Comments from the Center for Food Safety and the International Center for Technology Assessment-NanoAction Project on the proposed Environmental Protection Agency's conditional registration of a pesticide product Nanosilva, containing nanosilver/silica/sulfur particles, as a Materials Preservative in Textiles and Plastics.

September 26, 2013

Docket ID # EPA-HQ-OPP-2012-0594-0001

The Center for Food Safety (CFS) and its International Center for Technology Assessment-NanoAction Project[1] (ICTA) is a national, non-profit environmental organization of lawyers, scientists, and other professionals. CFS/ICTA presents these comments on behalf of our 325,000 members and online activists. CFS/ICTA does not have any financial interest in the topic of these comments. CFS/ICTA appreciates the opportunity to comment on the U.S. Environmental Protection Agency (EPA) Draft Decision Document for Proposed Conditional Registration of Nanosilva as a Materials Preservative in Textiles and Plastic, dated August 27, 2013 (Draft Decision Document).

CFS/ICTA strongly opposes the conditional registration of Nanosilva and requests that EPA not register Nanosilva until all relevant toxicity data are received. In its Draft Decision Document, EPA failed to provide rational bases for determining that the use of Nanosilva will not cause unreasonable adverse effects on the environment during the period when newly-required data are being developed; that Nanosilva is in the public interest; or that Nanosilva lacked sufficient time to generate the required data. Proceeding with a conditional registration based on the rationale provided in the Draft Decision Document would be an arbitrary and capricious action by EPA and contrary to law.

I. BACKGROUND

On August 27, 2013, EPA issued a 77-page Draft Decision Document for the Proposed Conditional Registration of Nanosilva as a Materials Preservative in Textiles and Plastics, which is available in the docket as EPA-HQ-OPP-2012-0594-0002.

EPA proposes to conditionally register a pesticide product containing nanosilver as a new active ingredient for a period of four years. The antimicrobial pesticide product, Nanosilva, is a silver-based product that is proposed for use as a preservative in plastics and textiles. Nanosilva LLC requested registration of the nanosilver in Nanosilva "because it was not an active ingredient in any currently registered pesticide product. Nanosilva is a silica-sulfur-nanosilver complex where

[1] The Center for Food Safety serves as the fiscal agent for the International Center for Technology Assessment-NanoAction Project.

the nanosilver active-ingredient is attached to crystalline silica via a thiolate bond."[2] We are concerned that crystalline silica is quartz, a highly toxic carcinogen. While we doubt that EPA would ever approve quartz, we suggest that Nanosilva may in fact be attached to synthetic amorphous silica. We wish to flag for EPA that the staff reviewing the data on Nanosilva have not adequately described the nanosilver material in Nanosilva, whether for lack of the necessary expertise in material chemistry or otherwise.

As a condition of registration, EPA proposes to require Nanosilva LLC to conduct additional testing to provide product chemistry, toxicity, exposure, environmental, and ecological data. The data requirements are based on the regulations governing the registration of pesticides and on an independent consultation EPA held with the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) Scientific Advisory Panel (SAP) in November 2009. In its final report, SAP addressed a number of questions associated with assessing the hazard of and exposure to nanosilver and other nanoscale metal-based pesticides.[3] Additionally, SAP acknowledged that "data gaps about potential exposures and hazards related to nanosilver are broad," noting that "there is very little information about nanosilver in the environment related to fate, transport, and transformation."

EPA states that it will "evaluate these data as they are submitted during the period of the conditional registration to confirm the agency's risk assessment" that there is a "low probability of adverse risk to human health and the environment" from Nanosilva during the four year review period and EPA's review of the submitted data.[4] If Nanosilva LLC fails to meet the conditions set forth in EPA's Draft Decision Document, EPA will issue a notice of intent to cancel Nanosilva LLC's registration under section 6(e).[5] Additionally, Nanosilva LLC's conditional registration for Nanosilva will automatically expire four years after being issued.[6]

II. SUMMARY OF CONTENTS

CFS/ICTA strongly opposes the conditional registration of Nanosilva and requests that EPA not register Nanosilva until all the relevant toxicity data are received. The emerging nanotechnology industry presents numerous new and unknown risks to human health and the environment. EPA cannot show that Nanosilva will not cause "unreasonable adverse effects on the environment." EPA lacks the required data to make such an assessment. Moreover, EPA fails to prove that Nanosilva LLC lacked the adequate time to provide required data or that Nanosilva is in the public interest. Thus, EPA does not meet the requirements needed to grant conditional registration.

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[2] Environmental Protection Agency (EPA), Draft Decision Document: Proposed Conditional Registration of Nanosilva as a Materials Preservative in Textiles and Plastics (Aug. 27, 2013) [*hereinafter* EPA, Draft Decision Document].

[3] FIFRA Scientific Advisory Panel, *A Set of Scientific Issues Being Considered by the Environmental Protection Agency Regarding: Evaluation of the Hazard and Exposure Associated with Nanosilver and Other Nanometal Pesticide Products* (2009) [hereinafter SAP Report] *available at* http://www.epa.gov/scipoly/sap/meetings/2009/november/110309ameetingminutes.pdf (last visited Sep. 26, 2013).

[4] EPA, Draft Decision Document at 1-2.

[5] *Id.* at 2.

[6] *Id.*

CFS/ICTA is opposed to conditional registration generally and to that of Nanosilva specifically. Conditional registrations of pesticides have been overused by EPA and the management of EPA's conditional registration program raises significant red flags about its ability to protect the American public while allowing products with known risks to remain on the market while undergoing further study.

Ultimately, EPA's Draft Decision Document relies on inadequate studies, ignores and fails to consider the aggregate risks of Nanosilva entering a market with other sources of nanosilver and nanosilver products, and makes improper conclusions based on faulty comparisons between Nanosilva and other silver or nanosilver based products.

III. SUMMARY OF NANOTECHNOLOGY AND ITS UNKNOWN RISKS

Nanotechnology is a powerful new set of platform technologies for observing, taking apart, and reconstructing nature at the atomic and molecular level. While the public generally thinks of nanotechnology in the future tense, consumer products containing manufactured nanomaterials have already arrived on market shelves, and comprise a product wave spanning many technologies. Nanosilver is the largest sector of these products, with hundreds of nanosilver products commercially available, although total numbers are unknown, since no labeling is required. These nanosilver products are properly defined and should be regulated as pesticides by EPA, since their only intended use is as an anti-bacterial, anti-microbial agent, i.e., to kill pests.

The same new properties that so excite industry—tiny size, vastly increased surface area to volume ratio, high reactivity—can result in new risks to human health and the environment. Swiss insurance giant Swiss Re noted: "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."[7] These risks essentially take two forms: increased potential toxicity and unprecedented mobility for a manufactured material.

First, nanoparticles' exceptionally large relative surface area creates increased surface reactivity and enhanced toxicity potential, which cannot be accurately predicted from larger material cousins.[8] As the European Commission's (EC) Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) explained:

> "[e]xperts are of 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."[9]

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[7] Swiss Re, *Nanotechnology: Small Matter, Many Unknowns* 37 (2004), *available at* http://media.swissre.com/documents/nanotechnology_small_matter_many_unknowns_en.pdf (last visited Sep. 26, 2013).

[8] Andre Nel *et al*., *Toxic Potential of Materials at the Nanolevel*, 311 Science 622-23 (2006).

[9] European Commission (EC), Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR), *Opinion on the appropriateness of existing methodologies to assess the potential risks associated with engineered*

It is accepted, therefore, that it is not possible to infer the safety of nanomaterials by using information derived from the bulk parent material."[10]

Scientists have yet to determine even what physicochemical properties will be most important in determining ecological and toxicological properties of nanomaterials.[11] Standard toxicological analysis correlates health risks with the mass to which an individual is exposed, resulting in an accumulated mass as an internal dose or 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, at least sixteen in fact, including: size, surface area, surface charge, solubility, shape or physical dimensions, surface coatings, chemical composition, and aggregation potential—a "far cry from the two or three usually measured."[12] Nanotoxicology is an emerging field in its own right, requiring new paradigms of predictive toxicology, which are only now being delineated. Yet EPA relied solely on mass as its risk metric for Nanosilva, despite being "aware" that "metrics other than mass (such as particle number or surface area) may be more suitable for assessing nanoparticle risks."[13]

Second, due to their tiny size, nanomaterials have unprecedented mobility for a manufactured material.[14] They are more easily taken up by the human body and can cross biological membranes, cells, tissues, and organs more efficiently than larger particles.[15] Once in the blood stream, nanomaterials can circulate throughout the body and can be taken up by the organs and tissues including the brain, liver, heart, kidneys, spleen, bone marrow, and nervous system.[16] 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, induce major structural damage, and result in DNA mutation.[17] EPA has, in fact, voiced its concerns regarding

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and adventitious products of nanotechnologies 6, 32 (adopted Sept. 28-29, 2005), *available at* http://ec.europa.eu/health/ph_risk/committees/04_scenihr/docs/scenihr_o_003.pdf (last visited Sep. 26, 2013).

[10] C. L. Tran *et al., A Scoping Study to Identify Hazard Data Needs for Addressing the Risks Presented by Nanoparticles and Nanotubes*, Institute of Occupational Medicine 34 (2005), *available at* http://randd.defra.gov.uk/Document.aspx?Document=CB01072_3060_FRP.doc (last visited Sep. 26, 2013).

[11] A. Maynard *et al., Safe Handling of Nanotechnology*, 444 Nature 267-69 (Nov. 2006); G. Oberdorster *et al., Nanotoxicology: An Emerging Discipline Evolving from Studies of Ultrafine Particles*, 113(7) Envtl. Health Perspectives 823-39 (2005).

[12] Andrew Maynard, *Nanotechnology: The Next Big Thing, or Much Ado about Nothing?*, 51 Annals of Occupational Hygiene 1-12, 7 (2006), *available at* http://annhyg.oxfordjournals.org/content/51/1/1.full.pdf+html (last visited Sep. 26, 2013).

[13] A. Nel *et al., Toxic Potential of Materials at the Nanolevel*, 311 *Science* 622-627 (2006); A. Maynard *et al., supra* note 11.

[14] Hoet *et al., Nanoparticles-known and unknown health risks*, 2 Journal of Nanobiotechnology 12 (2004); Swiss Re, *supra* note 7, at 7.

[15] *See, e.g.*, Holsapple *et al., Research Strategies for Safety Evaluation of Nanomaterials, Part II: Toxicological and Safety Evaluation of Nanomaterials, Current Challenges and Data Needs*, 88 Toxicological Sciences 12 (2005).

[16] Oberdorster *et al., supra* note 11.

[17] Li, N., *Ultrafine particulate pollutants induce oxidative stress and mitochondrial damage*, 111 Environ. Health Perspectives 455-60 (2003).

nanomaterials' ability to be absorbed into the body and cross the blood-brain barrier, as well as the high durability and reactivity of some nanomaterials.[18]

As little as is known about nanomaterials' health impacts, even less is known about their environmental impacts.[19] While EPA acknowledged that no fate or ecotoxicity studies are available for Nanosilva, EPA nonetheless proposes granting conditional registration of Nanosilva.[20]

Nanosilva is no ordinary pesticide that EPA has conditionally regulated, while simultaneously acknowledging it lacked critical data. Nanomaterials represent a new class of materials, materials for which the scientific community universally has concluded can act in fundamentally new ways, ways that experts are just starting to understand. Nanosilver pesticides are the first regulatory precedent for these materials, as well as the leading product type. If there were ever time for caution, in furtherance of the public interest, it must be here.

IV. EPA FAILS TO MEET THE REQUIREMENTS TO GRANT CONDITIONAL REGISTRATION TO NANOSILVA

FIFRA allows EPA to grant conditional registrations for active ingredients not contained in currently registered pesticides if EPA determines that the pesticide will not cause any "unreasonable adverse effects on the environment, and that the use of the pesticide is "in the public interest."[21] Such registrations may only last for a period reasonably sufficient for the generation and submission of required data, which are lacking because a period reasonable sufficient for generation of the data has not elapsed since EPA first imposed the data requirement.[22]

EPA proposes to grant the conditional registration for Nanosilva claiming that use of the pesticide will not cause unreasonable adverse effects on the environment during the period while the registrant develops the newly required data; use of Nanosilva is in the public interest; and that insufficient time has elapsed for Nanosilva LLC to generate and submit the required data.[23]

However, EPA has failed to satisfy the requirements for granting Nanosilva a conditional registration.

A. EPA cannot show that Nanosilva will not cause "unreasonable adverse effects on the environment" as required by FIFRA for conditional registration.

[18] W. Jordan, Office of Pesticide Programs, EPA, *Nanotechnology and Pestcides* 8-9 (2010), *available at* http://www.epa.gov/pesticides/ppdc/2010/april2010/session1-nanotec.pdf (last visited Sep. 26, 2013).
[19] Nanotechnology Working Group, EPA Science Policy Council, EPA *Nanotechnology White Paper* 33 (2007) ("The fundamental properties concerning the environmental fate of nanomaterials are not well understood, as there are few available studies on the environmental fate of nanomaterials."), *available at* http://www.epa.gov/osa/pdfs/nanotech/epa-nanotechnology-whitepaper-0207.pdf (last visited Sep. 26, 2013).
[20] EPA, Draft Decision Document at 70.
[21] 7 U.S.C. § 136a(c)(7)(C).
[22] *Id.*
[23] EPA, Draft Decision Document at 1.

Before granting a pesticide registration, EPA must determine that the pesticide will not cause any "unreasonable adverse effect on the environment."[24] The term "unreasonable adverse effects on the environment" means "any unreasonable risk to man or the environment, taking into account the economic, social, and environmental costs and benefits of the use of any pesticide."[25]

EPA's conditional registration of Nanosilva is unlawful because nanosilver poses unreasonable risks to man and the environment. The unreasonableness of the risks posed by nanosilver pesticides are further underscored by the dearth of health and safety data in the record.

1. EPA applies the wrong legal standard.

EPA applies the wrong standard in making its determination to conditionally register Nanosilva. EPA states that it "has determined that there is a low probability of adverse risk to human health and the environment from plastics and textiles incorporating Nanosilva."[26] Applying this "low probability of adverse risk" standard in granting Nanosilva conditional registration not only puts human health and the environment at risk, but is also indicative that EPA failed to consider the proper factors, and thus is arbitrary and capricious agency action on behalf of EPA.[27]

2. EPA fails to adequately address gaps in the scientific literature with regard to Nanosilva and nanosilver, more generally.

Beyond applying the wrong standard, EPA lacks adequate data to make its decision. As with nanomaterials more generally, there is a lack of research on the human health and environmental safety of nanosilver, and especially with a composite product like Nanosilva that the company plans to use more extensively than any existing nanosilver products. Indeed, it plans more extensive use than even any existing bulk silver products. Among other things, proposed incorporation of Nanosilva includes textiles, plastic films, sheets, slabs, and molded parts, as well as consumer products such as footwear, sportswear, uniforms, and auto parts, floor coverings, outdoor furniture, decking, and house siding.[28] To our knowledge, no other silver pesticide product registrations cover floor coverings, plastic films, slabs, and molded parts, such as those that would be found in outdoor furniture, decking and house siding.

SAP specifically acknowledged that "data gaps about potential exposures and hazards related to nanosilver are broad," noting that "there is very little information about nanosilver in the environment related to fate, transport, and transformation."[29] Further, EPA's Draft Decision Document admits that there are "no fate or ecotoxicity studies available for Nanosilva," which required EPA to estimate the fate and ecotoxicity using existing studies in the scientific literature.[30]

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[24] 7 U.S.C. § 136a(c)(7)(C).
[25] 7 U.S.C. § 136(bb).
[26] EPA, Draft Decision Document at 1 (emphasis added).
[27] *Motor Vehicle Mfrs. Assoc. v. State Farm Mutual Auto. Ins. Co.*, 463 U.S. 29, 43 (1983) ("Agency action is arbitrary and capricious if the agency relied on factors Congress has not intended it to consider.").
[28] EPA, Draft Decision Document at v.
[29] SAP Report at 9.
[30] EPA, Draft Decision Document at 70.

EPA acknowledged the existence of many gaps in scientific knowledge with regard to nanosilver's effects on health and the environment. These gaps include:

- no intermediate- or long-term human or environmental toxicity studies available for Nanosilva or for the nano-sliver released from products incorporating Nanosilva[31]
- no studies on environmental fate and transport[32]
- no studies in the scientific literature that investigate mutagenicity or carcinogenicity of nanosilver[33]
- no subchronic or chronic oral or dermal toxicity studies available for Nanosilva or on the nanosilver that might break away from products incorporating Nanosilva[34]
- no acceptable studies on the reproductive and developmental toxicity for nanosilver[35]
- inadequate information to assess mutagenic and carcinogenic potential of nanosilver due to differences in results between *in vitro* studies and *in vivo* studies, and limitations of the only available *in vivo* study[36]
- insufficient information on aggregate exposures to other nanosilvers currently in the market place.[37]

Yet the absence of data cannot replace the agency's burden to show, based on substantial evidence, that there will be no unreasonable impacts on the environment.

Several studies have raised significant red flags about nanosilver pesticides. As with some other nanomaterials, due to its size, the toxicity of nanosilver is greater than that of silver in bulk form; furthermore, nanosilver is more toxic then other metal nanoparticles.[38] EPA's SAP concluded:

> Nanoscale particles including nanosilver have been shown to be capable of penetrating biological barriers such as cell membranes and can enter into the cells themselves. Nanoparticles are able to attach to cell membranes, producing changes in membrane permeability, redox cycling in the cytosol, intracellular radical accumulation, and dissipation of the proton motive force for ATP synthesis. Each of these has been reported as a possible mechanism for nanoparticle toxicity. Evidence from scanning transmission electron microscopy also shows that smaller particles (< 10 nm) may enter the cell directly to inhibit microbial growth.[39]

[31] EPA, Draft Decision Document at vi.
[32] *Id.* at 55.
[33] *Id.* at 14
[34] *Id.* at 23.
[35] *Id.* at 24.
[36] *Id.* at 16.
[37] *Id.* at 52.
[38] Braydich-Stolle, L *et al*., *In Vitro Cytotoxicity of Nanoparticles in Mammalian Germline Stem Cells*, 88(2) Toxicological Sciences 412–419 (2005).
[39] FIFRA Scientific Advisory Panel Meeting, SAP Minutes No. 2010-01, *Evaluation of the Hazard and Exposure Associated with Nanosilver and Other Nanometal Pesticide Products*, (Nov. 3-5, 2009) (internal citations omitted).

Among documented potential harms to human health, *in vitro* (test tube) studies demonstrate that nanosilver is toxic to mammalian liver cells,[40] stem cells[41] and even brain cells.[42] One 2009 study discovered that absorption of nanosilver may interfere with the replication of DNA molecules, potentially creating genetic mutations.[43] Two other studies have demonstrated that exposure to nanosilver can reduce mitochondrial function.[44] The number of diseases associated with mitochondrial malfunction is increasing and includes Parkinson's, Alzheimer's, and Huntington's disease.[45]

Beyond the issue of toxicity, nanosilver may also create a public health burden by producing antimicrobial resistance.[46] The Centers for Disease Control and Prevention (CDC) recently acknowledged antimicrobial resistance as one of the world's most serious health threats, in part because of the use and overuse of antibiotics in medicine and food production.[47] As with antibiotics, the use and overuse of nanosilver may promote resistance to important antimicrobials, which must be addressed before it is too late.[48]

Nanosilver is also toxic to a variety of aquatic and terrestrial organisms.[49] EPA acknowledges that, even in its bulk form, silver is extremely toxic to fish and other aquatic species.[50] EPA

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[40] Hussain, S.M. *et al., In Vitro Toxicity of Nanoparticles in BRL 3A Rat Liver Cells*, 19 Toxicology in Vitro 975–983 (2005).

[41] Braydich-Stolle, L et al., *supra* note 38.

[42] Hussain, S.M *et al., The Interaction of Manganese Nanoparticles with PC-12 Cells Induces Dopamine Depletion*, 92(2) Toxocological Sciences 456–63 (2006); *see also* Bar-Ilan O., *et al*., *Toxicity Assessments of Multisized Gold and Silver Nanoparticles in Zebrafish Embryos*, 5 Small 1897-1910 (2009); Soto K., *et al*., *Cytotoxic Effects of Aggregated Nanomaterials*, 3 Acta Biomaterialia 351-358 (2007); Soto K., *et al*., *Comparative In Vitro Cytotoxicity Assessment of Some Manufactured Nanoparticulate Materials Characterized by Transmission Electron Microscopy*, 7 Journal of Nanoparticle Research 145-169 (2005); *and* AshaRani P., *et al*., *Cytotoxicity and Genotoxicity of Silver Nanoparticles in Human Cells*, 3 Acs Nano, 279-290 (2009).

[43] Wenjuan Yang *et al., Food storage material silver nanoparticles interfere with DNA replication fidelity and bind with DNA*, 20:8 Nanotechnology 85-102 (2009).

[44] Hussain *et al*., *supra* note 40; Hussain *et al., supra* note 42.

[45] Schapira *et al., Mitochondrial disease*, 368 (9529) Lancet 70-82 (2006).

[46] *See generally* Friends of the Earth (FoE), *Nanosilver: Policy Failure Puts Public Health At Risk* (2011), *available at* http://libcloud.s3.amazonaws.com/93/e2/8/549/NanoSilverUS.pdf (last visited Sep. 26, 2013).

[47] CDC, *Antibiotic Resistance Threats in the United States* 11 (2013), *available at* http://www.cdc.gov/drugresistance/threat-report-2013/pdf/ar-threats-2013-508.pdf (last visited Sep. 26, 2013).

[48] In the case of antibiotics in food production, the Food and Drug Administration (FDA) knew as early as 1972 that the sub-therapeutic use of antibiotics in animals favors the selection and development of antibiotic resistant bacteria. *See* 37 Fed. Reg. 2,444, 2,444-5. Yet, not until 2012 did FDA issue draft guidance to promote judicious use of antibiotics. *See* FDA, Draft Guidance for Industry on New Animal Drugs and New Animal Drug Combination Products Administered in or on Medicated Feed or Drinking Water of Food-Producing Animals: Recommendations for Drug Sponsors for Voluntarily Aligning Product Use Conditions With GFI #209, 77 Fed. Reg. 22,327 (Apr. 13, 2012) *available at* http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM299624.pdf (last visited Sep. 26, 2013).

[49] *See* FoE, *Nano & Biocidal Silver* 15-18, 20-24 (and citations therein) (2009), *available at* http://nano.foe.org.au/sites/default/files/Nanosilver%20Report%202009.pdf (last visited Sep. 26, 2013).

[50] EPA, Draft Decision Document at 55; *see also* Hogstrand *et al., The Toxicity of Silver to Marine Fish*, 4th International Conference Proceedings: Transport, Fate, and Effect of Silver in the Environment 109-112 (1996).

ignores that, at the nano-scale, nanosilver can be many times more toxic.[51] Swiss researchers recently modeled the environmental concentrations of several commercially available nanomaterials and predicted that nanosilver emissions may already pose risks to aquatic organisms.[52]

Further, the same property that makes these nanoparticles attractive to manufacturers—their highly enhanced antimicrobial properties—can be highly destructive to ecosystems, by threatening the bacteria-dependent processes that underpin natural systems. Microorganisms are the foundation of all ecosystems and provide key environmental services ranging from primary productivity to nutrient cycling and waste decomposition. Early studies show that nanosilver can reduce the activities of microbes employed in treating wastewater.[53] Widespread use of household products that release nanosilver into the sewage system could adversely affect waterways, exacerbated by the inability of public utilities and water treatment plants to properly treat the substance.[54]

In 2009, as a result of these and other potential adverse impacts on the environment, EMERGNANO, the first global review of environmental, health, and safety studies examining the risks of nanotechnology exposure, found that there is "sufficient evidence to suggest that silver nanoparticles may be harmful to the environment and therefore the use of the precautionary principle should be considered in this case."[55]

Given the improper standard that EPA applies to its decision, the acknowledged data gaps about potential exposures and hazards, significant red flags raised by existing data, and new broad uses proposed for Nanosilva, EPA has failed to show that conditional registration of Nanosilva will not cause unreasonable adverse effects on the environment.

B. Nanosilva has had sufficient time to generate and submit required data.

FIFRA allows EPA to grant conditional registrations of active ingredients not contained in any currently registered pesticides to allow registrants to generate and submit required data.[56]

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[51] Marambio-Jones *et al., A Review of the Antibacterial Effects of Silver Nanomaterials and the Potential Implications for Human Health and the Environment*, 12 J. Nanopart Res 1531-51 (2010); Wijnhoven *et al., Nanosilver – a review of available data and knowledge gaps in human and environmental risk assessment*, 3 (2) Nanotoxiocology 109-138 (2009).

[52] Gottschalk *et al., Possibilities and limitations of modeling environmental exposure to engineered nanomaterials by probabilistic material flow analysis*, 29 Envion Toxicology and Chemistry 1036-48 (2010).

[53] Choi *et al., The Inhibitory Effect of Silver Nanoparticles, Silver Ions, and Silver Chloride on Microbial Growth*, 42 Water Research 3066-74 (2008); Nanowerk, *Too Much Technology May Be Killing Beneficial Bacteria* (2008), *available at* http://www.nanowerk.com/news/newsid=5520.php (last visited Sep. 26, 2013).

[54] Letter from Ken Kirk, Executive Director, Nat'l Ass'n of Clean Water Agencies, to Stephen Johnson, Administrator, EPA (February 14, 2006), *available at* http://archive.nacwa.org/www.nacwa.org/getfile7128.html?fn=2006-02-14agltr.pdf (last visited Sep. 26, 2013); Benn, T. M., *et al. Nanoparticle silver released into water from commercially available sock fabrics*, 42 (11) Environmental Science & Technology 4133-4139 (2008).

[55] Aitken R, Hankin S, *et al*., *EMERGNANO: A Review of Completed and Near Completed Environmental, Health and Safety Research on Nanomaterials and Nanotechnology* 146 (2009), *available at* http:// http://randd.defra.gov.uk/Document.aspx?Document=CB0409_7911_FRP.pdf (last visited Sep. 26, 2013).

[56] 7 U.S.C. § 136a(c)(7)(C).

However, only when a data requirement is "first imposed" so recently that a registrant is unable to generate the data in time for the registration application may EPA grant a conditional registration. [57]

For example, EPA may require additional information from a registrant because those data specified in the regulations are insufficient for EPA to properly evaluate the product.[58] Upon such a request, the registrant should be given sufficient time to generate that data, and a conditional registration may be applicable. However, that is not the case here.

Nanosilva LLC applied in August 2009 to register this product. EPA concluded that because it had not yet reached a final decision as to which types of data would be required for Nanosilva, in part to apply the advice provided by SAP, that insufficient time had elapsed from the point at which EPA determined and informed Nanosilva LLC of the data requirements needed to assess Nanosilva LLC's application for Nanosilva LLC to have generated the data.[59] Nearly four years have passed since SAP convened in November 2009 and identified what would be needed to make a decision on Nanosilva's application. EPA now proposes to grant another three years to develop the newly required studies.[60] More than sufficient time has elapsed for the company to perform adequate toxicological testing of its product.

C. EPA failed to show that conditional registration of Nanosilva is in the public interest.

To grant a conditional registration, EPA must determine that the use of the pesticide is in the public interest.[61] EPA believes that the registration of this product benefits the public based on the following points: 1) conservation of the environment, 2) consumer benefits, and 3) innovation.[62]

For the first claim, EPA notes that a number of silver-based pesticide products are registered for use as materials preservatives, and that the use of Nanosilva could result in less environmental loading of silver than from currently registered silver-based pesticides.[63] However, because nanosilver is a more potent pesticide than traditional silver-based pesticides – that is, less nanosilver kills more microbes – even if Nanosilva results in a reduction in the overall mass of silver released into the environment, the potential for environmental damage and non-target impacts may still be greater than that resulting from currently registered silver-based pesticides. In fact, SAP noted that the rate and concentration of silver ions released from nanosilver will likely affect the acute or chronic toxicity of nanosilver compared with silver.[64] Moreover, EPA ignores the fact that there is no silver pesticide product on the market right now that is used as a material preservative in plastic for products like decking and plastic lumber, which have not previously relied on silver-based pesticides. Thus Nanosilva will be in addition to, rather than in

[57] *Id.*
[58] 40 CFR § 161.35(c).
[59] EPA, Draft Decision Document at 66.
[60] *Id.* Table 3b.
[61] 7 U.S.C. § 136a(c)(7)(C).
[62] EPA, Draft Decision Document at 67-69.
[63] *Id*. at 68.
[64] SAP Report at 10.

place of other silver-embedded products in the environment. Therefore, conditional registration of Nanosilva will necessarily increase, not reduce, the amount of silver ions that will be released into the environment

Additionally, SAP noted that nanosilver, but not silver, can penetrate cell membranes and deliver toxic ions directly inside of cells; the toxicity of silver nanoparticles appear to be much higher than that of silver nitrate; and that because of these differences in chemical properties, there are likely differences in exposure and environmental fate of nanosilver that should be considered.[65] Thus, in the case of Nanosilva replacing silver-based pesticides in commerce, any reduction in environmental loading of silver is not likely to result in conservation of the environment.

In its second claim, EPA asserts that conditional registration of Nanosilva will lead to consumer benefits, such that "plastics or textiles incorporating nanosilver may have longer-term ability to reduce the number of odor and stain causing bacteria as compared to other similar products on the market that contain conventional silvers."[66] However, EPA has failed to explain why consumers need antimicrobial plastics or textiles in the first case.

Moreover, EPA failed to provide an adequate characterization of the chemistry of Nanosilva, making it impossible for the public, and likely even for EPA staff, to "guesstimate" whether or not it would behave like other described nanosilver materials. EPA describes Nanosilva as, "a liquid suspension containing silica-sulfur-nanosilver particulates where the nanosilver active-ingredient is attached to crystalline silica via a thiolate bond."[67] First, the description of the silica as crystalline is likely in error; it is likely that the form of silica is synthetic amorphous silica. If this is not the case, and it is actually crystalline, then given crystalline silica's known cancer effects, EPA's determination of no cancer risk is certainly in error.

Presuming the error is in the description of the material, this error raises red flags about whether or not EPA staff that reviewed Nanosilva included material chemists, who would have the necessary expertise to characterize the material. Nanosilva appears to be a single silica particle surrounded by multiple nanoscale PVP-coated-silver particles connected together through weak thiol linkages. However, EPA fails to define the thiol linkages adequately and raises significant questions. What is the thiol linkage to? Is it to the PVP coating, or to the silver atoms, or to a silver ion that is separate from the surface? Research has demonstrated the PVP-coated-nanosilver particles, such as those used in the Nanosilva product, may be more toxic than uncoated particles.[68]

Last, EPA claims that it sees the emergence of nanotechnology as offering benefits for society including pest control products, and seeks to encourage innovative work to realize those benefits.[69] However, EPA does not provide any supporting data that suggests how or why it believes that nanotechnology "may allow for more effective targeting of pests and use of smaller

[65] SAP Report at 10-11.
[66] EPA, Draft Decision Document at 68.
[67] *Id.* Appendix B, p. 2.
[68] S. Kittler *et al.*, *Toxicity of Silver Nanoparticles Increases during Storage Because of Slow Dissolution under Release of Silver Ions*, 22 Chemistry of Materials 4548-4554 (2010).
[69] EPA, Draft Decision Document at 68-69.

quantities of pesticide."[70] Moreover EPA fails to assert how conditional registration of Nanosilva will encourage such innovative work, or in the alternative, how requiring sufficient data and studies of Nanosilva would discourage such innovative work.

Given the potential harm to human health and the environment, significant scientific unknowns, and lack of support for alleged benefits of Nanosilva, the conditional registration of Nanosilva is not in the public interest.

V. FUNDAMENTAL INADEQUACY, AND OVERUSE, OF CONDITIONAL REGISTRATION

Section 3(c)(7) of FIFRA provides EPA the authority to grant a "conditional registration" for a pesticide product under certain circumstances, even though some necessary data have not been provided by the registrant in the application.[71] By doing so, EPA allows pesticides into the marketplace without complete data, such as toxicity tests and studies that demonstrate the pesticides' impact on the environment. EPA's Office of Pesticide Programs (OPP) has overused conditional registrations, not in keeping with their original intent – to be used only in limited circumstances where a public need was established.[72]

In March 2011, an internal review conducted by OPP determined that of 16,156 active pesticide registrations, 11,205 (69 percent) were conditionally registered.[73] Of those, over 3,200 pesticides had been in conditional status since 1995, and 2,100 pesticides had been in conditional status since 1990. OPP officials allege that these numbers are inaccurate as a result of misclassifications and that the basis for many registration decisions was mischaracterized as conditional.[74]

The high numbers of products registrations that remain conditionally registered after so many years raises several concerns.

At best, EPA has poorly overseen its registration program to the point that its tracking system cannot even identify the status of conditionally registered pesticides to ensure that registrants submitted, and EPA reviewed, the required additional data upon which registration is conditioned, in a timely manner. As currently construed, the conditional registration program calls into question EPA's assertion that it will evaluate the additional required data "to confirm the Agency's risk assessment."[75]

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[70] EPA, Draft Decision Document at 68.
[71] 7 U.S.C. § 136a(c)(7).
[72] S.Rep.No. 95-334, 95th Cong., 1st Sess., 2 (July 6 (legislative day, May 18), 1977) at 21. (legislative history of the conditional registration process identifying that the "public interest" encompasses a narrow range of interests, such as "a significant pest control problem which cannot satisfactorily be handled by use of products which have been fully registered.").
[73] Government Accountability Office (GAO), *PESTICIDES: EPA Should Take Steps to Improve Its Oversight of Conditional Registrations* 13 (Aug. 2013) [hereinafter GAO Report], *available at* http://www.gao.gov/assets/660/656825.pdf (last visited Sept. 26, 2013)
[74] GAO Report at 13.
[75] EPA, Draft Decision Document at 2.

More importantly, OPP may be failing to meet its requirements under FIFRA to review each chemical every 15 years, allowing products to stay on the market despite lacking the data required by law.[76]

The Government Accountability Office (GAO) addressed these issues, amongst others, in a 2013 report entitled, "PESTICIDES: EPA Should Take Steps to Improve Its Oversight of Conditional Registrations." GAO made several conclusions regarding EPA's improper handling of conditional registration, including:

- EPA lacks a reliable system to track key information related to conditional registrations, including whether companies have submitted the additional data required by conditional registration within the required time frames.[77] Thus, EPA lacks an important registration management tool and cannot ensure that companies submit the required data, which may allow pesticides to remain on the market for years without EPA's receipt and review of these data.
- GAO has well documented OPP's problems with data management, with studies dating back to 1980, 1986, 1991, and 1992 noting problems with OPP data systems used to track the status of pesticide registrations.[78]
- GAO was unable to verify OPP officials' assertion that all actions mistakenly categorized as conditional registrations were legitimate program actions which were lawful under other sections of FIFRA.[79] EPA needs to correct misclassifications to ensure the accuracy and integrity of its data and make clear the statutory basis for these actions.
- OPP's use of conditional registrations for actions other than those that meet the criteria outlined in FIFRA Section 3(c)(7) has created confusion for its staff.[80] OPP lacks written guidance or a consistent methodology for maintaining its pesticide registration files, resulting in difficulty developing summary information about the status of pesticide registrations, and managing the pesticide registration program.[81]

Given the mishandling of EPA's conditional registration program, its usage here is troublesome. Specifically, because EPA cannot adequately track conditional registrations and assure that the requested data is timely submitted, the public cannot be assured what will happen upon the expiration of the four years which EPA has granted Nanosilva to supply the required data. EPA provides no clue as to what will happen upon expiration of this four year time period, such as Nanosilva products being removed from the market, or prosecution for continued production of Nanosilva incorporated products.

Thus, even if Nanosilva's conditional registration expires in four years there is no guarantee that EPA will take proper action to protect environmental safety and ensure that Nanosilva products are removed from the market or prevented from entering the market.

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[76] 7 U.S.C. § 136a(g)
[77] GAO Report at 19.
[78] *Id.* at 21.
[79] *Id.* at 14.
[80] *Id.* at 37.
[81] *Id.* at 38.

EPA has overused conditional registrations generally, failed to adequately oversee its conditional registration program allowing pesticide products to remain on the market without adequate and required studies, and should curtail its use of conditional registration to adhere to its original intent. Specifically, EPA's proposed conditional registration for Nanosilva is not supported by necessary elements as required by FIFRA.

VI. SPECIFIC COMMENTS

Proceeding with a conditional registration based on the rationale provided in the Draft Decision Document would be an arbitrary and capricious action by EPA, and contrary to law. Agency action must be set aside if it is arbitrary and capricious, an abuse of discretion, otherwise not in accordance with law, or without observance of procedure required by law.[82] Agency action is arbitrary and capricious if the agency relied on factors Congress has not intended it to consider, entirely failed to consider an important aspect of the problem, offered an explanation for its decision that runs counter to the evidence before the agency, or is so implausible that it could not be ascribed to a difference in view or the product of agency expertise.[83] EPA's Draft Decision Document overlooked important gaps in scientific data, applied faulty science to determine possible risks to conditional registration of Nanosilva, and if approved would be arbitrary and capricious agency action.

A. EPA's cursory look at aggregate effects is insufficient and fails to consider the other nano-scale antimicrobials which are on the market without having undergone a full chemical risk assessment on the nano-scale material.

EPA's proposed conditional registration of Nanosilva while turning a blind eye to other nanosilver pesticides currently on the market is contrary to its obligations under FIFRA.[84] The agency is legally obligated to adopt a consistent policy with regard to nanosilver products, because nanosilver is a pesticide requiring registration. These other nanosilver products, like Nanosilva, are properly classified as "pesticides" since the only purpose of the infused nanosilver is to fight bacteria, i.e., prevent pests. Nanosilver thus meets the definition of a pesticide.[85]

EPA argues that, because Congress specifically required consideration of aggregate exposures for registration under FIFRA for food-use pesticides, but not for non food-use pesticides, that such studies are not required to determine whether registration of Nanosilva will cause any unreasonable adverse effects on the environment.[86]

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[82] *Dickinson v. Zurko*, 527 U.S. 150, 152 (1999); 5 U.S.C. § 706(2)(A), (D).
[83] *Motor Vehicle Mfrs. Assoc. v. State Farm Mutual Auto. Ins. Co.*, 463 U.S. 29, 43 (1983).
[84] *See, e.g., Mayes v Massanari*, 276 F.3d 453, 459 (9th Cir. 2001) ("Whether substantial evidence supports a finding is determined from the record as a whole, with the court weighing both the evidence that supports and the evidence that detracts from [EPA's] conclusion.").
[85] 7 U.S.C. § 136(a)(1); 40 C.F.R. § 153.125 (defining "pesticide" broadly to be "any substance or mixture of substances intended for preventing, destroying, repelling, or mitigating any pest.").
[86] *See* EPA, Draft Decision Document at 50.

Thus, for the sake of "transparency," the extent of EPA's consideration of aggregate exposures involved Nanosilva and HeiQ AGS-20, "the only other pesticide which was knowingly registered as containing nanosilver."[87] In so doing, EPA concluded that if exposures to the two active nanosilver ingredients in Nanosilva and HeiQ AGS-20, were to occur concurrently, they would not result in margins of exposure that "would be of concern."[88] However, this fails to account for aggregate human and environmental exposures from other sources of nanosilver, which are many. Given that EPA's rationale for approving a conditional registration for this product is the purported environmental benefit to the environment from the release of silver ions, EPA must consider the cumulative and aggregate impact of all the various sources of silver ions in the environment.

According to the Woodrow Wilson International Center for Scholars, Project on Emerging Nanotechnologies (PEN), which maintains a registry of self-labeled products containing nanomaterials, there are over 300 nanosilver products already on the market.[89] Since no labeling or government registration is currently required, these self-labeled products are likely only the tip of the iceberg. PEN estimates that there are three to four new nanotech products hitting the market every week.[90]

EPA has acknowledged that it suspects it already approved the registrations of some like-situated products on the market that contain nanosilver as the active ingredient without knowledge that these products may contain nanosilver and without assessing any potential risks that might be associated with nanosilver.[91] Though EPA intends to seek more data from those products, such an admission should call for more caution, not less.[92]

Further, EPA acknowledged that it lacks the necessary information required to conduct an adequate aggregate risk assessment as to exposure to other nanosilver products in the market place.[93] Not only does EPA not have sufficient information to conduct an aggregate risk assessment, EPA asserts that it lacks adequate information on the composition of the nanosilver or potential nanosilver in other silver based pesticides to determine if all nanosilver should be treated as a single chemical.[94] Yet, EPA claims it had sufficient information to determine that Nanosilva would not pose unreasonable adverse effects on the environment.

Without including such increased aggregate exposure and cumulative risk, the agency's determination failed to ensure that the registration will not cause any "unreasonable adverse effects" on the environment or health, and is plainly contrary to the public interest.

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[87] EPA, Draft Decision Document at 51.
[88] *Id.*
[89] *See* Project on Emerging Nanotechnologies, Woodrow Wilson Int'l Ctr. for Scholars, *Nanotechnology Consumer Product Database Analysis, available at* http://www.nanotechproject.org/inventories/consumer/analysis_draft/ (last visited Sep. 26, 2013).
[90] Press Release, Project on Emerging Nanotechnologies, Woodrow Wilson Int'l Ctr. for Scholars, *New Nanotech Products Hitting the Market at the Rate of 3-4 Per Week* (Apr. 24, 2008), *available at* http://www.nanotechproject.org/process/assets/files/6697/pen_press_release_080422.pdf (last visited Sep. 26, 2013).
[91] EPA, Draft Decision Document at 64.
[92] *Id.*
[93] *Id.* at 51-52.
[94] *Id.* at 52.

B. EPA's reliance on available studies on the effect of nanosilver is misplaced because Nanosilva is unique as a nanosilver and nanosilicon based combination nano-particle, a combination for which there is no public data.

Nanosilva is a silica-sulfur-nanosilver complex where the nanosilver active-ingredient is attached to crystalline silica via a thiolate bond.[95] This configuration presents a more than substantial alteration to existing nanosilver combinations. Minimal public data exists on the unique combination of nanosilver and nanosilicon, such that any reliance on available studies on the effect of nanosilver by EPA is misplaced and inadequate in evaluating the risk to human health and the environment.

EPA acknowledged that SAP "cautioned about extrapolating from one nanosilver formulation to another when assessing hazards because differences in particle formulation (e.g., coating and inert ingredients) are likely to affect biological activity, among other things."[96] Yet, EPA has done exactly that. For example, because no repeated-dose subchronic or chronic toxicity studies exist for Nanosilva or the nanosilver in Nanosilva, the Agency relied on studies in the scientific literature on nanosilver toxicity based on the belief that they would be sufficient for assessing the risks of the unique Nanosilva complex.[97]

Until EPA has data which shows that Nanosilva is not a reproductive or development toxicant, a carcinogen, an endocrine disrupter, and that it is not toxic to the aquatic environment, EPA cannot allow this product to enter the market. Without these data, EPA cannot show that there are no unreasonable adverse effects to the environment and human health associated with the use of Nanosilva, and as such, cannot conditionally register this pesticide product.

C. EPA's reliance on available studies on the effect of silver is misplaced because it is not possible to infer the safety of nanomaterials by using information derived from the bulk parent material.

In its Draft Decision Document, EPA acknowledged the conclusions of SAP that:

> "existing information on conventional silver could be useful but would not necessarily be sufficient in assessing potential nanosilver risks. SAP recommended that the Agency treat nanosilver differently from its conventional silver counterpart in evaluating proposed nanosilver product applications (in terms of both data requirements and the conduct of risk assessments). Moreover, the Panel recommended that EPA require additional data on the physical chemistry, exposure potential, and the potential hazard to human health and the environment."[98]

Yet, EPA's conclusion that human health or ecological risk from exposure to silver ions derived

[95] EPA, Draft Decision Document at 4.
[96] *Id.* at 2.
[97] *See Id.* at 9, 55 (relying on studies available in the scientific literature as the basis for determining the fate of nanosilver in the environment because Nanosilva LLC has not conducted any studies to characterize the environmental fate of Nanosilva or the other particles that could be released during leaching or disposal of plastics and textiles incorporating Nanosilva).
[98] *Id.* at 3.

from products incorporating Nanosilva are not of concern, "relied on the existing reregistration decision for silver."[99] Similarly, despite known risks of silver's toxicity to aquatic life, Nanosilva did not submit any tests with aquatic organisms. However, after mentioning the concentrations of silver in surface waters, EPA summarily concluded that it does not expect any unreasonable adverse effects to the environment by citing a twenty year old assessment of conventional silver, from 1993, with no further explanation.[100] Such reliance is misplaced and fails to adequately assess the risk exposure from granting Nanosilva conditional registration.

VII. CONCLUSION

EPA's proposed conditional registration of Nanosilva would be an arbitrary and capricious agency action contrary to law and in violation of FIFRA. Given significant unknowns about nanotechnology generally, and Nanosilva specifically, EPA's proposed conditional registration would expose the environment to unreasonable adverse effects. These significant known and unknown risks provide all the more reason that EPA should require more testing before allowing Nanosilva on the market. EPA has overused and misused its authority under FIFRA in its use of conditional registrations, allowing untested products on the market while relying on improper science and ignoring significant data gaps about their effects. EPA must withdraw its proposal to conditionally register Nanosilva so as to act in accordance with its duties under FIFRA and to protect human health and the environment.

Thank you for the opportunity to provide comments.

Respectfully,

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[99] EPA, Draft Decision Document at v.
[100] EPA, Draft Decision Document at 57.