Metaplasia and Migration of Multi-Walled Carbon Nanotubes from the Lung After Subchronic Exposure*, 108 TOXICOLOGIST 457 (2009) (explaining that the fiber-like dimensions and durability of MWCNTs, as well as their ability to cause peritoneal inflammation, are reminiscent of asbestos); E. Kisin et al., *Pulmonary Response, Oxidative Stress and Genotoxicity Induced by Carbon Nanotubes*, 114 TOXICOLOGIST A793 (2010) (finding acute inflammation and interstitial fibrosis in mice exposed to carbon nanofibers); Robert R. Mercer et al., *Distribution and Persistence of Pleural Penetrations by Multi-Walled Carbon Nanotubes*, 7 PARTICLE & FIBRE TOXICOLOGY 1, 5–6 (2010) (showing that MWCNTs can have toxic effects as they frequently penetrate into both the alveollar epithelium and visceral pleura); Jürgen Pauluhn et al., *Subchronic 13-Week Inhalation Exposure of Rats to Multi-Walled Carbon Nanotubes: Toxic Effects are Determined by Density of Agglomerate Structures, not Fibrillan Structures*, 113 TOXICOLOGY SCI. 226, 226 (2010) (demonstrating reduced lung clearance in rats exposed to low mass concentrations of carbon nanotubes); Dale W. Porter et al., *Mouse Pulmonary Dose—and Time Course—Responses Induced by Exposure to Multi-Walled Carbon Nanotubes*, 269 TOXICOLOGY 136, 136–47 (2010) (observing that the long and thin structures of common carbon nanotubes and carbon nanofibres resemble asbestos fibres and migrate from pulmonary alveoli to pleural tissue which is the same site where malignant mesothelioma develops triggered by asbestos exposure).

[111] Caroline Scott-Thomas, *Food Companies Go Quiet on Nanotech Research Activity*, FOODNAVIGATOR-USA.COM (July 19, 2010), http://www.foodnavigator-usa.com/Financial-Industry/Food-companies-go-quiet-on-nanotech-research-activity.

a substance inside. Consequently, it appears possible that nanotubes may be being used in food packaging, dietary supplements, cosmetics, and sunscreens, in a similar fashion to the use of buckyballs. What is known is that carbon nanotubes have been proposed as a drug delivery device,[112] as a possible gene delivery vehicle,[113] and for use in combination with radiofrequency fields to destroy cancer cells.[114] In addition, at least one cosmetic company is exploring the use of nanotubes for cosmetics[115] and various uses for nanotubes in food and food packaging have been proposed.[116] Finally, researchers have developed a method for large-scale production of carbon nanotube filters for use in water quality improvement.[117]

3. *Presumptions of Safety*

According to toxicological principles, health risks normally correlate to the amount (or doses) to which an individual is exposed. In contrast, when evaluating health risks from exposure to nanoparticles, the concentration number and resulting total surface area predominately influence their interactions with biological systems, and are more reasonable parameters for doses of exposure.[118]

According to the EPA:

> [I]t is generally believed that nanoparticles can have toxicological properties that differ from their bulk material. A number of studies have demonstrated that

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[112] *Carbon Nanotubes that Look like Asbestos*, *supra* note 96.

[113] Ravi Singh et al., *Binding and Condensation of Plasmid DNA onto Functionalized Carbon Nanotubes: Toward the Construction of Nanotube-Based Gene Delivery Vectors*, 127 J. AM. CHEM. SOC. 4388, 4389 (2005).

[114] Christopher J. Gannon et al., *Carbon Nanotube-Enhanced Thermal Destruction of Cancer Cells in a Noninvasive Radiofrequency Field*, 110 CANCER 2654, 2654–55 (2007).

[115] Katie Schaefer, *Special Delivery: Clay Nanotubes for Skin*, COSMETICS & TOILETRIES (March 2008), http://www.cosmeticsandtoiletries.com/research/techtransfer/16119562.html.

[116] NANOBIO-RAISE, NANOTECHNOLOGY AND FOOD, *available at* http://files.nanobio-raise.org/Downloads/Nanotechnology-and-Food-fullweb.pdf (last visited Dec. 16, 2011); *see also Nanobiology: Responsible Action on Issues in Society and Ethics*, NANOBIO-RAISE, http://nanobio-riase.org (last visited Sept. 11, 2011) ("NanoBio-RAISE combines ethics research in nanobiotechnology with science communication. This interdisciplinary project brings together nanobiotechnologists, ethicists and communication specialists with the aims to anticipate the societal and ethical issues likely to arise as nanobiotechnologies develop and to use the lessons from the GM debate to respond to the probable public concerns. NanoBio-RAISE is a 6th Framework Programme Science & Society Co-ordination Action funded by the European Commission."); J.F. Graveland-Bikker & C.G. de Kruif, Review, *Unique Milk Protein Based Nanotubes: Food and Nanotechnology Meet*, 17 TRENDS FOOD SCI. & TECH. 196, 200–01 (2006) (providing an overview of potential applications of alpha-lactalbumin nanotubes in food and pharmaceuticals).

[117] *Nanotechnology's Miniature Answers to Developing World's Biggest Problems*, SCIENCEDAILY (May 12, 2005), http://www.sciencedaily.com/releases/2005/05/050512120050.

[118] *See* SCENIHR, *supra* note 54, at 22 (illustrating the importance of particle size).

> nanoparticle toxicity is complex and multifactorial, potentially being regulated by a variety of physiochemical properties such as size, chemical composition, and shape, as well as surface properties such as charge, area and reactivity. As the size of the particles decreases, a resulting larger surface-to-volume ratio per unit weight for nanoparticles correlates with increased toxicity as compared with bulk material toxicity.[119]

4. *Toxicological Screening*

To properly identify the safety risks of nanotech particles, established methods for testing normal size materials must be modified to address the unique properties of nanomaterials. Thus, the additional factors of size, shape, and surface properties will need to be examined.[120] As Günter Oberdörster explained,

> [t]here is a strong likelihood that the biological activity of nanoparticles will depend on physiochemical properties not routinely considered in toxicity screening studies. Physiochemical properties that may be important in understanding the toxic effects of test materials include particle size and size distribution, agglomeration state, shape, crystal structure, chemical composition, surface area, surface chemistry, surface charge, and porosity.[121]

A suggested strategy for screening for potential health effects is to use predictive toxicology. This method exposes cells in a culture to nanoparticles and then watches for subtle signs that the cells are starting to defend themselves.[122] A series of toxicity assays could be developed using this method that would include three key elements: "physiochemical characterization of [engineered nanomaterials], in vitro assays (cellular and noncellular), and in vivo studies."[123] According to scientists, there is a "strong likelihood that biological activity will depend on physiochemical characteristics that are not usually considered in toxicity screening

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[119] NANOTECHNOLOGY WHITE PAPER, *supra* note 58, at 78.

[120] *See* Nel et al., *supra* note 51, at 622 ("Particle size and surface area are important material characteristics from a toxicological perspective . . . . The change in the physiochemical and structural properties of engineered NM with a decrease in size could be responsible for a number of material interactions that could lead to toxicological effects.").

[121] Oberdörster et al., *supra* note 66, at 2.

[122] Nel et al., *supra* note 51, at 626 ("[P]redictive scientific model . . . focuses on target-specific, mechanism-based biological observations, rather than a descriptive approach.").

[123] *Id.*

studies."[124] Consequently,

> any test paradigm must attempt to characterize the test material with respect to size (surface area, size distribution), chemical composition (purity, crystalinity, electronic properties, etc.), surface structure (surface reactivity, surface groups, inorganic/organic coatings, etc.), solubility, shape and aggregation. This should be done at the time of [engineered nanomaterial] administration as well as at the conclusion, if possible.[125]

It is important to note that even this method could miss significant risks to health because it is very possible that, as scientific understanding grows and as new types of nanoparticles are created, new properties will be discovered that can lead to novel mechanisms of toxicity.[126] Moreover, not only should assays reflect portal-of-entry toxicity in skin, mucous membranes, and lungs, but, because of the mobility of nanoparticles, systemic responses must also be considered.

III. FDA REGULATION OF NANOTECH PRODUCTS FOR HUMAN CONSUMPTION AND THE PRESUMPTION OF BIOEQUIVALENCE

Ignoring a rapidly developing body of science to the contrary, the FDA opines that there is no scientific basis on which to conclude that "nanoscale" materials as a class are inherently more hazardous than "non-nanoscale" materials.[127] Its opinion that if the normal size material is safe, then its nanoscale counterpart is also safe is based on a now dated presumption of bioequivalence. Perhaps of even more concern, the FDA has also announced that the existing health and safety tests that it uses to assess the safety of normal size materials are "probably adequate" to assess the health effects of nanoparticles.[128] Consequently, nanotech products are being regulated exactly like their non-nanotech counterparts. The result is that manufacturers of nanotech food, dietary supplements, sunscreens, and cosmetics are not required to test their products for safety and are not required to obtain premarket approval from the FDA. The following sections describe the FDA regulation of each separate product category and explain why these regulations fail to protect public health when applied to

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[124] *Id.*

[125] *Id.*

[126] *See* SCENIHR, *supra* note 54, at 54–57 (emphasizing that critical gaps remain in the knowledge required for risk assessment purposes).

[127] U.S. FOOD & DRUG ADMIN., NANOTECHNOLOGY 11 (2007).

[128] *FDA Regulation of Nanotechnology Products*, *supra* note 23 (addressing FDA regulation of all nanoproducts).

nanotech products.

A. *Nanotech Drugs*

Under the current regulatory structure created by the Food, Drug and Cosmetic Act ("FDCA"), the FDA regulates products according to their intended use.[129] For example, products intended to treat diseases (referred to as "disease claims") or products intended to alter the structure and function of the body ("structure and function claims") are considered to be either drugs[130] or devices.[131]

> For drugs and devices, the modern FDA relies on a premarket enforcement process that places the majority of the cost and burden on the product manufacturer to establish safety and efficacy through the clinical trial process prior to distribution to the public. Without premarket approval from the FDA, these products will be deemed both adulterated and misbranded as a matter of law.[132]

The current regulatory scheme for drugs appears to be adequate to protect public health as the manufacturers bear the burden of proving that each new drug is both safe and effective for its intended use.[133] The FDA's

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[129] 21 U.S.C. § 321(g)(1)(B) (2006) (drugs); *id.* § 321(h)(2) (devices); *id.* § 321(i)(1) (cosmetics); United States v. Lane Labs-USA, Inc., 324 F. Supp. 2d 547, 567 (D.N.J. 2004) ("[T]he 'intended use' referred to within the FDCA framework contemplates 'the [objective] intent of those persons legally responsible for the labeling of drugs. . . . The intent is determined by such persons' expressions or may be shown by the circumstances surrounding the distribution of the article.'") (quoting 21 C.F.R. § 201.128); *see also* United States v. Storage Spaces Designated Nos. "8" & "49," 777 F.2d 1363, 1366 (9th Cir. 1985) ("[I]ntent may be derived or inferred from labeling, promotional material, advertising, or any other relevant source."); Katharine A. Van Tassel, *Slaying the Hydra: The History of Quack Medicine, the Obesity Epidemic and the FDA's Battle to Regulate Dietary Supplements Marketed as Weight Loss Aids*, 6 IND. HEALTH L. REV. 203, 229–30 (2009).

[130] *See* 21 U.S.C. § 321(g)(1)(B) (defining "drug" as an article "intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals"); *id.* § 321(g)(1)(C) (defining "drug" also as an "article[] (other than food) intended to affect the structure or any function of the body of man or other animals"); Van Tassel, *supra* note 129, at 229–30.

[131] 21 U.S.C. § 321(h)(2); Van Tassel, *supra* note 129, at 229–31.

[132] Van Tassel, *supra* note 129, at 230 (citing 21 U.S.C. §§ 355(a) & 360e(c) (regulating drugs and devices, respectively), and Richard A. Merrill, *The Architecture of Government Regulation of Medical Products*, 82 VA. L. REV. 1753, 1761–76 (1996)).

[133] One new ingredient is sufficient to trigger "new drug" status. "The newness of a drug may arise by reason (among other reasons) of: (1) The newness for drug use of any substance which composes such drug, in whole or part, whether it be active substance . . . or other component." 21 C.F.R. § 310.3(h)(1) (2010). The FDA's position that "particle size does not matter" and that the safety of the large particle version of an active ingredient can be used to predict the safety of the nanoparticle version of the same ingredient appears to lead to the conclusion that the nanotech version of a preapproved bulk component is not a "new substance." This renders this section inapplicable. Section

position that "particle size does not matter" and that the safety of the large particle version of an active ingredient can be used to predict the safety of the nanoparticle version of the same ingredient is less important in this context. A drug with an entirely new normal size ingredient must go through the premarket approval process. Similarly, if a drug that already has FDA approval is modified to add nanoparticles, even if the modified drug is being marketed to treat the same condition or disease, it will become a "new drug" because the proportion of the ingredients to each other will change.[134] In other words, the formula for the amount of each ingredient used to make the drug will change. Any change in the formula will cause the drug to be labeled a "new drug" which will trigger the pre-market approval process. All "new drugs" require testing for safety and effectiveness and premarket approval[135] from the FDA.[136] In addition, as the status of the nanotech version of the drug will change to that of a "new drug," notice of the fact that the drug is using a new formula will be provided to the physicians who are prescribing the new drug to their patients. The physicians must disclose any material health risks associated with the new drug.

On the other hand, the FDA's position that "particle size does not matter" is outcome determinative when it comes to devices. A pacemaker

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310.3 should be modified to include a section that renders a drug "new" if the mechanism of action of the drug is different. This would then trigger "new drug" status as the addition of nanoparticles to a drug is likely to change its mechanism of action.

[134] "New drug substance means any substance that when used in the manufacture, processing, or packing of a drug, causes the drug to be a new drug." *Id.* § 310.3(g). A substance can cause a drug to be considered a "new drug" if the proportion of one of the substances that is used in relation to the other ingredients, is new. *Id.* § 310.3(h)(3) ("The newness of a drug may arise by reason (among other reasons) of: . . . (3) The newness for drug use of the proportion of the substance in a combination, even though such combination containing such substance in other proportion is not a new drug."). Even if the FDA opines that the nanotech version of a preapproved bulk component is not a different component as they are bioequivalent, the proportion of the nanotech component to the other components of the drug will be different rendering it a "new drug" and triggering the pre-market approval process. *See id.*

[135] "No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed [with the FDA] is effective with respect to such drug." 21 U.S.C. § 355(a).

[136] A "new drug" is

> [a]ny drug . . . the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof . . . or . . . [a]ny drug . . . as a result of investigations to determine its safety and effectiveness for use under such conditions, has become so recognized, but which has not, otherwise than in such investigations, been used in a material extent or for a material time under such conditions.

Id. § 321(p)(1)–(2).

that already has undergone testing for safety and effectiveness will not need to be retested and undergo the FDA approval process again if it is modified to use nanoparticles in its design. This is because, unlike nanotech drugs, the nanotech device is likely to perform in the same way as the preapproved non-nanotech version. The FDA's position is that the two versions of the pacemaker are bioequivalent. On the other hand, devices are of less concern to public health than products that use free nanoparticles because devices are likely to contain nanoparticles that are fixed inside a solid matrix, which makes them less likely to move into the environment or the human body.

B. *Nanotech Food*

Unlike drugs and devices, traditional food products have their own special place in the FDA's regulatory structure as they can be placed directly upon the market without undergoing any testing for safety.[137] Government has little need to provide regulatory protection for consumers, "as thousands of years of use of traditional food provides consumers with the common knowledge, and thus the ability, to protect themselves from the ordinary risks associated with different traditional food products."[138] This common knowledge and ability to self-protect supports the presumption of safety that is granted to traditional food under the FDCA. If a particular food poses a safety risk over and above those which are normally associated with a food product, such as salmonella in peanut butter, the FDA carries the burden of proving that the food is adulterated or misbranded before it can be removed from the market.[139]

With the introduction of free nanoparticles to food, this rationale for minimal FDA regulation no longer holds true. Food and agricultural industries see opportunities to use nanoparticles for "more potent food colourings, flavourings and nutritional additives, antibacterial ingredients for food packaging, and more potent agrochemicals and fertilisers."[140] Nanoparticle additives are now found in sodas, dairy products, margarine, and sausages.[141] There is also wide use in food and beverage packaging of "nanoclay composites—plastics to which nanoscale clay platelets have been added . . . ."[142] These nanoclay composites are also being used "in agriculture pipes and plastics to allow controlled release of

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[137] Katharine Van Tassel, *The Introduction of Biotech Foods to the Tort System: Creating a New Duty to Identify*, 72 U. CIN. L. REV. 1645, 1651 (2004).

[138] Van Tassel, *supra* note 129, at 230.

[139] Van Tassel, *supra* note 137, at 1651.

[140] MILLER & SENJEN, *supra* note 15, at 4.

[141] *Id.* at 9.

[142] *Id.* at 4.

herbicides . . . ."[143] Analysts of the uses of nanotechnology in food estimate that more than six hundred food products contain nanoparticle additives.[144] In addition, between four hundred and five hundred foods have nanoparticle packaging, raising concerns regarding the migration of nanoparticles from the packaging into the food.[145]

1. *Nanotech Food Additives*

In the mid-twentieth century, there was an explosion in the growth of the food processing industry with a parallel increase in the number and variety of chemicals added to food.[146] In response to consumer concern over this increase in the number of new chemicals introduced into the food supply and an enhanced concern over rising cancer rates, Congress passed the Food Additives Amendment Act of 1958 ("FAAA").[147] The FAAA places the burden of proof on the manufacturers, rather than on the FDA, to show that a newly discovered substance added to food is safe if used within specified quantities.[148] This change fixed a major flaw in the 1938 FDCA that had originally placed the burden of proof on the FDA to prove that a food additive was unsafe.[149] Until the passage of the FAAA, the food industry could market potentially injurious chemical additions to the consuming public without interference from the FDA.[150] According to current FDA regulations, if substances added to food are "food additives," premarket testing for safety is required.[151] If a normal size version of a food additive has premarket approval, a modification using nanoparticles will also have approval as the FDA states that these two versions are bioequivalent.

The exception to this rule is when a food additive is generally regarded

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[143] *Id.*

[144] Stephen Daniells, *Think Big, Think Nano*, FOODNAVIGATOR.COM (Dec. 19, 2007), http://www.foodnavigator.com/Science-Nutrition/Think-big-think-nano.

[145] MILLER & SENJEN, *supra* note 15, at 10.

[146] Van Tassel, *supra* note 129, at 213–15.

[147] Joseph A. Levitt, *Keeping America's Food Supply Safe*, *in* FDA: A CENTURY OF CONSUMER PROTECTION 135, 140 (Wayne L. Pines ed., 2006).

[148] *Id.*

[149] *Id.*

[150] *Id.*

[151] A "food additive" is "any substance the intended use of which results . . . in it becoming a component or . . . affecting the characteristics of . . . food," unless the substance is generally regarded as safe (GRAS). 21 U.S.C. § 321(s) (2006). In response to the public's concern over the steadily increasing amounts of chemicals added to food as food processing technology developed, Congress enacted the Food Additives Amendment of 1958. Pub. L. No. 85-929, 72 Stat. 1784. The Food Additives Amendment established a pre-market approval requirement for "food additives." This placed the burden on the food processor to establish, through scientific methodology, that the additive was safe for its intended use before placing the food additive on the market. *Id.* This is referred to as the pre-market approval process.

as safe or "GRAS."[152] A substance is considered to be GRAS if there is a general consensus among informed experts that a substance is safe for human consumption.[153] If a substance added to food is considered to be GRAS, it will not require pre-market approval.[154] Examples are salt and sugar. The nanoparticle version of an already approved food additive also falls into this exception as the FDA's position on bioequivalency means that the safety of the normal size version is predictive of the safety of the nano scale version.

C. *Nanotech Dietary Supplements*

Congress passed the Dietary Supplement Health Education Act ("DSHEA") in 1994.[155] DSHEA was a victory to dietary supplement manufacturers who have claimed for decades that their products should be regulated like food.[156] By virtue of DSHEA, like traditional food, dietary supplements can now be placed directly on the market without any testing under a completely unsupported presumption of safety.[157] The term

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[152] 21 U.S.C. § 321(s).

[153] *Id.*

[154] A substance added to food is not a food additive and, therefore, does not require pre-market approval if it is "GRAS." *Id.* A substance that is "GRAS" is defined as a substance that is

> generally recognized, among experts qualified by scientific training and experience to evaluate its safety, as having been adequately shown through scientific procedures (or, in the case of a substance used in food prior to January 1, 1958, through either scientific procedures or experience based on common use in food) to be safe under the conditions of its intended use.

Id.

[155] Dietary Supplement Health and Education Act, Pub. L. No. 103-417, 108 Stat. 4325 (1994) (codified as amended in scattered sections of 21 U.S.C.). Under DSHEA, a dietary supplement is,

> a product (other than tobacco) intended to supplement the diet that bears or contains one or more of the following dietary ingredients: (A) a vitamin; (B) a mineral; (C) an herb or other botanical; (D) an amino acid; (E) a dietary substance for use by man to supplement the diet by increasing the total dietary intake; or (F) a concentrate, metabolite, constituent, extract, or combination of any ingredient described in clause (A), (B), (C), (D), or (E) . . . .

21 U.S.C. § 321(ff)(1); *see also* Van Tassel, *supra* note 129, at 239–41.

[156] Van Tassel, *supra* note 129, at 231–41.

[157] 21 U.S.C. § 321(s) (detailing the exemption from food additive provisions); Nutraceutical Corp. v. Von Eschenbach, 459 F.3d 1033, 1035 (10th Cir. 2006). This exemption covers dietary supplements that carry labels with "statements of nutritional support" and statements explaining how a supplement may *maintain* or *improve* the "structure and function" of the body. 21 U.S.C. § 321(g); *see also id.* § 343(r)(6) (allowing substantiation and disclaimer for structure and function claims); 27 C.F.R. § 101 (2010). A dietary supplement can also include on its label a statement that "describes the role of a nutrient or dietary ingredient intended to affect the structure or function in humans" or that "characterizes the documented mechanism by which a nutrient or dietary ingredient acts to maintain such structure or function." 21 U.S.C. § 343(r)(6)(A). Not only are dietary supplements cloaked with a

"dietary supplement" now encompasses both nutritional and non-nutritional substances by including not only vitamins, minerals, and amino acids, but also herbs or other botanicals which have no nutritional value.[158] Under the FDCA, the only way that the FDA can remove a dietary supplement from the market is to prove that it is adulterated by demonstrating that the product poses a "significant or unreasonable risk of illness or injury."[159]

1. *New Ingredients in Dietary Supplements*

DSHEA does provide the FDA with very limited premarket review power for a "new dietary ingredient for which there is inadequate information to provide reasonable assurance that such ingredient does not present a significant or unreasonable risk of illness or injury."[160] A dietary ingredient is defined as "new" if it was not on the market before October 15, 1994 when DSHEA was passed.[161] A new ingredient will be deemed to be adulterated if there is no history of use or "other evidence of safety."[162] The manufacturer must give the FDA seventy-five days notice prior to marketing and must provide the FDA with information indicating that the ingredient is reasonably expected to be safe.[163] Alternatively, the manufacturer may file a petition seeking an order from the FDA detailing the conditions under which the dietary ingredient will reasonably be expected to be safe.[164]

Under this system, if the FDA announces that all nanoparticles used in dietary supplements are "new" ingredients, the manufacturers who are currently distributing nanotech products must halt distribution for seventy-five days, must give the FDA seventy-five days notice that they plan to place their dietary supplement on the market, and must provide the FDA

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baseless presumption of safety, as if they were similar to traditional food, but DSHEA (as applied by the FDA) also grants an equally unwarranted presumption that dietary supplements for weight loss are effective as claimed. *See Nutraceutical Corp.*, 459 F.3d at 1039 n.5 ("The district court compared the language of DSHEA to the statutory language governing medical devices and drugs and concluded that, unlike manufacturers of medical devices and drugs, manufacturers of dietary supplements do not need to prove effectiveness prior to taking their product to market."); Van Tassel, *supra* note 129, at 240.

[158] However, dietary supplements do not include products that contain any other active ingredients such as synthetic ingredients that are regulated as over-the-counter medications or prescription drugs. Dietary Weight Loss Supplements: Limited Federal Oversight has Focused more on Marketing than on Safety: Before the Subcomm. on Oversight of Gov. Management, Restructuring, and the Dist. of Columbia, Comm. on Gov. Affairs, U.S. Senate, 1 (July 31, 2002) (statement of Janet Heinrich, Director, Health Care—Public Health Issues, U.S. Gen. Accounting Office); Van Tassel, *supra* note 129, at 239–41.

[159] *Nutraceutical Corp.*, 459 F.3d at 1035 (quoting 21 U.S.C. § 342(f)(1)).

[160] 21 U.S.C. § 342 (f)(1)(B).

[161] *Id.* § 350b(c).

[162] *Id.* § 350b(a).

[163] *Id.*

[164] *Id.* § 350b(b).

with the information that supports their position that the nanotech ingredient is reasonably safe.[165] However, unless the FDA can meet its burden of proof that "there is inadequate information to provide a reasonable assurance that such ingredient does not provide a significant or unreasonable risk of illness or injury," the manufacturer may automatically start to market its nanotech product seventy-five days after it provided the FDA with notice.[166] As the Ephedra case, discussed *infra* in Section IV.B, demonstrates, it is unlikely that the FDA will be able to meet this burden of proof until the risks associated with nanoparticles can be quantified using classic probability analysis.

D. *Nanotech Cosmetics*

Cosmetics[167] should be considered to be products that are marketed for human consumption as they are absorbed into the body indirectly through the skin when applied and are absorbed through the lungs as a result of the aspiration of aerosolized particles when washing off the cosmetic. Nanoparticles can be found in most personal care products including soap, deodorant, shampoo, hair conditioner, toothpaste, moisturizer, foundation, blush, lipstick, eyeshadow, perfume, nail polish, and after-shave lotion.[168] Manufacturers who use nanoparticles in their products include L'Oréal, Revlon, Estée Lauder, Chanel, Procter and Gamble, Beyond Skin Science LLC, SkinCeuticals, Dr. Brandt, Dermazone Solutions, and Shiseido, among many others.[169] Nanotech cosmetics that are rubbed onto the skin contain nanoparticles 1000 nm in size that are capable of absorption through intact skin.[170] When the skin is damaged, for example through blemishes, sun burn, eczema, shaving cuts, or other trauma, nanoparticles up to 7000 nm can penetrate the skin.[171] In fact, many nanotech cosmetics and sunscreens are especially formulated to be used on damaged skin. And an as yet unanswered question is what impact the "penetration enhancers"

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[165] SCHULTZ & BARCLAY, *supra* note 1, at 17.

[166] *Id.*

[167] The term "cosmetic" means

> articles intended to be rubbed, poured, sprinkled, or sprayed on, introduced into, or otherwise applied to the human body or any part thereof for cleansing, beautifying, promoting attractiveness, or altering the appearance, and . . . articles intended for use as a component of any such articles; except that such term shall not include soap.

21 U.S.C. § 321(i).

[168] *See* MILLER ET AL., *supra* note 17, at 18–26 (listing 116 products that contain nanoparticles).

[169] *Id.* at 14.

[170] Rouse & Yang, *supra* note 68; Tinkle et al., *supra* note 68, at 1202–03.

[171] Oberdörster et al., *supra* note 68, at 834.

that many cosmetic products use will have on this analysis.[172]

However, nanotech cosmetics are not required to be tested for safety because products that are intended to be used as cosmetics do not require premarket testing under the FDCA.[173] This treatment is a result of the belief held when the FDCA was first enacted that cosmetics were low-risk products because they are only spread onto the surface of the skin to improve attractiveness. That incorrect regulatory assumption persists today. In fact, Friends of the Earth has noted that "[a]lthough the FDCA has a lot of language devoted to cosmetics, it is not too much of an exaggeration to say that cosmetics in the USA are essentially unregulated."[174] Of the 10,500 normal size ingredients used in cosmetic products, only thirteen percent have been assessed for safety by the industry-funded Cosmetics Industry Review Panel.[175] The FDA can only remove an unsafe cosmetic from the market if the FDA can prove that the cosmetic is adulterated because "it bears or contains a poisonous or deleterious substance which may render it injurious" to users.[176]

E. *Nanotech Sunscreens*

Sunscreens fall into the "drug"[177] category as their intended use is to protect the skin from harm from the sun.[178] As a result, sunscreens, like other drugs, require pre-market testing for safety and effectiveness.[179] Consequently, sunscreens that are currently on the market have obtained FDA approval for human use.[180] The chemicals zinc oxide and titanium oxide have been major components in sunscreens for a long period of time.[181] The use of these chemicals in sunscreens has been screened for safety by the FDA and subsequently approved for use.[182]

The FDA has gone one step further and approved the use of sunscreens

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[172] *Nanotechnology & Sunscreens*, *supra* note 68, at 8.

[173] *Nanotechnology Consumer Products Inventory*, *supra* note 11, at 15.

[174] *Id.*

[175] *Frequently Asked Questions: Why Should I Be Concerned About the Safety of Personal Care Products? Doesn't the Government Regulate Them?*, ENVTL. WORKING GRP., http://www.ewg.org/skindeep/faq/ (last visited Nov. 26, 2011) ("On average, consumers use about 10 personal care products containing 126 ingredients per day. The Cosmetics Ingredients Review (CIR), the industry's self-policing safety panel, does not make up for FDA inaction. In 2007 EWG analysis found that over 30 years, the industry panel has reviewed the safety of just 13% of the 10,500 ingredients in personal care products.").

[176] 21 U.S.C. § 342(a)(1) (2006).

[177] *Id.* § 321(g)(1)(B).

[178] Sunscreen Drug Products for Over-the-Counter Human Use; Tentative Final Monograph, 58 Fed. Reg. 28194, 28195 (May 12, 1993).

[179] *See supra* Section III.A.

[180] *See* Final Monograph, *supra* note 48.

[181] *Id.*

[182] *Id.*

with these chemicals without a doctor's prescription so that consumers can purchase them over-the-counter without a doctor's prescription.[183] This over-the-counter ("OTC") status is achieved by giving each active component of the sunscreen "monograph" status.[184] In order to be placed in the OTC category, each active component is reviewed for use for safety and effectiveness by the FDA. The successful outcome of this review results in a regulation for each substance that is called a "monograph."[185] Sixteen active ingredients in sunscreens have monograph status, including zinc oxide and titanium oxide.[186]

A short-coming of zinc oxide and titanium oxide for the image-conscious user is that they make the sunscreen appear white and pasty due to a large amount of scattering of light from the particles.[187] The use of the engineered nanoparticle version of zinc oxide and titanium oxide has resolved these problems as they make the sunscreen "cosmetically clear" and easy to smooth onto the skin.[188] Seventy percent of the sunscreens that use titanium dioxide use engineered nanoparticles.[189] Thirty percent of sunscreens that use zinc oxide use engineered nanoparticles.[190]

The monograph that approves of the use of zinc oxide and titanium oxide does not expressly address sunscreen drug products that contain the nanoparticle version of these chemicals. However, the FDA states that it is aware that sunscreens are being marketed with nanoparticles.[191] In addition, in the sunscreen monograph, the FDA explains that:

> The agency is aware that sunscreen manufacturers are using micronized titanium dioxide to create high SPF products that are transparent and esthetically pleasing on the skin. The agency does not consider micronized titanium dioxide to be a new ingredient but considers it a

[183] *See* 21 C.F.R. § 330.10(a)(7)–(10) (2011) (allowing these sunscreens to be sold over-the-counter).

[184] Sunscreen Drug Products for Over-the-Counter Human Use, 43 Fed. Reg. 38206–07 (Aug. 25, 1978).

[185] *Id.* at 38207.

[186] *See* Final Monograph, *supra* note 48, at 27673.

[187] *Nanotechnology & Sunscreens*, *supra* note 68, at 3.

[188] *Id.* at 2.

[189] DEP'T OF HEALTH & AGEING, AUSTL. GOV'T, SAFETY OF SUNSCREENS CONTAINING NANOPARTICLES OF ZINC OXIDE OR TITANIUM OXIDE (2006), *available at* http://www.benev.com.tr/page/downloadfile.php?file=13.

[190] *Id.*

[191] Final Monograph, *supra* note 48, at 27676.

> specific grade of the titanium dioxide originally reviewed by the Panel.[192]

While it is not clear whether the FDA intended to include nanoparticles in its definition of "micronized," these monograph statements parallel the more general statements that the FDA has made in the context of nanoparticles that "particle size is not the issue."[193]

IV. FLAWS IN THE CURRENT FDA REGULATION OF NANOTECH PRODUCTS FOR HUMAN CONSUMPTION

A. *FDA Regulations on Ingredient Labeling*

The FDA takes the position that there is no need for labeling on products for human consumption that contain nanomaterials. Under the FDCA, a drug, device, food, dietary supplement, cosmetic, or sunscreen is deemed misbranded if its labeling is "false or misleading in any particular."[194]

> If an article is alleged to be misbranded because the labeling or advertising is misleading, then in determining whether the labeling or advertising is misleading . . . there shall be taken into account (among other things) not only representations made or suggested by statement, word, design, device, or any combination thereof, *but also the extent to which the labeling or advertising fails to reveal facts material in the light of such representations* or material with respect to consequences which may result from the use of the article to which the labeling or advertising relates under the conditions of use prescribed in the labeling or advertising relates under the conditions

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[192] *Id.* at 27671. The FDA explains that "micronized" simply refers to "a refinement of particle size distribution." *Id.* And that its position on bioequivalence is based on the fact that "fines" have been a part of titanium dioxide powders for decades. *Id.*; *see also Frequently Asked Questions on OTC Drugs*, FDA, http://www.fda.gov/Drugs/DevelopmentApprovalProcess/SmallBusinessAssistance/ucm069917.htm The FDA goes on to state that it was not "aware of any evidence at this time that demonstrates a safety concern from the use of micronized titanium dioxide in sunscreen products." Final Monograph, *supra* note 48, at 27671.

[193] *See supra* notes 127–28 and accompanying text (discussing the fact that the FDA does not see a scientific basis for the conclusion that nanoscale materials are any more inherently hazardous than non-nanoscale materials as well as the fact that the FDA announced that its existing health and safety tests are adequate assessors of health effects of nanoparticles).

[194] 21 U.S.C. § 362(a) (2006); *see also* 21 C.F.R. § 701.1 (2011).

> of use prescribed in the labeling or advertising thereof or under such conditions of use as are customary or usual.[195]

The FDA opines that product ingredient lists that refer to nanomaterial content by the same name as the normal size material counterpart are not false and misleading as there is no scientific basis on which to conclude that nanoscale materials as a class are inherently more hazardous than non-nanoscale materials. Thus, the FDA has taken the position that the fact that a product marketed for direct and indirect human consumption contains nanomaterials is not material and need not be disclosed on labels.

1. *Labeling, Notice, Distributional Justice, and Accountability*

Because nanotech ingredients are not listed on food, dietary supplements, cosmetic, or sunscreen labels, a consumer cannot choose to avoid products that contain nanotech ingredients. And yet, if there is an injury, who will bear the cost of the loss? Decision Analysis teaches that there are two significant types of error that can be made when dealing with scientific uncertainty. A type I error, also called an α error or an error of the first kind, occurs "if society regulates an activity that appears to be hazardous, but turns out later to be harmless (a 'false positive' in the parlance of experimental findings) and resources are needlessly expended."[196] A type II error, also referred to as a β error or an error of the second kind, occurs "if society fails to regulate an activity because the evidence is not initially thought to be strong enough, but that finally turns out to be harmful (a 'false negative')."[197] In the case of nanotech food, dietary supplements, cosmetics, and sunscreens, when a type I error occurs, the cost of that error is absorbed by the companies who produce the nanotech products. That cost, in turn, is shifted onto those consumers who purchase the products.

In contrast, when a type II error occurs, the cost is left squarely on the shoulders of those consumers who suffer a toxic injury from the consumption of a nanotech food, dietary supplement, cosmetic, or sunscreen. This result follows from the inability of the consumer to recover for those injuries under the tort system. The principle reasons for

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[195] 21 U.S.C. § 321(n) (emphasis added); *see also id.* § 331(a) (prohibiting the introduction into commerce of any food, device, or cosmetic that is misbranded); *id.* § 343(a) (stating that foods are misbranded if their labeling is "false or misleading in any particular"); *id.* § 352(a) (stating that drugs and devices are misbranded if their labeling is "false or misleading in any particular"); *id.* § 362(a) (stating that cosmetics are misbranded if their labeling is "false or misleading in any particular").

[196] Nicholas A. Ashford, *The Legacy of the Precautionary Principle in US Law: The Rise of Cost-Benefit Analysis and Risk Assessment as Undermining Factors in Health, Safety and Environmental Protection*, *in* IMPLEMENTING THE PRECAUTIONARY PRINCIPLE: APPROACHES FROM THE NORDIC COUNTRIES, EU AND USA 352, 369 (Nicolas de Sadeleer ed., 2007).

[197] *Id.*

this result are three-fold. First, as nanotech ingredients are not required to be listed on product labels, the consumer will not know that she was exposed to a nanotech ingredient. Thus, the consumer is unlikely to suspect that her injuries were caused by a novel substance.[198] Moreover, many of the health effects from toxic exposures are cumulative and generally do not appear for decades. Second, if the consumer learns that a nanotech ingredient was the cause of her injury, she will be required to establish fault under tort law by showing that the manufacturer could have foreseen the risk of harm.[199] As with many new technologies, the rate of the introduction of nanotech products into the market has far out-paced the science needed to demonstrate its associated risks. Under either the *Daubert* or *Frye* tests, this research lag acts to insulate a manufacturer from liability based on a lack of causation[200] and foreseeability.[201]

The final hurdle arises in the context of both negligence and strict liability claims. Unless the consumer can establish that she is a member of a substantial class of people who are at risk for the same type of adverse reaction, the case is likely to be dismissed under what is commonly referred to as the "idiosyncratic plaintiff defense."[202] This "*de minimus* harm" liability threshold can range from tens of thousands to millions of people.[203] Compounding this problem, as nanotech ingredients in food, dietary supplements, cosmetics, and sunscreens are unlabeled, injured consumers are unlikely to recognize what actually caused their injuries. As a result, these injuries will go unreported. Without this data, a consumer will be unable to establish that she is a member of a substantial class, creating an almost impassable barrier to recovery.[204] Even if the products were labeled, and a data collection system was established, it could be years before enough people were injured to reach the large threshold numbers expected under the burden of production created by this defense.[205]

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[198] Van Tassel, *supra* note 137, at 1681.

[199] *Id.* at 1683–84.

[200] Under the *Daubert* and *Frye* standards, evidentiary principles are likely to bar any introduction of scientific evidence to meet the burden of proof on causation as long as there is scientific uncertainty. Daubert v. Merrell Dow Pharm., Inc. 509 U.S. 579, 589 (1993); Frye v. United States, 293 F. 1013, 1014 (D.C. Cir. 1923). The *Daubert* factors counsel judges to ask the following questions in making decisions on the admissibility of scientific evidence: (1) Has the technique been tested in actual field conditions (and not just in a laboratory)?; (2) Has the technique been subject to peer review and publication?; (3) What is the known or potential rate of error? Is it zero, or low enough to be close to zero?; (4) Do standards exist for the control of the technique's operation?; and, (5) Has the technique been generally accepted within the relevant scientific community? *Daubert*, 509 U.S. at 580.

[201] Van Tassel, *supra* note 137, at 1683–84.

[202] *Id.* at 1680, 1683–84. This defense is basically a contention that a reasonable consumer would not have had the reaction and that the defect is in the consumer, not the product. *Id.*

[203] *Id.*

[204] *Id.*

[205] *Id.* at 1682–84.

The bottom line under the current system is that the personal injury costs associated with a type II error will be borne by innocent consumers and not the food, dietary supplements, cosmetics, and sunscreen manufacturers who reap the profits from product sales. This disconnect results in a morally suspect outcome under principles of distributive justice that counsel that one ought to act in such a manner that no one person or group bears a disproportionate share of benefits or burdens.

B. *Placing the Burden of Proof on the FDA*

An example of the implications of placing the burden of proof for safety on the FDA to prove that nanotech food, dietary supplements, and cosmetics are unsafe and ineffective is the case of a product called Ephedra, a dietary supplement which contained ephedrine-alkaloid ingredients.[206] Ephedrine alkaloids occur naturally in some plants, work as stimulants and fall into the same category as the street drug referred to as "Speed."[207] Products containing ephedrine alkaloids were marketed as dietary supplements for weight loss and to enhance sports performance.[208] Over time, the FDA began receiving adverse event reports ("AERs") from consumers which included numerous complaints of heart attacks, strokes, seizures, and deaths associated with the consumption of products containing ephedrine alkaloids.[209] One of the most highly-publicized cases of a fatal consequence from the use of ephedrine alkaloids in a dietary supplement was the death of Steve Belcher, a twenty-three-year-old baseball player with the Baltimore Orioles.[210]

In order to meet its burden of proof, the FDA took seven years to gather sufficient evidence on the safety of ephedrine alkaloids. The FDA compiled an administrative record of 130,000 pages, 19,000 AERs, and engaged in extensive notice and comment before it passed a regulation banning the sale of products containing ephedrine alkaloids in 2004.[211] In this final rule, the FDA stated that "[t]he best clinical evidence for a benefit . . . supports only a modest short-term weight loss, insufficient to positively affect cardiovascular risk factors or health conditions associated

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[206] Nutraceutical Corp. v. Von Eschenbach, 459 F.3d 1033, 1036 (10th Cir. 2006).

[207] Barry A. Palevitz, *Harmless Energizers or Dangerous Drugs?*, SCIENTIST, Dec. 9, 2002, at 18, 18–19 ("Ephedrine is a close relative of amphetamine, sometimes called benzedrene. A little chemical tinkering creates the street drugs methamphetamine and Ecstasy.").

[208] *Nutraceutical Corp.*, 459 F.3d at 1036.

[209] *Id.*

[210] FRAN HAWTHORNE, INSIDE THE FDA: THE BUSINESS AND POLITICS BEHIND THE DRUGS WE TAKE AND THE FOOD WE EAT 57 (2005).

[211] *Final Rule Declaring Dietary Supplements Containing Ephedrine Alkaloids Adulterated Because They Present an Unreasonable Risk*, 69 Fed. Reg. 6788 (Feb. 11, 2004) [hereinafter *Final Rule*]; *Nutraceutical Corp.*, 459 F.3d at 1036.

with being overweight or obese."[212] The manufacturer of Ephedra filed suit, arguing that the FDA had failed to meet its burden of proof of showing that products containing ephedrine alkaloids were unsafe.[213] The district court found for the manufacturer; however, in 2006, the FDA prevailed on appeal.[214] The total time and expense involved in this process, including the cost of the harm suffered by consumers, was tremendous.[215]

The rising concern that the FDA has been unable to keep pace with emerging science and technology magnifies the problem of placing the burden of proof for safety on the FDA. In 2006, the Commissioner of the FDA requested that the FDA's Science Board appoint a Subcommittee on Science and Technology. The assigned task of this thirty-three-member subcommittee was to evaluate "whether [the] FDA's scientific and technological infrastructure could support current and future regulatory needs."[216] In November of 2007, the subcommittee issued its report with the unanimous approval of the panel members.[217] The report "identified serious deficiencies in the present system, including too few scientists who understand emerging science and technology, a flawed system for regulating imports into the United States and an information infrastructure that was deeply flawed and unable to support various areas in the agency."[218] In its 2008 report in response to the request of Representatives Dingell, Waxman, Stupak, and Pallone, the subcommittee noted that

> the capacity of science to support the FDA mission is dangerously constrained from the effects of a long period of expanding Agency mandates and responsibilities, chronic under funding, the extraordinary advance of scientific discoveries, the complexity of new products and claims submitted to the FDA for premarket approval, the emergence of challenging safety problems, and the globalization of the industries that the FDA regulates.[219]

The report noted that "there is insufficient capacity in modeling, risk

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[212] *Nutraceutical Corp.*, 459 F.3d at 1036–37.

[213] *Id.* at 1043–44.

[214] *Id.* at 1038–39.

[215] *Final Rule*, *supra* note 211.

[216] SCHULTZ & BARCLAY, *supra* note 1, at 20.

[217] U.S. FOOD & DRUG ADMIN., FDA SCIENCE AND MISSION AT RISK; REPORT OF THE SUBCOMMITTEE ON SCIENCE AND TECHNOLOGY 7 (Nov. 2007) [hereinafter FDA SCIENCE AND MISSION AT RISK], *available at* http://www.fda.gov/ohrms/dockets/ac/07/briefing/2007-4329b_02_01_FDA%20Report%20on%20Science%20and%20Technology.pdf.

[218] SCHULTZ & BARCLAY, *supra* note 1, at 20.

[219] SCHULZ & BARCLAY, *supra* note 1, at 20 (referencing FDA SCIENCE AND MISSION AT RISK, *supra* note 217).

assessment and analysis" and that the "FDA['s] science agenda lacks a coherent structure and vision, as well as effective coordination and prioritization."[220] The report concluded that the FDA "cannot fulfill its mission because its scientific base has eroded, its scientific workforce does not have sufficient capacity and capability and its information technology infrastructure is inadequate."[221]

C. *Testing For Safety*

The past decade has elevated the level of scientific understanding of the health risks associated with nanoparticles from ignorance to indeterminacy. Scientists now know what they do not know about health risks and are able to plan the tests to discover those risks. The FDA can no longer ignore this large body of science and should begin the process of toxicological screening using predictive toxicology. Only then will the FDA have the body of evidence that it needs to meet its burden of proof under the current system to show that the nanotech products marketed for direct and indirect human consumption are unsafe and should be removed from the market.

D. *Ingredient Labeling and the Discovery of New Toxicants*

As a public health matter, the reality is that scaling up testing to a reasonable level, even with the use of predictive toxicology, will only detect a portion of all the potential toxicants associated with nanoparticles. There are two basic reasons for this conclusion. First, the science for testing for health risks of nanoparticles is in its infancy.[222] Second, additional significant risks to health may materialize because it is probable that, as scientific understanding grows and as new types of nanoparticles are created, new properties will be discovered that can lead to novel mechanisms of toxicity.[223]

As a result, many toxicants created by nanotech products will not be identified until after the product is introduced into the market and is exposed to the vast genetic diversity of the population. Over time, this exposure will reveal the type, severity, and statistical probability of any associated adverse reactions. For example, the drug industry regularly introduces novel substances into the general population recognizing that this is the only method that can fully identify the statistical probability of

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[220] SCHULZ & BARCLAY, *supra* note 1, at 20 (referencing FDA SCIENCE AND MISSION AT RISK, *supra* note 217, at 30, 33).

[221] SCHULZ & BARCLAY, *supra* note 1, at 20 (referencing FDA SCIENCE AND MISSION AT RISK, *supra* note 217, at i).

[222] Nel et al., *supra* note 51, at 626–27.

[223] SCENIHR, *supra* note 54, at 4.

adverse reactions.[224] This is because the clinical trials mandated by the FDA to establish premarket safety are fairly small and can have relatively low statistical power.[225] Consequently, even after FDA testing, serious adverse effects were not detected for approximately one-half of drugs on the market until after the drugs received regulatory approval and were made available to the general population.[226]

Thus, there is a regulatory recognition that premarket testing will not detect many adverse reactions when novel substances are distributed to the general population for use as drugs. For this reason, a very limited post-market surveillance system is in place to collect at least some data from some portions of the general population on their negative experiences with new drugs.[227] After the spate of highly-publicized drug withdrawals,[228] including Vioxx, this tracking system is being updated and strengthened.[229] Comparably, a system that pairs premarket safety testing with a post-market surveillance should be created as a pre-condition for the introduction of other novel, man-made substances into the market, such as nanotechnology used in consumer products that are absorbed by the body.

As the system exists today, there is no mechanism for public health officials to monitor whether nanotech products marketed for direct and indirect human consumption are triggering toxic reactions. The vast majority of consumers are unaware of the extent of their exposure to novel nanotech substances in spite of the extraordinary yearly growth in the national and global production of nanotech products. Consequently, it is currently highly unlikely that many of the health risks from this exposure can be identified and eliminated. For example, if a consumer uses a nanotech product and has a toxic reaction, the consumer will assume that the reaction is to the product itself, not an exposure to the nanoparticle ingredient. The only result is that the consumer will avoid that particular product in the future. A mild reaction will not merit a visit to a physician and will go unreported. If the reaction is moderate to severe, a physician may be consulted. However, there is no mandatory physician reporting of adverse effects to this type of product. And even if the physician has the time and inclination to report the adverse reaction, it will be incorrectly

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[224] Kevin Bullis, *Screening for Toxic Nanoparticles: Researchers Suggest a Strategy That Could Weed Out Dangerous Nanoparticles*, TECH. REV. (Feb. 7, 2006), http://www.technologyreview.com/NanoTech-Devices/wtr_16296,303,pl.html.

[225] Shelby D. Reed et al., *Use of Larger Versus Smaller Drug-Safety Databases Before Regulatory Approval: The Trade-Offs*, 27 HEALTH AFF. 360, 360–61 (2008).

[226] *Id.* at 366–67.

[227] Rena Steinzor & Margaret Clune, *The Hidden Lesson of the Vioxx Fiasco: Reviving a Hollow FDA*, CPR WHITE PAPER #514 (Center for Progressive Reform, Washington, D.C.), Oct. 2005, at 19, *available at* http://www.progressivereform.org/articles/Vioxx_514.pdf.

[228] Henry A. Waxman, *The Lessons of Vioxx—Drug Safety and Sales*, 352 NEW ENG. J. MED. 2576, 2576–78 (2005); Steinzor & Clune, *supra* note 227, at 1.

[229] Steinzor & Clune, *supra* note 227, at 19.

reported as a reaction to the particular product based on the information given by the patient, not to its nanotech content. And even if there was mandatory reporting, who would collect the report? The Centers for Disease Control and Prevention ("CDC") is neither required nor is set up to collect or monitor this type of data. Finally, some of the adverse health effects to nanotech toxicants may be delayed or latent (such as an increased occurrence of cancer). This lag time means that some long-term, serious adverse effects may not be connected to the nanoparticle exposures until a considerable period of time has passed.

Overall, as a public health matter, it appears that data collection for nanoparticle exposure should proceed in a manner that is similar to that which is used for other types of biologically active novel chemicals introduced into the market for absorption into the human body, such as drugs.

V. PROPOSALS FOR RESTRUCTURING THE REGULATION OF NANOTECH PRODUCTS FOR HUMAN CONSUMPTION

There are several steps that must be taken in order to update the FDA's regulation of nanotech products intended for human consumption to protect human health while supporting innovation. Drugs, food additives, and sunscreens already require premarket testing for all new chemicals. Consequently, the regulatory changes necessary to protect public safety will take less effort overall with these categories of products than the work that will be necessary in order to pass the new legislation that will be required in cases of dietary supplements and cosmetics.

A. *Drugs, Food Additives, and Sunscreens*

1. *FDA Acknowledgment That Nano Means Fundamentally Different*

Drugs, food additives, and sunscreens already require premarket testing for all new chemicals.[230] Consequently, if the FDA acknowledges that nano does not just mean small, it means fundamentally different as well, most of the rest of the needed changes will automatically fall into place. Under current regulations, this acknowledgment that nanotech versions of active ingredients are new chemicals will ensure that drugs, food additives, and sunscreens that have already been approved by the FDA, but are later modified to add nanotech particles, will undergo a new and complete round of safety testing in order to obtain premarket approval from the FDA.

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[230] *See supra* notes 129–36, 147–54, 177–93 and accompanying text.

2. *Nanotech Ingredient Labeling*

Under the current consumer product safety system, there is no mechanism in place for public health officials to monitor whether the heavy exposure of U.S. consumers to nanotech products marketed for direct and indirect human consumption is causing acute or latent toxic reactions. The new understanding that nanotech particles create novel, biologically active ingredients, in conjunction with the lack of definitive testing for toxicological effects of new nanoparticles, counsels for the establishment of a post-market surveillance system for monitoring for any unintended effects of nanotech food, dietary supplements, cosmetics, and sunscreens. Once the FDA acknowledges that nanotech particles are new chemicals, ingredient labeling will be required, removing the major obstacle to gathering data on toxicity.[231] Referring to nanomaterial content by the same name as the normal size material counterpart will then be false and misleading since nanoscale materials as a class will be recognized as inherently more hazardous than non-nanoscale materials. Thus, the fact that a product marketed for direct and indirect human consumption contains nanomaterials would become "material" and would have to be disclosed on labels.[232]

3. *Post-Market Surveillance*

As discussed above, requiring premarket testing is only a partial solution. Based on the current immature level of the science for health risk detection, many toxicants are unlikely to be identified until the general population is using these novel nanoproducts and adverse reactions begin to appear as a result of the exposure of the product to the enormously diverse U.S. gene pool. A post-market surveillance system, created through new legislation, will allow public health officials to monitor this data, thereby providing an early warning system to alert public health officials if there are toxic reactions to a particular nanotech product. This will allow a quick recall of the product preventing needless injuries to consumers. The proposed Food Safety Enhancement Act of 2009,[233] which

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[231] 21 C.F.R. § 101.18 (2011) (addressing the misbranding of food); *id.* § 201.6 (2010) (addressing drugs and misleading statements); *id.* § 701.1 (2011) (addressing cosmetics, labeling, and misbranding).

[232] *See supra* notes 194–95 and accompanying text.

[233] Food Safety Enhancement Act of 2009, H.R. 2749, 111th Cong. Introduced in early June, the Act would amend the Federal Food, Drug, and Cosmetic Act to require each food facility to: "(1) conduct a hazard analysis (or more than one if appropriate); (2) identify and implement effective preventive controls"; and (3) implement a food safety plan. *Id.* §§ 418(a), 418A. The Act would require the Secretary of Health and Human Services ("HHS") to: (1) "issue guidance or promulgate regulations to establish science based standards" to minimize the hazards from food borne contaminants, *id.* §§ 418A(b)(3)(A), 419(a); (2) "establish by regulation scientific and risk-based food safety standards for . . . raw agricultural commodities," *id.* § 419A(a); (3) inspect facilities at a

was passed by the House of Representatives in August of 2009, includes a requirement for the creation of a food tracking system[234] in order to quickly locate the source of any outbreak of food-borne illness.[235] A tracking system for all nanoparticle products marketed for human consumption could easily be grafted onto this food safety system.

B. *Dietary Supplements and Cosmetics*

1. *Switching the Burden of Proof for Safety, Labeling, and Post-Market Surveillance*

In order to remedy the regulation of nanotech dietary supplements and cosmetics, new legislation will be required that will place the burden of proof for safety onto the manufacturers by requiring that these products undergo the FDA premarket approval process. In the case of dietary supplements, this means a revision to the current legislation that places the burden of proof on the FDA to show that "new" ingredients are unsafe. This revision must switch the burden of proof from the FDA to manufacturers. In the case of cosmetics, it means creating entirely new legislation that requires that nanotech cosmetics undergo the FDA premarket approval process. Active ingredients are already required to be placed on dietary supplement and cosmetic labels.[236] A policy change by the FDA acknowledging nanotech ingredients as new chemicals, as recommended above, will result in nanotech ingredient labeling under current regulations. A post-market surveillance system for all nanotech products marketed for human consumption, as outlined above, should also be included in any new legislation.

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frequency determined pursuant to a risk-based schedule, *id.* § 105(a)(4)(A); (4) establish a food tracing system, *id.* § 107(c)(2); (5) assess fees relating to food facility re-inspection and food recall *id.* § 743A(a)–(b); and (6) establish a program for accreditation of laboratories that perform analytical testing of food for import or export, *id.* § 714(b). The proposed Act goes on to authorize the Secretary to: (1) order an immediate cessation of distribution, or a recall, of food, *id.* § 420(f)(1); (2) develop "safety and security guidelines applicable to the importation of food," *id.* § 805(b)(1); and (3) quarantine food in any geographic area within the United States, *id.* § 133(b)(i)(1).

[234] The HHS Secretary "shall by regulation establish a tracing system for food that is located in the United States or is for import into the United States." *Id.* § 107(c)(2). Direct sales by farms, restaurants, or grocery stores to consumers are exempted from the Act. *Id.* § 101(a)(1)(A)–(B). A facility shall recall an article of food or ingredient that presents a reasonable probability that it is a threat to human health. The HHS Secretary may request a recall if the Secretary "has reason to believe [the food] is adulterated, misbranded, or otherwise in violation of [the] Act." *Id.* § 420(a)(1). The HHS Secretary may order a facility to cease distribution of a food product "[i]f the Secretary ha[s] reason to believe that the use, consumption of, or exposure to, an article of food may cause serious adverse health consequences or death to humans or animals." *Id.* at § 420(b)(1). Similarly, the HHS Secretary may order a recall. *Id.* at § 420(e).

[235] The CDC "shall enhance food-borne illness surveillance . . . by coordinating Federal, State and local food-borne illness surveillance systems . . . ." *Id.* § 121(b).

[236] *See supra* note 231.

C. *Revisions to Analytical Tools Used to Evaluate the Need for Regulation of Innovative Technologies*

There are two hurdles that must be addressed in order for new legislation for the regulation of all nanotech products marketed for human consumption to be successfully adopted. First, the risk-benefit analysis used by the FDA to evaluate health risks must be revised. Second, the recent reliance by administrative agencies and legislators on cost-benefit analysis must be abandoned.

1. *Risk-Benefit Analysis*

As discussed in the following sections, the FDA conclusions to date with regard to nanotech particles are a function of its reliance on risk-benefit analysis in order to make regulatory decisions about innovative technologies. The problem with this reliance, as demonstrated clearly with the marketing of nanotech food, dietary supplements, cosmetics, and sunscreens, is that there is invariably a lag time between the production of the innovative technology and the development of the science necessary to identify the risks associated with that technology. Thus, the FDA has to wait to use its risk-benefit tool to regulate to protect public health until the state of the science on health risks catches up to the innovation itself. During this scientific lag time, manufacturers are free to market their products with no interference and no notice to unsuspecting consumers.

The FDA's regulatory reliance on risk-benefit analysis when there is insufficient evidence to actually quantify health risks—in other words, when there is uncertainty—results in several serious consequences for public health. First, the number of products containing nanotech particles that are marketed for direct and indirect human consumption grows daily. The FDA is not taking any steps to protect consumers by ensuring that these nanotech products are safe for direct or indirect human consumption. Second, the FDA is thwarting consumers' ability to protect themselves against any additional risks of harm by finding that manufacturers have no obligation to identify nanotech ingredients on product labels. Thus, consumers are not aware that they are being exposed to a novel substance with unique health risks. Finally, the FDA is failing to conduct the appropriate scientific testing in order to resolve the question of nanotech product safety. As long as the FDA relies on the tests for health risks created for and utilized on bulk materials to make determinations on the safety of nanoparticles, the data necessary to show that a nanotech product marketed for direct and indirect human consumption is unsafe and should be pulled from the market will never be developed.

a. Lessons Learned from History

There are numerous examples of the serious health consequences of this lag time between the introduction of new chemicals and technologies

into the market and the development of the science that defines the associated human health risks. The list includes the evolving understanding of endocrine disruption caused by tributylin ("TBT"), polychlorinated biphenyls ("PCBs"), diethylstilbestrol ("DES"), the Great Lakes pollution, and Thalidomide.[237] Illustratively, evidence existed in the 1930s that PCBs could cause serious harm to human health.[238] However, it was not until the 1970s that the first action was taken by Sweden to ban these chemicals; the European Union followed suit in 1996, implementing a phase-out to be completed by 2010.[239] Scientists are still grappling to understand the devastating consequences of a fifty year period of human and environmental exposure to organochlorine compounds used as pesticides in the Great Lakes area.[240] The marketing of these chemicals occurred in spite of the publication of the book *Silent Spring* in 1962 that warned of the negative health effects on humans and wildlife of this exposure.[241]

The time lag between the first scientific warnings over medical x-rays (1896), benzene (1897), and asbestos (1898), and when policy makers finally took action to reduce damage was between thirty and one hundred years.[242] The consequences of failure to act in time can have a "long tail" when there is a long latent period between exposure and negative health consequences. For example, the introduction of CFCs and the creation of the ozone hole are resulting in thousands of additional skin cancers that will only peak in number in the middle of this century. Another example is the introduction onto the market of DES to prevent miscarriages.[243] DES was introduced in 1947 and was widely distributed until 1970 when the first evidence that it produced human cancer appeared.[244] The fact that DES was an animal carcinogen was identified in 1938.[245] These are just a few examples[246] of the long lag time that can occur between the identification of an association between exposures to new technologies and negative health consequences, and the eventual understanding of how the

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[237] David Gee, *Late Lessons from Early Warnings: Toward Realism and Precaution with Endocrine-Disrupting Substances*, 114 ENVTL. HEALTH PERSP. 152, 156 (2006); *see also* Van Tassel, *supra* note 129, at 228–29 (discussing the case of Thalidomide).

[238] EUROPEAN ENV'T AGENCY, ENVTL. ISSUE REP. NO. 22, LATE LESSONS FROM EARLY WARNINGS: THE PRECAUTIONARY PRINCIPLE 1896–2000 66–69 (2001).

[239] *Id.*

[240] EUROPEAN ENV'T AGENCY, *supra* note 238, at 126.

[241] *Id.*

[242] Gee, *supra* note 237, at 155.

[243] *Id.* at 155–56.

[244] EUROPEAN ENV'T AGENCY, *supra* note 238, at 153.

[245] *Id.* at 152–53.

[246] For a comprehensive analysis of fourteen case studies of these types of scenarios, see generally EUROPEAN ENV'T AGENCY, *supra* note 238.

new technology actually causes the negative health effects.

2. *Dealing With Uncertainty in the Face of Clear Warnings*

While the use of engineered nanoparticles in products marketed for direct and indirect human consumption and the resultant exposure of consumers is growing daily, the body of science necessary to identify the health risks associated with engineered nanoparticles is still in its infancy. As has occurred so often in the past, this scientific lag time creates a period when there is an information void with regard to the risks to human health. As this information void is slowly filled through scientific experimentation, the level of uncertainty over health risks commonly progresses from ignorance (where scientists *don't know* what they don't know) to indeterminacy (where scientists *know* what they don't know but can plan the scientific experiments necessary to find out) to, finally, a tipping point in the state of knowledge when classic probability analysis can be applied to predict, or quantify, risk levels to human health.

When the FDA first made its decisions on how to regulate nanotech products, far less was known about the distinctive properties of nanoparticles, their uniquely high level of bioreactivity, and the resultant heightened potential for adverse health effects. Scientists simply "did not know what they did not know" about the health risks associated with nanotech particles. At that point in time, the FDA made its regulatory choices in an environment of ignorance, choosing to regulate based on what scientists now know to be a false assumption of bioequivalence. Over the past several years, a parade of major scientific discoveries has shifted the nature of the uncertainty over the public health risks of nanotech particles from ignorance to indeterminacy. In other words, scientists have progressed from *not knowing* what they do not know, to *knowing* what they do not know.

Scientists now understand that engineered nanoparticles may create novel health risks caused by powerful nano-bio interactions that have never before existed in nature. In order to move from indeterminacy to classic risk analysis, scientists must determine the nature and extent of the harm that occurs as a result of these nano-bio interactions. Then, using classic uncertainty principles, scientists must quantify the probability and degree of those harms. Thus, the new awareness on the part of scientists that nanoparticles can cause serious physical harm, and the identification of some of the potential mechanisms for causation, opens the door to the ability to plan out the systematic study of each new type of engineered nanoparticle in order to eliminate or confirm the associated health risks.

In spite of the fact that the state of the science has now moved into indeterminacy, the FDA's reliance on classic risk/benefit analysis in making decisions over whether to regulate for safety means that, until the science on the health risks associated with nanoparticles has matured to the

point that the risks can be quantified, the FDA will proceed as if this growing body of science did not exist. Taking note of lessons from past introductions of new technologies which involved clear warning signals, but also uncertainties over health risks, the FDA should modify its analysis to incorporate trade-off analysis.

3. *The Use of Trade-Off Analysis*

Applying trade-off analysis allows for the consideration of new kinds of uncertainties, as well as attendant risk mitigation strategies and factors into the analysis of the societal distribution of possible costs and benefits of policies and innovative technologies. Elements of trade-off analysis include:

- the seriousness and irreversibility of the harm addressed;
- the social distribution of possible costs and benefits of policies and technologies;
- the technological options for preventing, arresting, reversing or mitigating possible harm and the opportunity costs of selecting a given policy option;
- society's inclinations regarding erring on the side of caution and erring on the side of laxity; and
- the nature of uncertainty encountered: classical uncertainty, indeterminacy, or ignorance.[247]

Application of the above factors to nanotech products marketed for direct and indirect human consumption reveals the following: the harm is cumulative and causes irreversible damage to multiple different bodily functions that may, in the long run, be life threatening; the cost of the loss associated with any harm will be borne by the factory workers who handle the nanoparticles during the manufacturing process and consumers, while the nanotech product manufacturers reap the profits; the cost of identifying nanotech ingredients on product labels is very, very small and the cost of setting up a web based reporting system modeled on systems already in place at the FDA is even smaller; surveys indicate that consumers are tentatively supportive of nanotech products that have important benefits

[247] Ashford, *supra* note 196, at 371.

but have a clear preference for labeling and notice;[248] and, finally, scientists are no longer operating in ignorance as the state of the science has moved into indeterminacy and the possibility of serious health risks are no longer based on mere speculation. Therefore, as the risk of harm is serious, maybe even life threatening, and is cumulative and irreversible, the cost of the risk mitigation strategy of ingredient labeling and post market surveillance is small, the public will is to err on the side of caution, and the state of the science is indeterminacy not ignorance, trade-off analysis counsels for the implementation of the risk mitigation strategies of premarket testing, labeling, and post-market surveillance.

These risk mitigation strategies will allow for the creation of systems for the collection of data that will allow injured consumers to meet the *Daubert* and *Frye* admissibility standards necessary to establish causation.[249] In addition, the data will be available to allow an injured consumer to surmount the idiosyncratic plaintiff defense and the foreseeability pre-condition to tort recovery. These strategies will also encourage a more appropriate level of private investment into research to test for public health effects of this innovative technology. This investment will be passed on to increase the price of the use of nanotechnology in products, putting the brakes on the current free-for-all and allowing for a more measured growth of the type of products that use nanotechnology during this period of scientific uncertainty regarding the risks to public health.

4. *Abandonment of the Cost-Benefit Analysis*

A risk-benefit analysis performed today, that factors in different levels of uncertainty as reflected in trade-off analysis, suggests that the benefits of nanotech products for human consumption only outweigh human health risks if risk mitigation strategies, such as premarket testing, nanoparticle ingredient labeling, and post-market surveillance, are employed. Unfortunately, even if a trade-off analysis is adopted by the FDA, modern day risk assessment used to evaluate public health regulations has been functionally co-opted and has become a two-step process. The first step is the risk-benefit step discussed above. The second step entails the performance of a cost-benefit analysis of all new legislation. The use of cost-benefit analysis is both inappropriate and destructive in the context of evaluating the impact of new technologies on public health, discourages

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[248] *Study Points Way to Communicating Nanotech*, SCIENCEDAILY (Feb. 3, 2007), http://www.sciencedaily.com/releases/2007/01/070131211717.htm. *But see Nanotechnology: To Know it is not Necessarily to Love it*, SCIENCEDAILY (Dec. 8, 2008), http://www.sciencedaily.com/releases/2008/12/081208114302.htm (reporting the findings of a study indicating that consumer support may be tied to cultural predispositions).

[249] *See supra* notes 200–01 and accompanying text.

investment into health risk research, and short circuits the injury recovery system.

Triggered in 1994 by then Speaker of the House Newt Gingrich's "Contract with America,"[250] a series of legislative and executive orders mandated that all new federal regulatory proposals include a cost-benefit analysis[251] justifying the cost of regulation.[252] Lessons from the past demonstrate that this cost-benefit hurdle has undermined public health and safety as it is common for the development of new technologies to far outpace the development of the science necessary to test for the risks associated with those technologies.[253] Health risks take time to quantify. Until they are quantified, risk mitigation strategies have no measurable benefit to out-balance the associated costs. Thus, the result of a cost-benefit analysis for any proposed public health measure to monitor the health effects of new technologies is a non-starter when many new technologies first enter the market.[254]

As the type of uncertainty over public health risks of nanotech products marketed for direct and indirect human consumption is indeterminacy, the FDA and Congress should avoid the application of

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[250] Ashford, *supra* note 196, at 356–57 (internal quotation marks omitted).

[251]

> In theory, cost-benefit analysis of a policy option enumerates all possible consequences, both positive and negative; estimates the probability of each; estimates the benefit or loss to society should each occur, expressed in monetary terms; computes the expected social benefit or loss from each consequence by multiplying the amount of the associated benefit or loss by its probability of occurrence; and computes the net expected social benefit or loss associated with the government policy by summing over the various possible consequences. The reference point for these calculations is the state of the economy in the absence of the government policy, termed the 'baseline.'

Id. at 366.

[252] Cost-benefit analysis attempts to describe the consequences of a candidate regulation in monetary terms.

> This poses two problems. One is the difficulty, even arbitrariness, of placing a monetary value on human life, health and safety and a healthy environment. Another is that by translating all of these consequences into equivalent monetary units, discounting each to current value (since a US$/Euro invested now is expected to earn interest over time), and aggregating them into a single US$/Euro value intended to express the net social effect of the government policy, the effects on the economy from investing now in future health, safety and environmental benefits are weighted far more heavily than those benefits that occur in the future, including those to future generations.

Id. at 367.

[253] EUROPEAN ENV'T AGENCY, *supra* note 238, at 194.

[254] Steffen Foss Hansen et al., Commentary, *Late Lessons from Early Warnings for Nanotechnology*, 3 NATURE NANOTECHNOLOGY 444, 444–47 (2008).

formulaic cost-benefit analysis when performing a risk assessment to decide whether such a system is warranted. In addition to other shortcomings,[255] cost-benefit analysis leads to a quick and dirty "if you cannot quantify it, it does not exist" conclusion and produces a single number that fails to reveal who benefits and who pays.[256] The FDA should uncouple cost-benefit analysis from risk assessment to avoid being in the position of reacting to public health crises rather than preventing them. Instead, regulators should apply a risk assessment that uses trade-off analysis.

The mistakes made with prior introductions of new chemicals and technologies into society are looking progressively more similar to the concerns now being raised regarding various forms of nanotechnologies, including nanotech food, dietary supplements, cosmetics, and sunscreens. Until recently, even a pure risk assessment coupled with trade-off analysis has counseled against the need for premarket testing, labeling, and post-market surveillance. The risks to public health appeared to be based on little more than speculation. The past decade has brought a dramatic change in this picture in the form of the new scientific understanding of the health effects of nanotech particles. The FDA is now faced with more than just speculation over the possible health risks associated with nanoparticles used in products marketed for human consumption. While still not quantified, the level and extent of the risk of unintended health consequences from nanoparticle exposure is now quantifiable. When regulating new technologies, such as engineered nanoparticles,[257] if the FDA continues to rely on rigid cost-benefit analysis when the risk is not yet quantified, but is quantifiable through scientific testing, the FDA will be continuously operating behind the curve, reacting to public health crises rather than preventing them. Instead, the FDA should learn from the lessons of past technologies, abandon the use of cost-benefit analysis and apply trade-off analysis when engaging in risk assessment to evaluate new technology regulations designed to protect public health.

IX. CONCLUSION

The number of nanotech products marketed for direct and indirect human consumption is increasing yearly. This growth is paralleled by steadily increasing human exposure to these novel, highly bioreactive substances. At the same time, the current regulatory system discourages the proper level of investment into research for public health risk

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[255] *See supra* note 253 and accompanying text.

[256] *Id.*

[257] *See* Katharine A. Van Tassel, *Genetically Modified Plants Used for Food, Risk Assessment and Uncertainty Principles: Does the Transition from Ignorance to Indeterminacy Trigger the Need for Post-Market Surveillance?*, 15 B.U. J. SCI. & TECH. L. 220 (2007) (evaluating the FDA's regulation of genetically modified food in light of the new scientific understanding of the networked gene).

identification and avoidance leaving the true cost of nanotech products artificially low and creating an overuse of this potentially high risk nanotechnology. While the present regulatory scheme has created a health risk information void, collectively, the public health protection systems simultaneously act to defeat the consumer's ability to engage in self-protection, a current requirement of the tort system. Ironically, this inability to self-protect runs directly contrary to the movement by tort reformers to require even more individual responsibility.

Now that the nature of the uncertainty over the public health risks associated with these nanoparticles is indeterminacy rather than ignorance, premarket testing of nanotech products for human consumption, nanotech ingredient labeling, and post-market surveillance should be required in order to provide for both the transparency and accountability necessary to protect public health. In order to achieve this result, risk assessments should be modified to use trade-off analysis and the use of cost-benefit analysis should be abandoned altogether.

Revising the legislative decision-making process in these ways will permit consumers to engage in self-protection and will open the door to the creation of systems for the collection of data that will allow any injured consumers to meet the *Daubert* and *Frye* admissibility standards necessary to establish causation. In addition, this data will be available to any injured consumers to use to meet the idiosyncratic plaintiff defense and the foreseeability pre-condition to tort recovery. These strategies will also encourage a more appropriate level of private investment into research to test for the public health effects of this innovative technology. This investment will be passed on to increase the price of the use of nanotechnology in products, putting the brakes on the current "free-for-all" and allowing for a more measured growth of the type of products that use nanotechnology during this period of scientific uncertainty over the risks to public health.

In conclusion, the application of trade-off analysis results in a recognition that these risk mitigation strategies will fill the critical gaps in our public health system and will supply the accountability that is necessary to maintaining safe consumer products as each new nanotech product is introduced into the market.