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UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF CALIFORNIA

CV 11 6592

INTERNATIONAL CENTER FOR TECHNOLOGY ASSESSMENT, FRIENDS OF THE EARTH, THE ACTION GROUP ON EROSION, TECHNOLOGY AND CONCENTRATION, THE CENTER FOR ENVIRONMENTAL HEALTH, FOOD AND WATER WATCH, and THE INSTITUTE FOR AGRICULTURE AND TRADE POLICY *Plaintiffs,* vs. MARGARET A. HAMBURG, M.D., *Defendant.*	**Case No.** **COMPLAINT FOR DECLARATORY AND INJUNCTIVE RELIEF** **Administrative Procedure Act Case**

INTRODUCTION

1. This is an action for declaratory and injunctive relief regarding the failure by the Food and Drug Administration ("FDA" or "the agency") to respond within a reasonable time to a petition filed by the International Center for Technology Assessment, Friends of the Earth, The Action Group on Erosion, Technology and Concentration, and The Center for Environmental Health (collectively, "Petitioners") for rulemaking requesting that FDA regulate nanotechnology products under its statutory purview, including but not limited to sunscreen drug products composed of manufactured nanomaterials. Petitioners are joined by Food and Water Watch and The Institute for Agriculture and Trade Policy (collectively "Plaintiffs") in this action.

2. Nanotechnology is a powerful new set of technologies for observing, taking apart and reconstructing nature at the atomic and molecular level. Consumer products containing manufactured nanoparticles have already arrived on market shelves, and numerous products that fall under FDA's jurisdiction, like nano-cosmetics and nano-sunscreens, are now widely available. Manufactured nanomaterials have fundamentally different properties from their bulk material counterparts—properties that also create unique human health and environmental risks—which necessitate new health and safety testing paradigms. Yet FDA has failed to address the risks of nanomaterials.

3. On May 16, 2006, Petitioners submitted a petition to FDA for rulemaking. Docket No. FDA-2006-P-0213, attached as Ex. A ("2006 Petition"). The 2006 Petition requested, *inter alia*, that the agency take several regulatory actions pursuant to the Federal Food Drug and Cosmetic Act ("FDCA") with respect to nanomaterial products, including nano-sunscreens. It also requested that FDA conduct a Programmatic Environmental Impact Statement ("PEIS") pursuant to the National Environmental Policy Act ("NEPA") to assess the impacts of nanotechnology in products under its statutory purview on human health and the environment.

4. Over five and a half years have now passed since FDA received the 2006 Petition for rulemaking. FDA has not meaningfully responded to or taken action on the 2006 Petition, in violation of the Administrative Procedure Act ("APA"). In the interim, nanomaterial consumer products have continued to proliferate without oversight. This Court should order the agency to

respond to Plaintiffs' 2006 Petition without further unlawful delay.

JURISDICTION

5. This Court has jurisdiction over this action pursuant to 28 U.S.C. § 1331 (federal question) and 28 U.S.C. § 1346 (United States as Defendant).

6. The relief requested is specifically authorized pursuant to 28 U.S.C. § 1651 (writs) and 28 U.S.C. §§ 2201–02 (declaratory relief). An actual controversy exists between the parties within the meaning of 28 U.S.C. § 2201 (declaratory judgments).

7. Plaintiffs have a right to bring this action pursuant to the Administrative Procedure Act (APA), 5 U.S.C. §§ 551, *et seq.*, 702–706.

VENUE

8. Venue properly lies in this Court pursuant to 28 U.S.C. § 1391(e) because one or more of the Plaintiffs reside in this District.

PARTIES

9. Plaintiff International Center for Technology Assessment ("CTA") is located at 660 Pennsylvania Ave., S.E., Suite 302, Washington, D.C. 20003. Formed in 1994, CTA seeks to assist the public and policy makers in better understanding how technology affects society. CTA is a non-profit organization devoted to analyzing the economic, environmental, ethical, political, and social impacts that can result from the application of technology or technological systems. CTA works towards adequate oversight of nanotechnology through its Nanotechnology Project, NanoAction.

10. CTA develops and disseminates to its members, policymakers, members of local, state, and federal government, international governmental officials, non-profit organizations, and interested members of the general public a wide array of educational and informational materials that address the environmental, economic, and social and public health impacts associated with the use of new technologies like nanotechnology. These materials include, but are not limited to, reprints of news articles and agency regulatory positions, press releases, fact sheets, action alerts, electronic mail alerts, and investigative or technical reports. CTA's materials often analyze the legal and regulatory means by which federal agencies address the various economic,

environmental, pubic health, and social impacts associated with new technologies such as nanotechnology.

11. Along with its function as an information clearinghouse, CTA also serves in an advocacy function to, among other things, protect human health and the environment from the impacts and risks raised by novel technologies like nanotechnology. Accordingly, CTA's activities seek to encourage full public participation in local, state, and federal policymaking and rulemaking proceedings so that public concerns over the use of novel technologies are duly considered and acted upon by governmental decision making bodies.

12. Plaintiff Center for Environmental Health ("CEH") is located at 528 61st Street, Suite A, Oakland, California 94609. Founded in 1996, CEH is a non-profit organization dedicated to protecting the public from environmental and consumer health hazards. CEH is committed to environmental justice, reducing the use of toxic chemicals and practices, supporting communities in their quest for a safer environment, and corporate accountability.

13. Plaintiff Friends of the Earth ("FoE"), is located at 1100 15th, NW, 11th Floor, Washington D.C. 20005. FOE is a non-profit organization with offices in Washington, D.C. and San Francisco, California that seeks to create a more healthy, just world. FOE is the U.S. voice of Friends of the Earth International, the world's largest federation of democratically elected grassroots environmental groups, located in 76 countries.

14. In conjunction with the 2006 Petition FoE released a groundbreaking report, "Nanomaterials, Sunscreens and Cosmetics: Small Ingredients, Big Risks", *available at* http://libcloud.s3.amazonaws.com/93/ce/0/633/Nanomaterials_sunscreens_and_cosmetics.pdf. Since then, FoE has released updated reports every year, sharing more and more about the alarming risks concerning nanomaterial sunscreens, which could affect consumers, workers, and the environment. Most recently, FoE released a report entitled "Manufactured Nanomaterials and Sunscreens: Top Reasons for Precaution", *available at* http://libcloud.s3.amazonaws.com/93/14/0/632/Manufactured_nanomaterials_and_sunscreens_reasons_for_precaution.pdf. This report highlights subsequent scientific findings.

15. Plaintiff Action Group on Erosion, Technology and Concentration ("ETC

Group") is an international civil society organization headquartered in Canada, with offices in the USA and Mexico. ETC Group is dedicated to the conservation and sustainable advancement of cultural and ecological diversity and human rights. To this end, ETC Group supports socially responsible developments in technologies useful to the poor and marginalized, and it addresses governance issues affecting the international community. ETC Group also monitors the ownership and control of technologies and the consolidation of corporate power.

16. Plaintiff Food and Water Watch ("FWW") is a Washington, D.C.-based national non-profit public interest consumer organization with offices throughout United States, including San Francisco, California. FWW works to ensure consumer access to affordable, healthy, and wholesome food and clean water. Through research, public and policymaker education, media, and lobbying, the organization advocates policies that guarantee safe, wholesome products produced in a sustainable manner. To that end, FWW has advocated against various government proposals and polices that would limit consumers' right to healthy and safe products, and negatively impact human health and the overall environment.

17. Plaintiff the Institute for Agriculture and Trade Policy ("IATP") is a non-profit organization with offices in both Washington, D.C. and Minneapolis, Minnesota. IATP works locally, nationally and globally to promote fair, healthy and sustainable food, farm and trade systems. On June, 2011, IATP published a report examining nanotechnology, entitled "Racing Ahead, U.S. Agri-Nanotechnology in the Absence of Regulation."

18. Defendant Dr. Margaret A. Hamburg is sued in her official capacity as FDA Commissioner. As Commissioner, Dr. Hamburg has the ultimate responsibility for FDA's activities and policies.

19. Dr. Hamburg and the Food and Drug Administration are collectively referred to herein as "FDA" or "the agency."

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LEGAL BACKGROUND

Administrative Procedure Act

20. Under the Administrative Procedure Act ("APA"), agencies are required to "give an interested person the right to petition for the issuance, amendment, or repeal of a rule." 5 U.S.C. § 553(3).

21. The APA requires an agency to conclude a matter presented to it "within a reasonable time." 5 U.S.C. § 555(b). "Prompt notice shall be given of the denial in whole or in part of a...petition...." *See* 5 U.S.C. § 555(e).

22. The APA, 5 U.S.C. § 702, grants a right of judicial review to "a person suffering legal wrong because of agency action, or adversely affected or aggrieved by agency action."

23. Courts "shall compel agency action unlawfully withheld or unreasonably delayed," 5 U.S.C. § 706(1), and "hold unlawful and set aside agency action, findings, and conclusions found to be arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." 5 U.S.C. § 706(2)(A). Courts may only review a final agency action, 5 U.S.C. § 704, and "agency action" includes a "failure to act." 5 U.S.C. §551(13).

STATEMENT OF FACTS

Nanotechnology and Nanomaterials

24. Nanotechnology is the design, characterization, production and application of structures, devices and systems by manipulating shape and size at the nanoscale.

25. The nanoscale refers to nanometer (nm) measurement, which equals one billionth of a meter. This size is remarkably tiny for a manufactured material. A human hair is roughly 80,000 nanometers wide, a sheet of paper is about 100,000 nm thick, and a red blood cell is approximately 7,000 nanometers wide.

26. A nanoparticle or nanomaterial refers to a particle or manufactured substance that has at least one component at the nanoscale.

27. However nano means more than just tiny, a billionth of a meter in scale: the radical reduction in size means that seemingly ordinary materials may behave completely

differently than their larger bulk or macro form.

28. The U.S. National Nanotechnology Initiative ("NNI"), which coordinates Federal nanotechnology research and development between agencies (including FDA) defines nanotechnology as "the understanding and control of matter at dimensions of roughly 1 to 100 nanometers, where unique phenomena enable novel applications. Encompassing nanoscale science, engineering and technology, nanotechnology involves imaging, measuring, modeling, and manipulating matter at this length scale."[1]

29. The U.S. Patent Office has established a Patent Classification Class, Class 977, for Nanotechnology patents, which it defines as

> i. Nanostructure and chemical compositions of nanostructure;
> ii. Device that include at least one nanostructure;
> iii. Mathematical algorithms, e.g., computer software, etc., specifically adapted for modeling configurations or properties of nanostructure;
> iv. Methods or apparatus for making, detecting, analyzing, or treating nanostructure; and
> v. Specified particular uses of nanostructure.
>
> As used above, the term "nanostructure" is defined to mean an atomic, molecular, or macromolecular structure that:
>
> a) Has at least one physical dimension of approximately 1-100 nanometers; and
> b) Possesses a special property, provides a special function, or produces a special effect that is uniquely attributable to the structure's nanoscale physical size.[2]

30. These definitions illustrate that nanomaterials have novel properties and functions because of their small size. Congress also recognized this basic fact in passing the 2004 Nanotechnology Research and Development Act, 15 U.S.C. § 7501, defining nanotechnology as "the science and technology that will enable one to understand, measure, manipulate and manufacture at the atomic, molecular, and supramolecular levels, aimed at creating materials,

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[1] National Nanotechnology Initiative, Factsheet: What Is Nanotechnology?, http://www.nano.gov/html/facts/whatIsNano.html.

[2] Patent office Classification Definitions, Class 977, Nanotechnology, (November 2005), *available at* http://www.uspto.gov/web/patents/classification/uspc977/defs977.htm#C977S000000.

devices and systems with fundamentally new molecular organization, properties, and functions." 15 U.S.C. § 7509(2).

Nanomaterial Development and Commercialization

31. Over the last decade, governments worldwide have invested over 40 billion U.S. dollars (USD) in nanotechnology. The U.S. has invested a total of around $12 billion USD of public funds. Private research and development spending reached $6.6 billion USD in 2007, surpassing government spending for the first time. However government health and safety risk research is less than 4% of the total NNI funding in the U.S.

32. Commercialization is well underway. In 2008, $166.6 billion USD in nano-enabled products were produced; by 2012 that figure is expected to grow to $263 billion USD worldwide. Thousands of tons of nanomaterials are already being produced each year.

33. Products containing nanomaterials have been and continue to enter the market at a steady pace: One public inventory developed in 2005 by the Woodrow Wilson International Center for Scholars and the Pew Charitable Trusts, through their Project on Emerging Nanotechnologies, averages at least three to four new nano-consumer products per week, and lists over a 1,300 products total.[3]

34. The current nano-product market is not limited to a particular product or nanomaterial ingredient, instead spanning many industries. Nano-products currently available include: paints, coatings, sunscreens, sporting goods, cosmetics, clothing, dietary supplements, food packaging, kitchenware, electronics and battery components, light emitting diodes used in computers, cell phones, and digital cameras, children's toys, detergents, personal hygiene products, cleaning agents, pet products, lubricants and foams, and waxes.

35. Most of these commercialized nano-products fall under FDA's broad statutory purview.

36. Many of these products infuse nanomaterials in "free" rather than "fixed" form, are intended for human consumption, either directly or indirectly, for example through lotions,

[3] http://www.nanotechproject.org/inventories/consumer/analysis_draft/

sunscreens, and cosmetics that are absorbed by the skin.

37. Notably, the largest nanomaterial commercial sectors are personal care products and antimicrobial products.

38. Other studies have focused specifically on nano-personal care products: the Australian Therapeutic Goods Administration ("TGA") concluded in 2006 that several hundred sunscreen products containing manufactured nanoparticles of zinc oxide or titanium dioxide are currently on the market in Australia.

39. Plaintiff FoE also published a 2006 report on the prevalence of nanomaterials in personal care products, detailing 116 currently available cosmetics, sunscreens, and other personal care products that incorporate nanomaterials.

40. These are only the self-identified products. Since no labeling is required, the known nano-products likely represent only a small fraction of the actual commercialized applications.

Nanotechnology's Novel Properties and Concomitant Risks

41. These nanomaterials are being infused in existing products because they have different properties from their bulk material counterparts—electrical, optical, magnetic, toxicity, chemical, photoreactive, persistence, bio-accumulation, and explosiveness, to list a few. These novel properties excite industry by creating new commercial potential as well as patentability. However these same properties also create unique human health and environmental risks that necessitate new health and safety testing paradigms.

42. Swiss Insurance giant Swiss Re noted that "Never before have the risks and opportunities of a new technology been as closely linked as they are in nanotechnology. It is precisely those characteristics which make nanoparticles so valuable that give rise to concern regarding hazards to human beings and the environment alike."

43. Nanomaterials differ in several important ways from larger particles of the same materials. First, reduction in size to the nanoscale level results in an enormous increase of surface to volume ratio, giving nanoparticles a much greater surface area per unit mass compared

to larger particles.[4] Because growth and catalytic chemical reactions occur at the particle surface, this leads to increased potential for biological interaction and increased reactivity than in the same material made up of larger particles, as well as increased potential for toxicity, resulting in DNA mutation, structural damage within the cell, and cell death.

44. Second, at the nanoscale quantum physics comes into play, potentially affecting *inter alia*, the optical, electrical and magnetic behavior of materials.

45. Third, because of their tiny size nanomaterials also have unprecedented mobility in the body and environment for a manufactured material. The human species has evolved mechanisms of protection against environmental agents; size is an important factor in the efficacy of these mechanisms. The exposure to manufactured nanoparticles, having characteristics not previously encountered, presents new challenges to the normal defense mechanisms of the body's immune and inflammatory response systems.

46. For example, manufactured nanoparticles can enter the body and pass through biological membranes—like cell walls, cell tissue, and organs—more easily than larger particles. They readily enter the body via inhalation and ingestion. Once in the blood stream, nanomaterials can move around the body and accumulate in organs and tissues including the brain, heart, liver, kidneys, spleen, bone marrow, and nervous system. Research has highlighted nanoparticles' movement from the lungs into the blood stream, the gastro-intestinal tract to other organs, and the nose via olfactory nerves into the brain. In addition, unlike larger particles, nanoparticles are transported within cells and taken up by cell mitochondria, and the cell nucleus, where they can interfere with cell signaling and induce structural damage, including DNA damage.

Nanotoxicology

47. The scientific expert consensus is that the properties of a substance when in bulk form cannot predict how that substance will behave at the nanoscale. For example, substances

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[4] *See, e.g.*, Andre Nel *et al.*, *Toxic Potential of Materials at the Nanolevel*, 311 SCIENCE 622-27, 622, 623 Fig. 1 (2006).

change colors at various nano-levels (e.g., gold); substances that were stable as bulk materials can become reactive when engineered to nanoparticle level (e.g., aluminum); substances can become highly elastic, stretching to 50 times their original length without breaking (e.g., copper); and substances that were insulators can become conductors (e.g., silicon). Zinc oxide and titanium dioxide, two metal oxides used in sunscreens, become transparent at the nanoscale.

48. The same features that industry finds marketable can create unpredictable risk to human health and the environment.

49. At the time of Plaintiffs' 2006 Petition filing, FDA's position was that, while it acknowledged that products under its jurisdiction contained nanomaterials, it believed that its "existing battery of pharmacotoxicity tests is probably adequate for most nanotechnology products that we regulate. Particle size is not an issue." *See* Ex. A, at 13-14, 19. Yet such testing is based on and completed regarding bulk material states of many nanomaterials.

50. The agency's conclusion is at loggerheads with the consensus view of the scientific community, which is that the adverse effects of nanoparticles cannot be reliably predicted or derived from the known toxicity of the bulk material. For example, the European Commission's Scientific Committee on Emerging and Newly Identified Health Risks ("SCENIHR") concluded: "Experts are of the unanimous opinion that the adverse effects of nanoparticles cannot be predicted (or derived) from the known toxicity of material of macroscopic size, which obey the laws of classical physics."[5] Similarly, the U.K. Royal Society and the Royal Academy of Engineering, the world's oldest scientific organization, has emphasized: "Free particles in the nanometre size range do raise health, environmental, and safety concerns and their toxicology cannot be inferred from that of particles of the same

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[5] European Commission's Scientific Committee on Emerging and Newly Identified Health Risks, Opinion on the Appropriateness of Existing Methodologies to Assess the Potential Risks Associated with Engineered and Adventitious Products of Nanotechnologies, at 6 (adopted September 28-29, 2005) (emphasis added); *id.* at 34 (existing regulatory tests do not anticipate the significance of the new nanoparticle physicochemical parameters in play, and as a result "safety evaluations of nanoparticles and nanostructures cannot rely on toxicological and ecotoxicological profile of bulk material that has been historically determined").

chemical at a larger size."[6] The British Institute for Occupational Medicine similarly concluded: "[B]ecause of their size and the ways in which they are used, they [manufactured nanomaterials] have specific physical-chemical properties and therefore may behave differently from their parent materials when released and interact differently with living systems. It is accepted, therefore, that it is not possible to infer the safety of nanomaterials by using information derived from the bulk parent material."[7]

51. Toxicology normally correlates health risks with the mass to which an individual is exposed, resulting in an accumulated mass as an internal dose/exposure. However, the biological activity of nanoparticles is likely to depend on physicochemical characteristics that are not routinely considered in toxicity screening studies. There are many more factors affecting the toxicological potential of nanoscale materials than the two or three factors normally analyzed, including: particle size, surface area, surface charge, solubility, shape or physical dimensions, surface coatings, chemical composition, and aggregation potential.[8]

52. The novel properties of manufactured nanomaterials make them different, for all purposes relevant to FDA's statutory mandate, from existing materials of the same chemical composition. Accordingly, the U.K. Royal Society concluded that manufactured nanomaterials should be treated as new chemicals/new substances: "Substances made using nanotechnology should be considered new chemicals and undergo extra safety checks before they hit the market to ensure they do not pose a threat to human health.... We recommend that chemicals produced in the form of nanoparticles and nanotubes be treated as new chemicals ...."[9]

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[6] The Royal Society and the Royal Academy of Engineering, Nanoscience and Nanotechnologies: Opportunities and Uncertainties, London, July 2004, at 49, *available at* http://www.nanotec.org.uk/finalReport.htm.

[7] Tran *et al.*, *A Scoping Study to Identify Hazard Data Needs For Addressing The Risks Presented By Nanoparticles and Nanotubes*, Institute of Occupational Medicine Research Report (December 2005), at 34.

[8] *See, e.g.*, Oberdorster *et al.*, *Principles for Characterizing the Potential Human Health Effects From Exposure to Nanomaterials: Elements of a Screening Strategy*, 2 Particle and Fibre Toxicology 8, at 1.0 (2005).

[9] The Royal Society and the Royal Academy of Engineering, *supra* note 6, at 6 (summary and recommendations), 43, 73, & 83.

53. Despite this consensus, FDA has concluded that its previous testing is "probably adequate" and has not instituted any regulatory changes to account for these critical differences, such as classifying them as new substances or requiring specific nano-toxicity testing or labeling for nano-products.

Nanomaterials and the Environment

54. For these same reasons, nanomaterials in products under FDA's jurisdiction have foreseeable potential significant environmental impacts. Nanomaterials are entering the environment in numerous ways over their lifecycle, including during manufacture, transport, use and disposal of products. For example, sunscreens, cosmetics, and other consumer products under FDA's jurisdiction will enter the environment as they are disposed of after use, washed off in showers, or directly dispersed from skin into waterways.

55. Once in the environment, manufactured nanomaterials constitute a new class of non-biodegradable pollutants. The same unique mobility and toxicity concerns that apply to human health risks apply to environmental risks. Potential impacts include but are not limited to: mobility, reaching places larger particles cannot, moving through aquifers and soils; transport, the ability to absorb or bond to harmful chemicals and carry them places they would not otherwise reach; reactivity, interacting with natural substances to develop toxic compounds; fate and persistence; and bioaccumulation. Plaintiffs' 2006 Petition included numerous studies presenting environmental red flags from nanomaterials in products overseen by FDA. *See* Ex. A, at 30-32.

56. Other federal agencies have acknowledged the risks posed by nanotechnology. In its 2007 "White Paper" on nanotechnology,[10] the Environmental Protection Agency ("EPA") concluded that nanomaterials' "special properties" can "cause some nanomaterials to pose hazards to humans and the environment, under specific conditions." EPA stated that "at this point not enough information exists to assess environmental exposure for most engineered nanomaterials" and that "the fundamental properties concerning the environmental fate of

[10] http://www.epa.gov/osa/pdfs/nanotech/epa-nanotechnology-whitepaper-0207.pdf

nanomaterials are not well understood."

57. EPA concluded that there are numerous sources of potential direct and indirect nanomaterial release into the environment, including, inter alia, "releases resulting from the use and disposal of consumer products containing nanoscale materials." Further, the "high durability and reactivity of some nanomaterials raise issues of their fate in the environment." EPA has noted that "the use of nanomaterials in the environment may result in novel by-products or degradates that also may pose risks." In general, EPA acknowledged that "there is a significant gap in our knowledge of the environmental, health, and ecological implications associated with nanotechnology."

58. For these reasons, the U.K. Royal Society concluded regarding the release of naonomaterials into the environment: "Until more is known about their environmental impact, we are keen that the release of nanoparticles and nanotubes in the environment be avoided as far as possible. Specifically we recommend as a precautionary measure that factories and research laboratories treat manufactured nanoparticles and nanotubes as hazardous, and seek to reduce or remove them from waste streams."[11]

Nano-Sunscreens

59. Nano-personal care products present perhaps the most immediate cause for concern, given their prevalence on markets, their use of "free" rather than "fixed" nanoparticles, and their repeated, intimate use by consumers. Crucial safety questions based upon nanoparticles' toxicity and mobility characteristics as well as the existing data are still unanswered.

60. Zinc oxide and titanium oxide nanoparticles used in sunscreens have quickly become two of the most commonly used nanomaterials in consumer products and one of the fastest growing sector of nanomaterial commercialization. Unlike bulk-sized amounts of the same substances, UV blockers titanium dioxide and zinc oxide become transparent or "cosmetically clear" at the nanoscale. The new optical properties of the nanoparticles make the

[11] The Royal Society and the Royal Academy of Engineering, *supra* note 6, at 46.

clear sunscreens more marketable, and the manufactured nanoparticle ingredients are patented for their novelty.

61. The 2006 Petition lists a number of these nano-sunscreens (*see* Ex. A, at 38-42), documents the scientific evidence of their potential risks to human health and the environment (*id.* at 49-64), and enumerates the U.S. patents granted on these materials (*id.* at 65-68).

62. Concurrently with the 2006 Petition, Plaintiff FoE published a 2006 guide to nano-cosmetics and nano-sunscreens, documenting the evidence of their risks.[12] Another 2009 report from FoE, CTA, and Consumers Union build on that analysis and updated further scientific evidence of harm.[13]

63. As discussed above and in the 2006 Petition, many types of nanoparticles have proven to be toxic to human tissue and cell cultures, resulting in oxidative stress, inflammatory cytokine production, DNA mutation and even cell death.

64. Researchers have published more red flags since the 2006 Petition's filing, showing that manufactured nanomaterials (such as zinc oxide and titanium dioxide) used in these nano-sunscreens can:

a. Damage human colon cells: A study from the University of Utah[14] showed that nano zinc oxide is toxic to colon cells even in small amounts. The scientists called for more research and warned that the evidence is especially concerning for children who are more likely to accidently ingest sunscreen. The colon is vital because it eliminates food waste and absorbs important nutrients;

b. Damage brain stem cells in mice: A study from China found that zinc oxide nanoparticles can damage the brains of mice by killing important brain stem cells.[15] In another study, Japanese scientists injected pregnant mice with nano titanium dioxide and recorded changes in gene expression in the brains of their fetuses.[16] These changes have been associated with autistic disorders, epilepsy and Alzheimer's disease. Though more studies are necessary to know if this damage to would occur in humans, these studies with mice serve as important

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[12] http://libcloud.s3.amazonaws.com/93/ce/0/633/Nanomaterials_sunscreens_and_cosmetics.pdf

[13] http://libcloud.s3.amazonaws.com/93/14/0/632/Manufactured_nanomaterials_and_sunscreens_reasons_for_precaution.pdf

[14] http://www.nanowerk.com/news/newsid=15676.php

[15] http://www.natureasia.com/asia-materials/highlight.php?id=438

[16] http://www.azonano.com/news.asp?newsID=12847

warnings. Such studies have encouraged scientists in the United Kingdom to explore the link between manufactured nanomaterials and Alzheimer's disease. At the end of last summer, scientists at the University of Ulster were funded by the European Union to conduct more research; [17]

c. Travel up the food chain from smaller to larger organisms: A study by researchers at Arizona State University, the Georgia Institute of Technology, and Tsinghua University in China found through a dietary experiment that Daphnia (a "water flea" that provides important nutrition for aquatic life) can transfer nano titanium dioxide to larger organisms (in this case Zebrafish). [18] This study is of great concern because it shows that manufactured nanomaterials with toxic properties could end up in the animal food chain at large;

d. Damage important microbes in the environment: Scientists at the University of Toledo found that nano titanium dioxide inhibited the function of bacteria after just an hour of exposure.[19] Manufactured nanomaterials from sunscreens can easily wash off of the body in the shower and end up in wastewater and the wider environment, which could affect microbes that are helpful to ecosystems and sewage treatment plants; and

e. Travel from mothers to unborn fetuses: Nanoparticles up to 240 nm in size can cross into human placentas, meaning that the toxicity of manufactured nanomaterials could extend across generations.[20]

FDA and Plaintiffs' 2006 Petition

65. FDA regulates numerous products that contain manufactured nanomaterials, including sunscreens and cosmetics. Yet the agency has taken no regulatory steps to formally address the inherent, fundamental differences of nanomaterials, nor has the agency addressed their associated new risks to human health and the environment pursuant to the Federal Food, Drug and Cosmetic Act ("FFDCA" or "Act").

66. On May 16, 2006, Petitioners submitted a petition for rulemaking to FDA.[21] The eighty-page 2006 Petition, and approximately 500 pages of supporting administrative record,

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[17] http://news.ulster.ac.uk/releases/2009/4573.html

[18] http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6V74-4YS6P6N-4&_user=10&_coverDate=05%2F31%2F2010&_rdoc=1&_fmt=high&_orig=search&_sort=d&_docanchor=&view=c&_acct=C000050221&_version=1&_urlVersion=0&_userid=10&md5=876fe797ee7c05dd32c1d7b64334b93b

[19] http://www.environmentalhealthnews.org/ehs/news/nanoparticles-damage-microbes

[20] http://www.nanowerk.com/news/newsid=15414.php

[21] http://www.icta.org/doc/Nano%20FDA%20petition%20final.pdf

documents the then-existing body of scientific evidence studying nanomaterial risks stemming from their unpredictable toxicity and unprecedented mobility.

67. The 2006 Petition's first half requests FDA to issue a formal Commissioner opinion on manufactured nanoparticles in light of this evidence; amend its regulations to include nanotechnology definitions necessary for proper regulation; enact comprehensive nano-product regulations, including treating nanomaterials as new substances, using nanomaterial-specific toxicity testing paradigms, and requiring nano-product labeling; and comply with NEPA by assessing the human health and environmental impacts of its nano-related actions and regulatory program.

68. The 2006 Petition's second half focuses specifically on nano-sunscreens, part of the growing nano-personal care market. Sunscreens are classified by FDA as human drugs, unlike many other personal care products, and consequently should be subject to more rigorous FDA regulation, including the requirement of premarket "new drug product" applications supporting the drug's safety and efficacy before any commercialization is permitted. *See* 21 U.S.C. § 321(g)(1). The commercial allure of nano-sunscreens is that they appear transparent because of the nanoparticles' fundamentally different properties. The manufactured nanoparticles are also patented for their profitable novelty.

69. Yet in the agency's first and only word on nano-sunscreens, a 1999 regulation, FDA considered manufactured nanoparticle ingredients in these sunscreens a mere reduction in size and not a new drug ingredient, permitting sunscreen manufacturers to sell nano-sunscreens based on the agency's safety assessment of bulk material sunscreens. [22]

70. The 2006 Petition demands FDA reconsider its 1999 equivalency stance on nanoparticle sunscreen ingredients and for the agency to instead classify nano-sunscreens as new drug products which require premarket review of health and safety evidence. Nanoparticle ingredients in sunscreens have raised red flags for scientists because it is unknown how easily

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[22] U.S. Food and Drug Administration, HHS, Sunscreen Drug Products For Over-The-Counter Human Use; Final Monograph, 64 Fed. Reg. 27,666-27,693, 27,671 (1999).

they can penetrate the skin and circulate throughout the body,[23] and studies have shown them to be photoactive in some cases, producing free radicals and causing DNA damage to human skin cells.[24]

71. Because nano-sunscreens are currently sold without such premarket testing or review by FDA, the 2006 Petition called on FDA to declare that those products an imminent hazard to public health and to request that manufacturers cease production until FDA nanomaterial product regulations are developed and implemented. *See* 21 C.F.R. §§ 2.5(a) (imminent hazard), 7.45(a) (recall).

72. Specifically, the 2006 Petition requested that FDA take the following actions:

a. Amend FDA regulations to include nanotechnology definitions necessary to properly regulate nanomaterial products, including the terms "nanotechnology," "nanomaterial," and "engineered or manufactured nanoparticle;"

b. Issue a formal advisory opinion explaining FDA's position regarding manufactured nanoparticles in products regulated by FDA;

c. Enact new regulations directed at FDA oversight of nanomaterial products establishing and requiring, *inter alia,* that nanomaterials be subjected to nano-specific health and safety testing, and that nanomaterial products be labeled to delineate all nanoparticle ingredients;

d. Prepare a Programmatic Environmental Impact Statement ("PEIS") assessing the impacts of nanotechnology and nanomaterials on the human environment;

e. Reopen the Administrative Record of the Final Over-the-Counter ("OTC") Sunscreen Drug Product Monograph for the purpose of considering and analyzing information on manufactured nanoparticles of zinc oxide and titanium oxide currently used in sunscreens.

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[23] *See, e.g.,* European Commission's Scientific Committee on Cosmetic Products and Non-Food Products (SCCNFP), Statement on Zinc Oxide In Sunscreens, adopted September 20, 2005 http://europa.eu.int/comm/health/ph_ risk/committees/04_sccp/docs/sccp_o_00m.pdf (last visited July 7, 2006) (finding insufficient evidence presented for a finding of safety).

[24] *See, e.g.,* 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 Journal of Photochemistry and Photobiology 205-213 (1997); Dunford *et al.*, Chemical Oxidation and DNA Damage by Inorganic Sunscreen Ingredients, 418 FEBS Letters no. 1-2, pp. 87-90 (1997); *Donaldson et al., Free Radical Activity Associated with the Surface of Particles: A Unifying Factor in Determining Biological Activity?*, 88 Toxicology Letters 293-98 (1996).

f. Amend the OTC Sunscreen Drug Monograph to address nanoparticles, instructing that sunscreen products containing nanoparticles are not covered under the Monograph and instead are "new drugs" for which manufacturers must complete a New Drug Application in accordance with 21 U.S.C. § 335.

g. Order entities using the nanoparticles in sunscreens regulated by FDA to cease manufacture until FDA's Sunscreen Drug Monograph is finalized and broader FDA nanotechnology regulations are developed and implemented.

h. Request a recall from manufacturers of all publically available sunscreen drug products containing nanoparticles of titanium dioxide and/or zinc oxide until the manufacturers of such products complete New Drug Applications.

FDA's Failure to Respond to Plaintiffs' 2006 Petition

73. On November 9, 2006, FDA provided an Interim Response in accordance with 21 C.F.R. § 10.30(e)(2), fulfilling the requirement to provide a response within 180 days. The Interim Response stated that FDA was unable to reach a decision on the 2006 Petition "because it raises complex issues requiring extensive review and analysis by Agency officials, and in relation to which the Agency is seeking public input." In addition, the Interim Response indicated that FDA "formed an internal task force, the FDA Nanotechnology Task Force, to consider issues related to the safety and effectiveness of FDA-regulated products that use nanotechnology materials."

74. FDA's Nanotechnology Task Force issued a report on nanotechnology on July 25, 2007 ("Task Force Report"). The Task Force Report references the 2006 Petition and, under footnote 20 states, "[w]hile this report addresses some issues raised in the [2006] petition, this report reflects only the views of the Task Force, and does not constitute an agency answer to the [2006] petition in whole or in part."

75. Since that time the agency has given no further information concerning when, or if, Petitioners may expect a response to the 2006 Petition.

76. In June 2011, FDA issued several draft guidance documents and proposed rules regarding sunscreen. All of the June 2011 OTC Documents ignored the 2006 Petition and issues it tabled. None of these documents take or initiate any of the actions requested in 2006 Petition:

a. FDA's June 14, 2011 draft guidance, "Considering Whether an FDA-Regulated Product Involves the Application of Nanotechnology" ("June 14, 2011 Draft

Guidance"), will not—by its own terms—"create or confer any rights for or on any person and does not operate to bind FDA or the public," nor will it "establish any regulatory definitions," "[n]or does this guidance document address the regulatory status of products that contain nanomaterials or otherwise involve the application of nanotechnology." The June 14, 2011 Draft Guidance makes no mention of the 2006 Petition.

b. FDA's June 17, 2011 draft guidance, "Enforcement Policy: OTC Sunscreen Drug Products Marketed Without an Approved Application" ("June 17, 2011 Draft Guidance"), makes no reference to nanotechnology, nor does it mention particle size as a relevant consideration for evaluating the safety of sunscreens. The June 17, 2011 Draft Guidance makes no mention of the 2006 Petition.

c. The remainder of the documents published by FDA on June 17, 2011, similarly fail to reference or address the 2006 Petition. *See* "Proposed Rule to limit the labeling of sunscreens with SPF content higher than 50"; "Advance Notice of Proposed Rulemaking and Request for Data regarding dosage forms for OTC sunscreen"; "Notice soliciting comments on SPF labeling and testing requirements and FDA's proposed collection of data from industry"; and "Final Rule addressing labeling and effectiveness testing for certain OTC sunscreen products containing specified active ingredients and marketed without approved applications" (collectively, "June 2011 OTC Documents").

77. Despite finalizing the OTC Drug Sunscreen Monograph in 1999, FDA has postponed or stayed the effective date for the final monograph, twice: in 2000 and 2001. The stay remains in effect. In 2007, FDA issued a proposed rule to amend the final monograph. It has not been implemented. Neither the final monograph, nor the proposed rule to amend it, address nanotechnology or nano-sunscreens in any form whatsoever.

78. Over 65 months have passed since FDA received the 2006 Petition. To date, FDA has not directly responded to or acted on the 2006 Petition.

79. The public has filed approximately 15,000 comments in the FDA docket for Plaintiffs' 2006 Petition, the overwhelming majority calling on the agency to respond and address this pressing issue.

80. Since Petitioners submitted the 2006 Petition, hundreds of new nanomaterial products have entered the US market. The Woodrow Wilson International Center for Scholars has documented the dramatic increase in nanotechnology materials in consumer products from

2006 until 2011.[25] In particular, an increasing number of sunscreens containing manufactured nanoparticles of titanium dioxide and zinc oxide have reached the shelves. Also recently cosmetic lotions containing nanomaterials in the form of incorporated sunscreens have also proliferated on the market. Researchers have published new studies indicating potential health and environmental impacts of these materials.

81. Spray-on sunscreens have become particularly prevalent in the marketplace since FDA received the 2006 Petition. The nature of these spray-on products allows sunscreen to be misted into the air, where it is often inhaled by the user. In effect, the user of the sunscreen is inhaling zinc oxide and titanium oxide nanoparticles.

Harm to Plaintiffs

82. The interests of Plaintiffs are being and will be adversely affected by Defendants' continued failure to respond to or act on the 2006 Petition. In particular, Defendants' unreasonable delay in responding to the 2006 Petition injures Plaintiff organizations by, *inter alia*, abridging their procedural right to petition a federal agency for rulemaking under the APA. Defendants' unreasonable delay also directly harms Plaintiffs' goals and functions by impeding their ability as public interest non-profit organizations to further facilitate public involvement in governmental decision-making and by foreclosing the statutory right that allows for public participation through petitions for rulemaking.

83. The interests of Plaintiffs' members are being and will be adversely affected by Defendants' continued failure to respond to the 2006 Petition. Members of Plaintiffs' organizations suffer procedural injury based on the agency's undue delay in responding to their 2006 Petition. Plaintiffs' members are also suffering or will suffer an ongoing threat to their health and the health of their environment so long as nanomaterial products remain unaddressed by FDA.

84. The requested relief will redress this harm by forcing FDA to respond to the 2006 Petition and address these issues, resulting in either (1) a response fulfilling FDA's statutory

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[25] *See* http://www.nanotechproject.org/inventories/consumer/analysis_draft/

duties, aimed at protecting the public health and environment from the growing and unregulated risks from nanomaterials, particularly sunscreen products manufactured with nanomaterials; and/or (2) by providing a final agency action that Plaintiffs may challenge if Plaintiffs disagree with the agency's response, in whole or in part.

CAUSE OF ACTION

85. Plaintiffs incorporate by reference all allegations contained in paragraphs 1 through 84 *supra.*

86. The Administrative Procedure Act, 5 U.S.C. § 553(3), requires agencies to "give an interested person the right to petition for the issuance, amendment, or repeal of a rule." *See also* 5 U.S.C. § 551(4) (defining "rule" as "the whole or part of an agency statement of general or particular applicability and future effect designed to implement, interpret, or prescribe law or policy"). The APA right to petition encompasses the right to petition for a new, revised or final rule concerning FDA regulation of nanotechnology products under its statutory purview, including but not limited to sunscreen drug products composed of manufactured nanomaterials. *See* 5 U.S.C. § 551, *et seq.*

87. Upon receipt of an APA petition, the Commissioner and FDA have a duty to respond to the petitioners promptly. *See* 5 U.S.C. § 555(e) ("Prompt notice shall be given of the denial in whole or in part of a...petition..."). Such response must be substantive, *i.e.*, it must either grant or deny the petition. *See id.*

88. The APA, 5 U.S.C. § 702, grants a right of judicial review to "a person suffering legal wrong because of agency action, or adversely affected or aggrieved by agency action." Plaintiffs and their members are adversely affected by FDA's past and continued failure to respond to the 2006 Petition.

89. The APA, 5 U.S.C. § 706(1), states that a reviewing court "shall" interpret statutes, and "compel agency action unlawfully withheld or unreasonably delayed." FDA's failure to respond to and take action on the 2006 Petition constitutes unlawfully withheld and unreasonably delayed agency action. *See id.*

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RELIEF REQUESTED

WHEREFORE, Plaintiffs respectfully request that this Court enter an Order:

(1). Declaring that Defendants have violated the Administrative Procedure Act by failing to respond to the 2006 Petition within a reasonable time;

(2). Declaring that Defendants continue to be in violation of the Administrative Procedure Act by failing to respond to the 2006 Petition;

(3). Ordering Defendants to respond to the 2006 Petition as soon as reasonably practicable;

(4). Retaining jurisdiction of this action to ensure compliance with its decree;

(5). Awarding Plaintiffs attorney's fees and all other reasonable expenses occurred in pursuit of this action; and

(6). Granting other such relief as the Court deems just and proper.

Respectfully submitted this 21st day of December, 2011.

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