Comments of the Natural Resources Defense Council on EPA's Proposed Conditional Registration of Nanosilva as a Materials Preservative in Textiles and Plastics

September 26, 2013

Docket ID: EPA-HQ-OPP-2012-0594

The Natural Resources Defense Council (NRDC) is a national, non-profit environmental organization of lawyers, scientists, and other professionals. NRDC presents these comments on behalf of our 1.4 million members and online activists. NRDC does not have any financial interest in the topic of these comments. NRDC appreciates the opportunity to comment on the U.S. Environmental Protection Agency's ("EPA's") Draft Decision Document for Proposed Conditional Registration of Nanosilva as a Materials Preservative in Textiles and Plastic, dated August 27, 2013 (hereinafter referred to as "Draft Decision Document").

These comments are supported by the following public interest, community, and environmental health organizations:

Beyond Pesticides (Nichelle Harriott)
Center for International Environmental Law (David Azoulay)
Food and Water Watch (Patty Lovera)
Friends of the Earth Australia (Louise Sales)
Friends of the Earth U.S. (Ian Illuminato)
Glynn Environmental Coalition (Daniel Parshley)
Health Care Without Harm (Paul Bogart)
Healthy Building Network (Tom Lent)
Healthy Child Healthy World (Gigi Lee Chang)
Institute for Agriculture and Trade Policy (Steve Suppan)
Midwest Environmental Justice Organization (Maria Powell)
TEDX, The Endocrine Disruption Exchange (Lynn Carroll)

NRDC and the above organizations that have signed on to these comments strongly oppose the conditional registration of Nanosilva and requests that EPA not register Nanosilva until all the relevant toxicity data are received. Throughout the Draft Decision Document, EPA provide little to no rational basis 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. Proceeding with a conditional registration based on the rationale provided in the Draft Decision Document would be an arbitrary and capricious action by the Agency.

I. Introduction

In August 2009, the company Nanosilva LLC applied to register a new active ingredient called Nanosilva, which is a "liquid suspension containing silica-sulfur-nanosilver particulates where the nanosilver active-ingredient is attached to crystalline silica via a thiolate bond."[1] We are concerned that crystalline silica is quartz, which is highly toxic carcinogen. We doubt that EPA would ever approve quartz, and suggest that Nanosilva is in fact attached to synthetic amorphous silica. We will address the issue of the poorly defined material later in these comments, but here wish to flag for EPA that the staff reviewing the data on Nanosilva seem not to have the necessary expertise in material chemistry required to adequately describe the Nanosilver material. This is not the training of toxicologists.

On August 27, 2013, the EPA proposed to conditionally register Nanosilva under the Federal Insecticide, Fungicide, and Rodenticide Act ("FIFRA"). 7 USC §136a(c)(7)(C). Among other things, Nanosilva is proposed to be incorporated into textiles, plastic films, sheets, slabs, and molded parts, meaning it can end up in consumer products such as footwear, sportswear, uniforms, and auto parts, floor coverings, outdoor furniture, decking, and house siding. To our knowledge, no other silver pesticide product registrations cover floor coverings, plastic films, slabs, and molded parts as would be found in outdoor furniture, decking and house siding.

II. Legal Standard

FIFRA requires that pesticides be registered before they can be legally sold in the U.S. 7 U.S.C. §136a. EPA evaluates a pesticide application to assess any potential risks it may pose to human health or the environment. Only if EPA determines that a pesticide will "perform its intended function without unreasonable adverse effects on the environment" can a pesticide be approved for use. 7 U.S.C. §136a(c)(5). The term "unreasonable adverse effects on the environment" is defined by statute to mean "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…." 7 U.S.C. §136(bb). EPA's assessment is based on the results from a series of studies that the registrant (the company seeking to register the pesticide) submits as part of the application packet. If EPA determines that a pesticide will cause unreasonable adverse effects on the environment, EPA must deny its registration. 7 U.S.C. §136a(c)(5)(C).

In very limited circumstances, EPA may conditionally register a pesticide without the full set of data required by FIFRA. 7 U.S.C. §136a(c)(7)(C). EPA may grant a conditional registration to a new active ingredient that is not contained in any currently registered pesticide only if all three of the following things are true: The registrant has not had sufficient time to generate the required data because not enough time has passed since the data requirement was imposed to generate the data (such as when EPA requests submission of a study that is not normally required as part of the core study requirements), the use of the pesticide during this time will not cause any unreasonable adverse effect on the environment, and the use of the pesticide is in the public interest, such as to prevent a disease outbreak.

[1] U.S. Environmental Protection Agency. "Draft Decision Document for Proposed Conditional Registration of Nanosilva as a Materials Preservative in Textiles and Plastic," August 27, 2013 (hereinafter referred to as "Draft Decision Document") at 4.

III. Background

Silver metal is a well-recognized non-specific antimicrobial metal. Silver ions (positively charged atoms, Ag+) are more toxic to aquatic organisms than any other metal except mercury.[2] Silver is toxic, persistent in the environment, and has the potential to bioaccumulate in ocean plants at concentrations 10,000 to 70,000 times higher than in the surrounding sea water. [3] Its historical use in developing film for traditional photography proved that the release of silver into the waste stream is deadly for aquatic biota. Silver is acutely toxic to aquatic organisms at exquisitely low concentrations, as low as 50 ng/L (parts per trillion, ppt); a study in fish embryos reported toxicity down to 10 ng/L.[4] Because of its extreme toxicity to aquatic organisms, discharges of silver effluent into lakes, streams, ponds, or any public water is subject to National Pollutant Discharge Elimination System permit restrictions, and any water that has been treated with silver pesticide cannot be discharged into the sewage systems without first notifying the sewage treatment authorities.[5]

EPA's 1993 Reregistration Eligibility Decision ("RED") for silver notes that in humans when it is inhaled or ingested, it can be absorbed from the lungs and the gastrointestinal tract into the blood stream, where it causes a permanent skin discoloring condition called argyria.[6] [7] The oral reference dose, considered the acceptable daily intake limit over a lifetime, established by EPA in 1991 for silver is 0.005 mg/kg/day.

Nanosilver, or silver nanoparticles, are made up of clusters of silver atoms that must be oxidized to dissolve and then become ions, which are charged particles. Silver nanoparticles are intentionally engineered to release silver ions, which is the mechanism of their enhanced microbe-killing activity. In addition to releasing more antibacterial ions, silver nanoparticles appear to be able to penetrate into cells better than silver, or possibly, to deliver ions directly into cells. These are believed to be the properties that make nanosilver a much more efficient antimicrobial than silver and much more toxic.[8] In cultured mouse sperm stem cells, a 48 hour treatment of nanosilver (15 nm diameter) was 45-fold more toxic than silver carbonate (EC50 of 8.75 versus 408 µg/ml) in a concentration-dependent manner; nanosilver was the most toxic of the nanomaterials tested, and drastically reduced mitochondrial function and cell viability.[9]

---

[2] Luoma SN. Silver nanotechnologies and the environment: old problems or new challenges. A report by Woodrow Wilson International Center for Scholars and The Pew Charitable Trusts. 2008. Available at http://www.pewtrusts.org/uploadedFiles/wwwpewtrustsorg/Reports/Nanotechnologies/Nano_PEN_15_Final.pdf, last accessed September 24, 2013.

[3] *Id.*

[4] *Id.*

[5] EPA Reregistration Eligibility Document Facts. Silver. June, 1993. Available at http://www.epa.gov/oppsrrd1/REDs/factsheets/4082fact.pdf, last accessed September 24, 2013.

[6] *Id.*

[7] Papp T, Schiffmann D, Weiss D, Castranova V, Vallyathan V, Rahman O. Human health implications of nanomaterial exposure. Nanotoxicology, 2008. 2:1, 9 – 27.

[8] FIFRA SAP, 2009. FIFRA Scientific Advisory Panel Meeting held November 3-5, 2009 on the Evaluation of Hazard and Exposure Associated with Nanosilver and Other Nanometal Pesticide Products *available at* http://www.epa.gov/scipoly/sap/meetings/2009/november/110309ameetingminutes.pdf, last visited September 26, 2013 at 10 (hereinafter referred to as "SAP Report.")

[9] Braydich-Stolle L, Hussain S, Schlager JJ, Hofmann MC. In vitro cytotoxicity of nanoparticles in mammalian germline stem cells. Toxicol Sci. 2005 Dec;88(2):412-9. Epub 2005 Jul 13.

The FIFRA Scientific Advisory Panel ("SAP") reported in 2010 that several major differences between silver and nanosilver were likely to result in a distinct hazard profile for nanosilver. However, the SAP noted that there are no studies that are definitive regarding a comparison of silver and nanosilver toxicity, and more research is required. [10] These findings showcase the problem with EPA's proposal to put nanosilver on the market essentially untested, with an inadequate hazard database, while knowing that it is likely to be more hazardous than silver.

IV. EPA 's conditional registration program is too flawed to be used at this time

At this time, EPA has so many unsolved problems with conditional registrations that it should not grant *any* conditional registration of a new pesticide active ingredient. EPA is inappropriately using the conditional registration process and should not do so until it can fix the problems and ensure that it is protecting the environment and public health from dangerous pesticides.

a. NRDC report on conditional registrations

In March, 2013, NRDC released its report "Superficial Safeguards: Most Pesticides are approved by a flawed EPA process."[11] The report indicates that the majority of pesticides registered by EPA were conditionally registered. In fact, NRDC's review of the EPA database showed that 65 percent of all registered pesticides were done so through the conditional registration process.

In addition to the misuse of conditional registrations, NRDC also found that EPA's database to track these conditional registrations was a mess. EPA was unable to tell whether requested data had been submitted in a timely manner, whether the data had been reviewed by the agency, or whether any review of the data resulted in changes to the pesticides registration designation.

NRDC further highlighted two specific examples of pesticides that were improperly registered conditionally, including AGS-20, which is also a nanosilver pesticide product that EPA conditionally registered in 2011. In response to news articles about this report, EPA stated "We will continue to work on improving record-keeping and have developed a plan to update the IT (information technology) systems to address that need."[12]

b. GAO report on conditional registrations

On September 9, 2013, the U.S. Government Accountability Office ("GAO") released its report, "PESTICIDES: EPA Should Take Steps to Improve Its Oversight of Conditional Registrations" (hereinafter referred to as the "GAO Report.")[13] Similar to NRDC's report, the GAO found that EPA

[10] SAP Report at 10.
[11] Attached as Appendix A.
[12] Koch, Wendy. "Study: Two-thirds of pesticides got flawed EPA approval." USA Today. March 28, 2013. Available at http://www.usatoday.com/story/news/nation/2013/03/27/pesticides-get-flawed-epa-approval/2024991/, last accessed September 26, 2013.
[13] U.S. Government Accountability Office. "PESTICIDES: EPA Should Take Steps to Improve Its Oversight of Conditional Registrations." August 2013, available at http://www.gao.gov/assets/660/656825.pdf, last accessed September 26, 2013. NRDC incorporates the entirety of the GAO Report as part of these comments.

had inaccurate data on the total number of conditional registrations that have been granted due to "insufficient guidance and training, management oversight, and data management."[14]

The GAO found that EPA does not have a way to track the status of conditional registrations. Although EPA officials believed that routine program operations would provide a suitable quality control check, the GAO found that "they fall short of what is needed because they are neither comprehensive nor do they ensure the timely submission of these data."[15]

For example, EPA believed that "good faith submissions" by registrants would satisfy the data requirement, despite the fact that EPA had found cases where "required data were not submitted or were submitted late."[16] EPA also relied on individual product managers to develop their own tracking systems, including "electronic spreadsheets or reminder notices, handwritten notes, and memory," which opens up to many problems especially when managers retire, resign, or take extended absences.[17]

The GAO further explained that "without a reliable tracking system, [EPA] may miss conditional pesticides where, had the additional required data been submitted and reviewed, [EPA] might have altered the terms of a registration."[18] "[W]ithout the ability to systematically track conditional registrations, [EPA] is not well-positioned to produce summary data to enable it to easily identify situations for priority follow-up; enforce FIFRA and its implementing regulations; and report to Congress and others on program status."[19]

c. **EPA's response is not encouraging**

GAO recommended three major changes that EPA should undertake to improve this program. The most important of the three was the first: "Complete plans to automate data related to conditional registrations to more readily track the status of these registrations and related registrant and agency actions and identify potential problems requiring management attention…."[20]

While EPA responds that it is taking some steps to achieve this goal, it hedges its bets by saying "it plans to develop a more comprehensive system for tracking conditional registrations; however, the agency's ability to do so depends on the availability of funding and the complexity of incorporating changes in the databases."[21]

In the Draft Decision Document, EPA states that Nanosilva's registration will automatically expire after four years and that Nanosilva will have to submit another application to obtain an unconditional registration. If this is EPA's weak attempt to circumvent the systemic problems with its conditional registration program, it is not enough. There is no indication that Nanosilva products will automatically be removed from the market at expiration of the four year time period. While

[14] GAO Report at 12.
[15] *Id.* at 19.
[16] *Id.* at 22.
[17] *Id.* at 23.
[18] *Id.* at 20.
[19] *Id.*
[20] *Id.* at 39.
[21] *Id.*

EPA may argue that any Nanosilva products still on the market after four years would be there illegally, this argument is not comforting. As EPA acknowledged in conditionally registering AGS-20, there are many nanosilver products illegally on the market. Hei-Q was merely the first company to take steps to legally register its product. To our knowledge, EPA has never prosecuted or taken any other actions to ensure that illegal nanosilver products are removed from the market. Therefore, even if the Nanosilva registration were to expire in four years, there is no guarantee that EPA would take any action to ensure that all Nanosilva products are actually removed from the market.

V. EPA applied the wrong standard

Early in the Draft Decision Document, EPA explains its decision to conditionally register Nanosilva. It states "EPA has determined that there is a *low probability of adverse risk* to human health and the environment from plastics and textiles incorporating Nanosilva…"[22] This is the wrong standard. FIFRA allows a pesticide to be conditionally registered only if the Administrator has determined that "use of the pesticide will not cause any unreasonable adverse effect on the environment…" 7 U.S.C. §136a(c)(7)(C). The standard is not "low probability" of adverse risk – it is no unreasonable adverse effect. EPA's finding of "low probability of adverse risk" weakens the statutory standard and is impermissible.

VI. Nanosilva had a reasonable period of time to generate data

In August 2009, Nanosilva applied to register Nanosilva as a new active ingredient.[23] EPA may only conditionally register a new active ingredient for a period of time to allow the registrant to generate required data because "a period reasonably sufficient for generation of the data has not elapsed since the Administrator first imposed the data requirement…." 7 U.S.C. §136a(c)(7)(C). EPA relies on the fact that it had to consult with its SAP to determine the data requirements needed to assess Nanosilva's application.[24] The SAP convened in November, 2009 meaning that almost four years have passed since EPA would have identified the data requirements that would be needed to make a decision on Nanosilva's application. EPA is now granting Nanosilva another three years to develop the requisite health effects studies including the health effects toxicity tests, the ecological effects tests, and the environmental fate studies.[25] The time that has transpired between the SAP meeting when EPA developed the list of tests that are necessary and now does provide a reasonably sufficient period of time for generation of the data, and argues against granting a conditional registration.

VII. There is no public interest to warrant conditionally registering Nanosilva

The conditional registration of Nanosilva is not in the public interest. It provides no measurable medical or health benefits to consumers, but puts them in harm's way. There seems to be little doubt that consumers will come in direct contact with the pesticide while wearing treated clothing, and that children have a high likelihood of ingesting the pesticide while mouthing the clothing in addition to direct dermal contact. It is also possible that nanosilver that breaks away from the

[22] Draft Decision Document, p. 1, emphasis is added.
[23] *Id* at 1.
[24] *Id* at 6.
[25] *Id* Table 3B.

Nanosilva product will be another source of exposure – potentially from floor coverings, outdoor furniture, or other uses. Because the proposed application is to treat textiles and plastics that consumers will come into direct contact with, exposure will be unavoidable. The potential harm from such contact is poorly understood and untested, which is a direct violation of FIFRA's requirement for a safety finding.

a. Conditional Registrations are to be used in very narrow, limited situations

To grant a conditional registration for a new active ingredient, EPA must show that use of the pesticide is in the public interest. The legislative history of the conditional registration process is clear that the "public interest" encompasses a narrow, not broad, range of interests, such as when there "is a significant pest control problem which cannot satisfactorily be handled by use of products which have been fully registered."[26] As explained by the then-EPA Administrator, the conditional registration would be important when "there may be a real need for use of the pesticide to avoid pest outbreaks."[27] Furthermore, he noted that "[a]lthough we think that the exercise of this conditional registration authority for new chemicals would be rare, we feel that it should be available in appropriate cases.[28]

To ensure that conditional registration for new chemicals only occurred in the limited situations when the public interest was at stake, the House of Representatives agreed during conference to adopt a version of the amendment similar to the Senate's that would require the Administrator to "determine as a condition to granting the registration that use of the pesticide is in the public interest."[29]

In the GAO report on EPA's use of conditional registrations, EPA also acknowledges that the conditional registration is to be used sparingly. EPA explains that in creating the conditional registration process, "Congress also recognized that it would be appropriate to give EPA discretionary authority, *in very narrow circumstances,* to approve the registration of a product containing a new active ingredient for which EPA requires additional data."[30]

Despite the requirements that the conditional registration not be overused, EPA is proposing to conditionally register this pesticide product using an improperly generic and broad definition of public interest. Furthermore, some of the conclusions that EPA makes about the benefits associated with Nanosilva are wrong.

b. The environmental loadings are more dangerous with Nanosilva

EPA contends that one of the public interest benefits of Nanosilva is "Conservation of the Environment." However, EPA's explanation actually points to a greater adverse impact on the environment from Nanosilva, not lower.

[26] S.Rep.No. 95-334, 95th Cong., 1st Sess., 2 (July 6 (legislative day, May 18), 1977) at 21.
[27] H.Rep.No. 95-343, Part. 2, 95th Cong., 1st Sess., 10 (June 1, 1977).
[28] *Id.*
[29] H.R.Conf.Rep.No. 95-1560, 95th Cong., 2d Sess., 35 (Sept. 12, 1978).
[30] GAO Report, p. 46, emphasis is added.

EPA states that because a smaller mass of silver is used in Nanosilva than in other products, "the overall potential environmental loading of silver from the lower-volume use of Nanosilva "should be smaller than from a comparable use of currently registered silver-based pesticides."[31] However, EPA ignores the fact is 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. The Nanosilva will be incorporated into wholly new products, not taking the place of other silver-embedded products. Therefore, the introduction of Nanosilva into commerce – no matter the amount – will necessarily increase, not reduce, the amount of silver ions that will be released into the environment.

More problematically, EPA acknowledges that more silver ions will be released because the nanosilver particles are smaller and therefore have higher surface area per unit mass of silver. Since nanosilver is much more potent (effective) than conventional sized silver, less nanosilver kills more microbes. While Nanosilva may possibly lead to a reduction in the overall mass of silver released into the environment, its killing potential is greater and therefore the potential for environmental damage and non-target impacts is greater. In fact, the SAP noted that the rate and concentration of deadly silver ions released from nanosilver is different and will likely affect the acute or chronic toxicity of nanosilver compared with silver. The data referenced by SAP show that nanosilver, but not silver, can penetrate cell membranes and deliver toxic ions directly inside of cells and that this may be its mechanism for killing microbes so effectively. The SAP also noted that "when compared as a function the Ag+ concentration, toxicity of silver nanoparticles appeared to be much higher than that of silver nitrate."[32] Moreover, the SAP noted that because of these differences in chemical properties, there are likely to be differences in exposure and environmental fate of nanosilver that should be considered.

Silver is highly toxic to aquatic organisms. Increasing the amount of silver ions that will enter rivers and streams through our wastewater system or from run-off during rainstorms will only harm the environment. It does not conserve the environment.

a. EPA provides no efficacy data to support its consumer benefits claim

EPA contends that benefits inured to consumers by Nanosilva contribute to the public interest enough to warrant a conditional registration of a product missing critical toxicity data. Part of this argument is grounded in EPA's assumption that Nanosilva products "are reported to retain the ability to reduce the number of odor and stain causing bacteria."[33] EPA also assumes that Nanosilva "*should* be able to maintain its ability to reduce" bacteria longer than other silver active ingredients.[34] EPA assumes that products using nanosilver "*may* have longer-term ability" to reduce the bacteria compared to conventional silver embedded products.[35]

EPA's contention that nanosilver provides a consumer benefit is grounded in assuming nanosilver's efficacy. EPA provides no evidence and does not indicate that any data regarding Nanosilva's efficacy exist. Without such evidence, EPA's claim that consumers benefit from the presence of

[31] Draft Decision Document at 68
[32] SAP Report at 10.
[33] Draft Decision Document at 68.
[34] *Id.* emphasis is added.
[35] *Id.* emphasis is added.

Nanosilva on the market is mere conjecture and is an inappropriate basis for making a regulatory determination.

b. Conditional registrations are not the proper way to encourage innovation

EPA wishes to encourage innovation in nanotechnology, but allowing untested pesticides into products to be used in ways that are potentially harmful is not the appropriate way to do so. EPA's mission is to ensure that products that are brought to market will be used in ways that will not harm the environment or public health. But in this case, EPA is turning a blind eye to all the possible environmental and health hazards associated with Nanosilva in an effort to encourage broadly the field of nanotechnology. EPA has many other opportunities to actually encourage innovation through supporting research and through its existing programs to ease market access for pesticide products that are adequately tested and shown to be reduced risk.[36] EPA has even established criteria for determining that pesticides are reduced risk,[37] which include compatibility with Integrated Pest Management (IPM) strategies.[38] Ironically, the pivotal principle of IPM is to avoid using pesticides if they are not necessary – an approach undermined by this prophylactic integration of nanosilver into consumer products. By EPA allowing an untested product like Nanosilva on the market where consumers learn after-the-fact that it might cause unreasonable health or environmental effects will only stifle real innovation, undermine desirable IPM strategies, pose unknown environmental risks, and undermine consumer confidence.

VIII. EPA does not have the data to determine that these uses of Nanosilva will not have any unreasonable adverse impacts on human health or the environment

To conditionally register a new active ingredient, EPA must determine that that use of the pesticide during the period of the conditions will not cause any unreasonable adverse effect on the environment. 7 U.S.C. §136a(7)(C). In the case of nanosilver (and specifically Nanosilva), the flaws in the studies relied on by EPA and the critical data gaps especially on reproductive toxicity, carcinogenicity, and endocrine disruption (among many others) mean that, scientifically, EPA cannot make that determination.

a. EPA has failed to characterize Nanosilva

Fundamentally, 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 (equally poorly) described nanosilver materials. EPA describes Nanosilva

[36] U.S. Environmental Protection Agency, "Reducing Pesticide Risk" September 27, 2011, available at http://www.epa.gov/pesticides/health/reducing.htm, last accessed September 26, 2013.
[37] U.S. Environmental Protection Agency, "Pesticide Registration (PR) Notice 97-3: Guidelines for Expedited Review of Conventional Pesticides under the Reduced-Risk Initiative and for Biological Pesticides". Sept.4, 1997, available at http://www.epa.gov/pesticides/PR_Notices/pr97-3.html, last accessed September 26, 2013.
[38] U.S. Environmental Protection Agency, "Pesticides and Food:
What 'Integrated Pest Management' Means," available at http://www.epa.gov/pesticides/food/ipm.htm, last accessed September 26, 2013.

as "a liquid suspension containing silica-sulfur-nanosilver particulates where the nanosilver active-ingredient is attached to crystalline silica via a thiolate bond."[39]

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 EPA did not make an error, and the silica is actually crystalline, then given crystalline silica's known cancer effects, EPA's determination of no cancer risk is in error. If EPA did make an error in describing the material, then it 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.

Furthermore, Nanosilva appears to be a single silica particle surrounded by multiple nanoscale PVP-coated-silver particles connected through weak thiol linkages. The thiol linkages have not been defined in the sense of "linkage to what?" Is it to the PVP coating or to the silver atoms or to a silver ion that is separate from the surface? In a product, these may be in some sort of equilibrium relationship, but in a realistic environmental exposure scenario, one is likely to dominate. This would mean that the chemistry – and therefore the toxicology – depends on the route of exposure. Moreover, Lee et al (2006) (referenced by EPA) describes Nanosilva as a material with 4% PVP, only 0.1% silica, and even less thiol.[40] This means that there is a much greater chance of nanosilver reacting with PVP than silica particles. It is arguably much more likely that the PVP outnumbers the number of thiol groups on the silica surface. EPA's description of a nanosilver active ingredient coated with PVP and sulfur[41] is wholly unsupported, unlikely, unscientific, and inadequate to predict the behavior of the material under real-world conditions relevant to a hazard assessment.

There is no scientific evidence to support statement that "the resulting liquid suspension contains 1% nanosilver by weight where the nanosilver surface is coated with sulfur and PVP, and is attached to silica."[42] First, for that to be true, the sulfur connected to a thiol connected to a silica particle would need to surround the silver particles (instead of silver particles surrounding the silicon dioxide particle). Second, that would mean the sulfur has disengaged from the thiol, meaning disengaged from the silicon dioxide. It is unknown if the above complex would survive the temperature and chemical conditions of a master batch. If disengaged (broken at the point of contact with the silicon dioxide or chemically attacked and "corroded" through at a neck point) then the silver and silicon dioxide may migrate to separate locations within the fiber.

In short, the Nanosilva is not characterized well enough to determine with confidence that data on other nanosilver materials can be used to predict the toxicology of Nanosilva. Scientific support for extrapolating from one nanosilver to another is lacking. EPA should use science, not speculation, to evaluate pesticide hazards.

b. It is unreasonable to rely on data on nanosilver particles that are not Nanosilva.

[39] Draft Decision Document, Appendix B, 2.
[40] *Id*.
[41] *Id.*
[42] *Id.*

In August 2009, EPA turned to its SAP regarding some open questions about the hazard of and exposure to nanosilver. The 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."[43] Despite the warnings from the SAP, EPA appears to rely on studies of different nanosilver formulations to make the determination that Nanosilva could be used without any adverse effects on the environment or on human health.

The SAP also noted that "not enough literature is available to draw any firm conclusions regarding human (occupational or consumer) and environmental exposures to nanosilver under realistic use scenarios."[44]

c. There are no studies that properly address the oral toxicity of Nanosilva

EPA identifies five studies in the scientific literature that investigate the oral toxicity of nanosilver in rodents. Three of the most robust studies are not complete enough to determine regulatory limits. The other two are even less well described, and therefore less useful for supporting regulatory decisions. As such, EPA does not have a reliable study that addresses the oral toxicity of Nanosilva.

i. EPA rejects Park et al. (2010) for oral and dermal POD

In December 2011, EPA conditionally registered HeiQ AGS-20 containing nanosilver as a materials preservative in textiles. As part of its final decision to register the product[45], EPA relied on Park et al. (2010)[46] for the point of departure ("POD") of 0.5 mg/kg-day to calculate the oral and dermal POD for the nanosilver in HeiQ AGS-20.

In this proposed conditional registration of Nanosilva, EPA has determined that Park et al. (2010) is no longer reliable for calculating a POD. EPA states that in its recent review of the study for this assessment of Nanosilva, EPA reversed its reliance on the study, and now finds that it lacks enough analysis of the cellular changes to draw conclusions with confidence. EPA says, "In the absence of histopathological findings, the clinical chemistry changes observed [in Park et al. 2010] are insufficient evidence of an adverse effect."[47]

ii. Kim et al. (2008) lacks analysis of cellular effects, has poor methodological reporting, and fails to follow stated guidelines

EPA calculated a POD from Park et al. (2010) of 0.5 mg/kg/day for oral and dermal toxicity, based on effects observed in mice that ingested nanosilver for 28 days. After discarding that study for this current assessment of Nanosilva, EPA calculated a POD of 30 mg/kg/day, based on the 28-day oral

[43] *Id.* at 2.
[44] *Id.* at 3.
[45] NRDC has challenged EPA's final decision to conditionally register AGS-20. These comments do not condone any of the decisions made by EPA in that final decision, but are raised to highlight further flaws in EPA's assessment of Nanosilva.
[46] Park, E.J., Bae, E., Yi, J., et al. 2010. Repeated-Dose Toxicity and Inflammatory Responses in Mice by Oral Administration of Silver Nanoparticles. *Environmental Toxicology and Pharmacology* 30: 162-168.
[47] Draft Decision Document at 21.

toxicity study by Kim et al. (2008).[48] This result weakened oral and dermal exposure limits by 60-fold.

The scientific community has identified Kim et al. (2008) as not useful for derivation of a POD.[49] The study provides no information on the form or shape of the silver nanoparticles in the solution that was used to dose the animals. Further, the study misstated that it was performed in accordance with OECD 407 study guidelines. In fact, no neurotoxicity endpoints were investigated, and the histopathology (observation of cellular damage) failed examine the spinal cord, peripheral nerve, bone marrow, lymph nodes, stomach or small or large intestines.

EPA moved away from the more protective POD from Park et al. (2010) claiming that the histopathology analysis was too weak, and unjustifiably proposes to rely on this less-protective study by Kim et al. (2008) that lacks any histopathology analysis on so many critical organs and tissues.

Importantly, Kim et al. (2008) reported a dose-dependent accumulation of silver content in a broad range of tissues including blood, liver, lungs, kidneys, stomach, testes and brain. Cellular damage in the liver of male and female rats included dose-dependent bile-duct hyperplasia, dilation of the central veins, and inflammation. However, the authors failed to specify which dose groups had these effects. Silver concentrations were dose-dependent in blood and all examined tissues, with the kidney concentrations in females being 2-fold higher than males.

That ingested nanosilver is accumulating in many critical organs, where its antimicrobial activity may lead to significant cellular damage that has not been adequately studied, is evidence that EPA cannot determine that there are no unreasonable adverse effects associated with the use of Nanosilva.

iii. Hadrup et al. (2012) cannot be used to determine a POD

EPA identified Hadrup et al. (2012) as another study that investigates the oral toxicity of nanosilver in rats.[50]

First, EPA itself determined that the study lacked histological support for determining a POD.[51] Second, the nanoparticles studied by Hadrup et al. are silver nanoparticles stabilized with polyvinylpyrrolidone (PVP), whereas the particles in Nanosilva are very different, formed of a composite of silica-sulfur-nanosilver particles. The PVP-coated nanosilver particles are likely to disengage and transport separately from the silica. This is also significantly different from the HEiQ product that EPA recently conditionally approved, which probably transports in the environment more like a silica particle carrying along the silver. In short, the scientific support for extrapolating

[48] Kim YS, Kim JS, Cho HS, Rha DS, Kim JM, Park JD, Choi BS, Lim R, Chang HK, Chung YH, Kwon IH, Jeong J, Han BS, Yu IJ. Twenty-eight-day oral toxicity, genotoxicity, and gender-related tissue distribution of silver nanoparticles in Sprague-Dawley rats. Inhal Toxicol. 2008 Apr;20(6):575-83.

[49] RIVM, 2009. Nanomaterials under REACH, Nanosilver as a case study. Report 601780003, National Institute for Public Health and the Environment. Netherlands. Available at http://www.rivm.nl/bibliotheek/rapporten/601780003.pdf

[50] Hadrup N, Loeschner K, and Mortensen Al, et al. 2012. The similar neurotoxic effects of nanoparticulate and ionic silver in vivo and in vitro. *NeuroToxicology* 33, 416-423.

[51] Draft Decision Document at 24.

from one nanosilver composite type to another is lacking. EPA should use science, not speculation, to evaluate pesticide hazards.

d. Critical data gaps for nanosilver prevent a finding of no unreasonable adverse effects

EPA acknowledges that it is missing data on entire categories of hazards. These missing studies are essential to a complete assessment of the potential adverse effects associated with the proposed uses of Nanosilva. Therefore, because EPA lacked essential data, its determination that Nanosilva will not have unreasonable adverse effects on the environment is unreasonable, unsupported, and arbitrary and capricious.

i. EPA has no acceptable studies on reproductive and developmental toxicity

Reproductive and developmental toxicity are essential components of a full human health risk assessment, and without information about that hazard, EPA cannot determine whether a pesticide will have unreasonable adverse impacts on human health. ("Disorders of reproduction and hazards to reproductive health have become prominent public health issues."[52] Developmental toxicity is manifested as "death, structural abnormality, altered growth, and functional deficit," all critical to a complete human health risk assessment.[53])

Information about the hazard characterization is a crucial component to a complete risk assessment. "A statement of the potential for human risk and the consequences of exposure can come only from integrating the hazard characterization and quantitative dose-response analysis with human exposure estimates in the risk characterization."[54]

In proposing to conditionally register Nanosilva, EPA states that it has enough information to determine that Nanosilva will not have any unreasonable adverse impacts on human health. However, EPA highlights the critical data gaps on reproductive and development toxicity in its assessment of nanosilver. Specifically, EPA states,

> There are studies showing significant, dose-dependent increases in the concentration of silver in the testes of rats after oral ingestion, inhalation, and injection of nanosilver…; however there are few studies available on the reproductive and development toxicity of nanosilver.[55]

To counter this data gap, EPA is requiring Nanosilva to submit the results of a Modified Reproduction/ Development Toxicity Screening Test 37 months after the conditional registration is issued. EPA's rationale is that this test "will provide *initial information* on possible effects on reproduction and/or development."[56] To make a first determination whether Nanosilva has any unreasonable adverse impacts on human health, EPA needs to be able to assess whether there are

[52] Guidelines for Reproductive Toxicity Risk Assessment, 31 Fed. Reg. 56274, 56275 (Oct. 31, 1996).
[53] Guidelines for Developmental Toxicity Risk Assessment, 56 Fed. Reg. 63798, 63802 (Dec. 5, 1991).
[54] Guidelines for Reproductive Toxicity Risk Assessment, 31 Fed. Reg. 56274, 56276 (Oct. 31, 1996).
[55] Draft Decision Document at 14.
[56] *Id.*, Appendix B, 10, Table 1B

any reproductive or developmental toxicity concerns. Reproduction and development are essential components of human health, and therefore, without even basic "initial" information about reproductive and developmental toxicity, EPA cannot complete its safety determination of Nanosilva.

ii. EPA has no acceptable studies on mutagenicity

For the mutagenicity of nanosilver, EPA states that "there are *no studies* in the scientific literature that investigate the potential of nanosilver to cause cancer…."[57] After reviewing the *in vitro* studies that exist, EPA concludes that "there is *inadequate information* to assess mutagenic (and hence carcinogenic) potential of nanosilver due to differences in results between the *in vitro* studies and *in vivo* studies, and the limitations of the only available *in vivo* study."[58] Without a full suite of mutagenicity tests on the material of interest, Nanosilva, EPA cannot determine with scientific confidence whether or not Nanosilva may be mutagenic to DNA, and therefore pose a risk of cancer, intergenerational effects, disease, birth defects, or other severe adverse health endpoints related to mutagenicity.

iii. EPA has no information on environmental fate and transport or environmental toxicity

According to EPA, Nanosilva "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" [59]and "has not conducted any studies to characterize the ecotoxicity of Nanosilva or other particles that could be released during leaching or disposal of plastics incorporating Nanosilva"[60] These are critical components of an environmental assessment to determine where the Nanosilva goes into the environment and what harm it causes when it is there. As a result, EPA is left to rely on studies of conventional silver and nanosilver particles that are different from Nanosilva.

Furthermore, EPA acknowledges that silver "may become toxic to aquatic life at elevated concentrations."[61] However, after mentioning the concentrations of silver in surface waters, EPA concludes that it does not expect any unreasonable adverse effects to the environment, citing a twenty year old assessment of conventional silver from 1993.[62] That old assessment never contemplated the presence of nanoscale silver particles – nanotechnology had barely begun as a scientific endeavor at that point. Therefore, EPA's reliance on the old assessment is wholly improper, and EPA has failed to provide any explanation for its determination at the nanoscale.

Nanosilva did not submit any tests with aquatic organisms, and EPA is left to assess the scientific literature addressing aquatic organisms and other nanosilver particles – despite the SAP's admonition that the differences in particle sizes cannot be underestimated. After identifying six

[57] *Id.* at 14, emphasis is added.
[58] *Id.* at 16, emphasis is added.
[59] *Id.* at 55.
[60] *Id.* at 57.
[61] *Id.*
[62] *Id.*

studies in the scientific literature on aquatic animals, EPA concludes that the data "do not characterize the effects from longer-term exposure to nanosilver."[63] One study did look at long term effects, and while it did not show lethal effects, the authors reported non-lethal effects at all nanosilver concentrations tested.[64] Non-lethal effects can also reflect an unreasonable impact on the environment and cannot be summarily dismissed. EPA fails to address this finding in discussing the environmental toxicity of Nanosilva.

iv. The Greenscreen™ for Safer Chemicals finds that nanosilver products have too many data gaps to be assessed

The Greenscreen™ for Safer Chemicals (GS) is a comparative chemical hazard assessment framework. It builds on the EPA Design for the Environment (DfE) approach, along with the OECD Globally Harmonized System (GHS) and other accepted systems.[65] It is being used by industry, government and non-governmental organizations ("NGOs") to support product design and development, materials procurement, and as part of alternatives assessment to meet regulatory requirements.

A GS assessment of a chemical looks at eighteen hazard endpoints (including chronic and acute toxicity, ecotoxicity, and physical characteristics such as flammability and reactivity), scores each endpoint according to the available data or lack thereof (i.e. a data gap), and assigns a Benchmark score (BM) from 1 to 4, with 1 being the most hazardous. Where there are no data for an endpoint, GS can use analogues, modeled data, or other available reasonable substitutes to inform that endpoint. Confidence in the score is identified as high (bold), low (italics), or very poor ("DG" for data gap). Chemicals that are carcinogens, mutagens, reproductive and/or developmental toxicants, endocrine disruptors, and PBTs (persistent, bioaccumulative, and toxic) are considered substances of high concern and receive a BM of 1.

Nanosilver, silver, and the silver-silica composite AGS-20 were put through the GS and those assessments compared. The three GS assessments were all conducted by independent scientists at NSF International, which is an approved GS profiler.[66] They found an extensive lack of data on critical endpoints for nanosilver, and by extension for Nanosilva.[67]

The specific materials evaluated for the silver case study were nanoscale metallic silver, a silica-silver nanocomposite, and conventional low-solubility dispersed silver and silver salts. Both silver and nanoscale silver scored a benchmark of 1(high concern), based on high aquatic toxicity, high persistence, and acute inhalation toxicity. The identified data gaps for nanoscale silver include reactivity, flammability, carcinogenicity, reproductive toxicity, and endocrine disruption.

---

[63] *Id.* at 59
[64] *Id.*
[65] *See generally* GreenScreen™ v 1.2 (October 2011) available at http://www.cleanproduction.org/Greenscreen.php, last accessed September 26, 2013.
[66] *See generally* NSF International Press Release, "NSF International Offers GreenScreen™ Evaluations to Help Organizations Identify Safer Chemicals," February 2, 2012, available at http://www.nsf.org/newsroom/nsf-offers-greenscreen-evaluations, last accessed September 26, 2013.
[67] Attached here as Appendix B.

The HeiQ AGS-20 silica-nanosilver composite received a BM of U (unspecified) due to the large number of data gaps. Unfortunately, EPA approved the AGS-20 for textiles in 2011, on the assumption that hazard data on silver nitrate and other soluble salts could be used as analogues to fill data gaps. It was not scientifically justifiable for EPA to substitute data on other nanosilver particles in its AGS-20 assessment. The SAP noted that "when compared as a function of Ag+ [ion] concentration, toxicity of silver nanoparticles appeared to be much higher than that of silver nitrate."[68] Because of these differences in chemical properties, there are likely to be differences in exposure and environmental fate. For this reason, the GS assessment did not use silver nitrate or other soluble silver salts as analogs to fill data gaps, because the screen sought to examine particle size-specific hazards.

The results of these three GS assessments demonstrates that there are numerous critical areas of information that EPA lacks knowledge about regarding the potential health and safety impacts of Nanosilva for people and the environment.

Altogether, these critical health endpoints and environmental impacts are essential to making a determination about registering this pesticide. Until EPA has data specific to Nanosilva on reproductive and developmental toxicity, carcinogenicity, endocrine disruption, and environmental toxicity, EPA cannot allow this product to enter the market. In the absence of these data, EPA cannot show that there are no unreasonable adverse impacts to the environment and human health associated with the use of Nanosilva, and as such, cannot register this pesticide product.

e. EPA ignores other sources of nanosilver

In the aquatic risk portion of the risk assessment, EPA states that it "only considers silver that could be released by Nanosilva and does not include other sources of silver which will contribute to the environmental loading of silver."[69] Given that part of EPA's rationale for conditionally registering this product is the purported benefit to the environment from the release of silver ions, EPA should consider the cumulative and aggregate impact of all the various sources of silver ions loading to the environment.

f. EPA's Calculated Inhalation POD is not a true No Observable Adverse Effect Level

EPA relies on Song et al. (2012) for the short- and intermediate-term inhalation No Observable Adverse Effect Level ("NOAEL").[70] [71] The study by Song et al. (2013) exposed six week old male and female Sprague Dawley rats with either no dose (control group) or one of three dose groups (49, 117, and 381 μg/m^3; each group consisted of 17 male rats and 12 female rats) with silver nanoparticles 14-15 nm in diameter in an inhalation chamber for 6 hours per day over 12 weeks.

[68] SAP Report at 10.
[69] Draft Decision Document at 62.
[70] Note that this study was available online in 2012, but was actually published in 2013 and therefore the proper reference is Song et. al 2013)
[71] Song KS, Sung JH, Ji JH, Lee JH, Lee JS, Ryu HR, Lee JK, Chung YH, Park HM, Shin BS, Chang HK, Kelman B, Yu IJ. Recovery from silver-nanoparticle-exposure-induced lung inflammation and lung function changes in Sprague Dawley rats. Nanotoxicology. 2013 Mar;7(2):169-80.

The authors report a statistically significant decrease in various measurements of lung function in the male rats – but not females – in the middle and high dose groups throughout both the exposure period and the recovery period. Moreover, the authors report that the female rats gradually recovered from lung inflammation, whereas the males in the high dose group showed persistent inflammation throughout the 12 week recovery period. Sex differences were also observed for the distribution of silver across organs, with five times more silver accumulated in the kidneys of females compared with males in the same treatment group. There was a statistically significant dose-dependent increase in lung tissue silver concentration in both males and females after the exposure period, which was not completely cleared by the end of the 12 week study. The authors also reported that signs of inflammation were present in the middle-dose group after 12 weeks of exposure. Statistically significant accumulation of silver compared to the control group was reported in the liver and spleen in male rats after 12 weeks of recovery, and the kidneys in female rats contained five times more accumulated silver than the male kidneys.

Maybe most important, the male rats in the high-dose group showed persistent inflammation throughout the 12 week study period. Because the males did not completely recover during the study period, and because gender differences remain unexplained by either the authors or EPA, this study seems to raise more questions than it answers, and lacks confidence in the ability to rely on it to determine a POD.

Importantly, the nanoparticles studied by Song et al. are uncoated silver nanoparticles, whereas the particles in Nanosilva are very different, formed of a composite of silica-sulfur-nanosilver particles. It is not clear how the rate of ion release may differ between these two markedly different materials. The scientific support for extrapolating from a nanosilver composite to an uncoated nanosilver particle is lacking. EPA should use science, not speculation, to evaluate pesticide hazards.

NRDC does not support using Song et al. to determine a POD. However, if EPA is going to rely on Song et al. to determine a POD, an uncertainty factor must be applied to adjust for the lack of a NOAEL. An uncertainty factor of *at least* 10X should be incorporated because EPA has neither pharmacokinetic nor pharmacodynamic information to warrant lowering the default 10x factor in adjusting for the lack of a NOAEL.

IX. Conclusion

Over the years, EPA has abused the conditional registration provision in FIFRA and allowed pesticides to market that are inadequately tested and have wreaked havoc on the environment. Imprelis reportedly caused billions of dollars of damage in dead trees. Clothianidin is part the family of neonicotinoid pesticides that are partly implicated in the massive bee death crisis. Examples of other pesticides allowed to enter the market based on flawed or insufficient data continue to emerge.

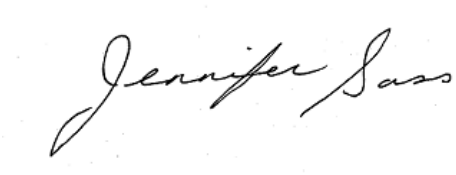
Separate reports by NRDC and the GAO exposed the flaws in the EPA conditional registration to the public's scrutiny for the first time. Pesticides littering the market have been fast-tracked through the conditional registration process and EPA has not developed a method for properly tracking

them. Despite the outcry against this misuse of conditional registrations, EPA once again turns to this fast track system to let another pesticide to market where many consumers will become unknowing guinea pigs for the benefit of one company whose only duty is to its financial bottomline.

Because EPA does not have an established program in place at this time, granting this conditional registration means that Nanosilva could become the next poster child for a conditional registration system gone seriously wrong. The only unknown at that point will be the extent of the damage that ensues. If EPA continues down this path, the public confidence in the safety of pesticide products will erode further. EPA must fix its program before it can go forward with this – or any other – conditional registration. For this, and the other reasons stated above, NRDC strongly opposes the conditional registration of Nanosilva.

Thank you for considering these comments.

Respectfully submitted,



Dr. Jennifer Sass, Senior Scientist

Mae Wu, Program Attorney

Health and Environment Program

Natural Resources Defense Council

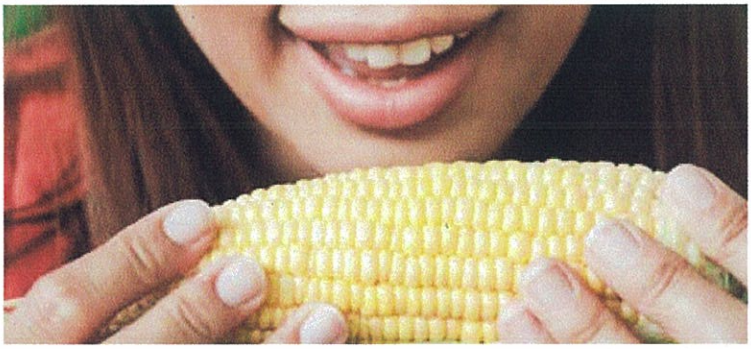
APPENDIX A

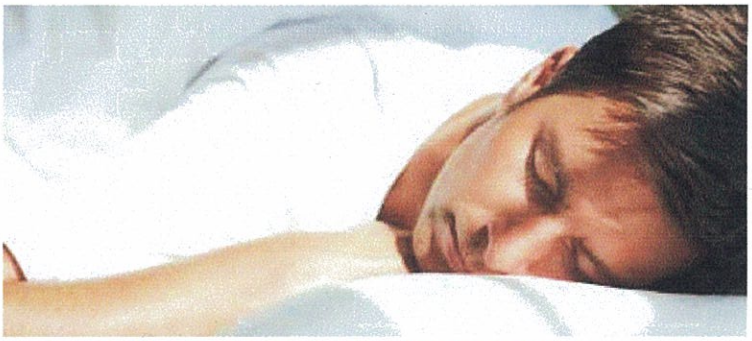
NRDC ISSUE BRIEF

MARCH 2013
IB: 13-01-B

Superficial Safeguards: Most Pesticides Are Approved by Flawed EPA Process

AUTHORS: Jennifer Sass, Ph.D., and Mae Wu, J.D.





Conditional registration approves some pesticides before they have been rigorously tested. They end up in some of our most basic household items.

The public may think pesticides are only allowed onto store shelves and for use in agriculture and into consumer products if they have been approved by the U.S. Environmental Protection Agency (EPA) in a transparent and scientifically rigorous process. Recent investigations by the Natural Resources Defense Council (NRDC), however, reveal a deeply flawed system, indicating that the public's trust is misplaced. NRDC spent several years examining federal government data and interviewing key officials, and has determined that the government has allowed the majority of pesticides onto the market without a public and transparent process and in some cases, without a full set of toxicity tests, using a loophole called a conditional registration. In fact, as many as 65 percent of more than 16,000 pesticides were first approved for the market using this loophole. This issue brief explains how the conditional registration program differs from full registration and provides case studies of two pesticides—nanosilver and clothianidin—to show how the conditional registration has been misused. The case of nanosilver, approved by the EPA as an antimicrobial agent in textiles, highlights the ways that some new pesticides can obtain a conditional registration without thorough toxicity testing to evaluate risk. The case of clothianidin—a pesticide that is designed to be absorbed into plant tissue but is then unintentionally passed on to bees and other pollinators, and consequently is linked to widespread bee deaths—illustrates the types of problems that may arise after a pesticide has been conditionally approved, and are often hidden from public scrutiny. Finally, NRDC has found significant shortcomings in the EPA's data-gathering system. We cannot determine how many pesticides were first conditionally approved, allowed onto the market, and then lingered there for years while toxicity testing data was being submitted; or how many pesticides were subsequently withdrawn for various reasons; or how many were given full registration.

PESTICIDE REGISTRATION

Pesticides are poisons. They are designed to kill things. Unfortunately, they often harm more than the intended targets, such as weeds or insects; they can also harm, or even kill, non-target species, including frogs, fish, birds, bees, other beneficial insects, and people. Recognizing this danger decades ago, Congress passed the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), which requires that all pesticides be registered by the EPA before they can be legally sold or distributed in the United States. Under FIFRA, the EPA cannot register a pesticide until it ensures that the pesticide's use will not pose unreasonable adverse effects on the environment or human health. The EPA currently interprets this provision to mean that some level of harm is allowed. For example, the EPA often considers the risk of one person out of 1 million getting cancer to be acceptable.

By law, to register a pesticide, a company must submit results from a list of specified studies to the EPA. These results make up the core data that help the EPA determine human exposure, effects on human health and wildlife, and environmental fate. The government uses these data to determine whether or how the pesticide can be used without endangering human health or the environment.

The EPA may also consider data from peer-reviewed scientific journals, other governments, or other sources, oftentimes receiving these additional sources from public comments. This whole process can last several years and includes data review by the agency's in-house science experts, opportunities for public comment, and discussions with the registrant and grower groups.

In 1972, Congress amended FIFRA to impose more stringent testing requirements to register pesticides. Registrants subsequently struggled to meet the new data requirements by the law's deadlines. To address this problem, Congress in 1978 created the conditional registration procedure with the intention that it would be used only in rare, specific instances.

THE CONDITIONAL REGISTRATION

Even though industry often claims that all registered pesticides have been thoroughly assessed, the EPA has used conditional registration as a loophole to register some pesticides without all the necessary data. The conditional registration allows a new active ingredient to enter the market for an unspecified period of time during which the registrant must generate missing data requested by the EPA.[1] By law, to grant an active ingredient conditional registration, the EPA must determine that 1) the registrant did not have sufficient time to generate the required data because not enough time has passed since the data requirement was imposed; 2) the use of the pesticide during this time will not cause any unreasonable adverse effect on the environment; and 3) the use of the pesticide is in the public interest, such as to prevent a disease outbreak.[2] Properly used, conditionally registering a new pesticide provides an important benefit in special situations such as allowing new pesticides on the market to address a public health emergency. However, improper use of conditional registration means that scores of untested or undertested pesticides may litter the market, potentially threatening human health.

THE ENVIRONMENTAL PROTECTION AGENCY IS MISUSING CONDITIONAL REGISTRATIONS

Despite the intention of Congress that conditional registration be used sparingly, NRDC's investigations of the EPA's pesticide registration database revealed that as of August 2010, more than 11,000—about 65 percent—of the 16,000-plus currently active pesticide products have been conditionally registered and allowed on the market.[3] Soon after NRDC submitted its findings to the EPA, the agency conducted its own analysis, and confirmed NRDC's findings.[4]

For pesticides registered between 2004 and 2010, the EPA's own analysis found that it had misused the conditional registration provision for other registration activities such as "requiring label changes" and other actions that are "beyond the scope" of the conditional registration.[5] In fact, according to the EPA's analysis, they misused it 98 percent of the time.[6] In 2011 and 2012, of more than 1,400 new registrations, 300-plus pesticides were conditionally registered—about 20 percent overall—a dramatically reduced rate from previous years, but still too many for comfort. By examining EPA data, NRDC has determined that as of October 2012, conditionally registered pesticide products still made up about 65 percent (10,640 out of 16,500) of total pesticide registrations.

THE ENVIRONMENTAL PROTECTION AGENCY IS NOT TRACKING CONDITIONAL REGISTRATIONS

The EPA's database is seriously disorganized. Once a pesticide is conditionally registered, the EPA does not have a system to track the data it had requested as a condition of the registration. In addition, the agency does not follow whether those data were received, what the data show regarding the pesticide's potential for harm or other aspects of the registration decision, or what, if any, changes were made in response to the received data. These problems suggest that conditional registrations may last many years with no trigger to remind the EPA to review the status of the required studies or assess their meaning.

The EPA defends the integrity of its conditional registration program by noting that between 2004 and 2010, it had never altered its previous regulatory decision for any conditional registrations based on the subsequent data it received, suggesting that all its conditional decisions were right to begin with. However, there is no public notice of, or comment period on, the EPA's ultimate decision. The lack of both tracking and public engagement makes it impossible to know 1) if the requested studies were submitted in a timely manner; 2) whether the submitted studies were reliably conducted; 3) if the EPA's conclusions concerning safety were well-founded; and 4) if the EPA should have altered its regulatory decision for any of those pesticides. This process lacks accountability and transparency and compromises the public trust.

Given the poor tracking, lack of public accountability, absence of a transparent process, the failure to provide a public response to submitted data, and the failure to provide a public notice and comment period, the EPA's use of conditional registrations to usher inadequately assessed pesticides onto the market is an abdication of the agency's duty to protect public health and the environment.

Two case studies of pesticides—nanosilver and clothianidin—highlight a conditional registration program gone wrong. Nanosilver is toxic to brain cells and its use on clothing will lead to exposures to people, including pregnant women and children; it is a significant public health concern. Clothianidin comes from a family of pesticides connected to widespread bee deaths, but was approved based on a poorly conducted bee field test, which will be discussed later in this report.

THE ENVIRONMENTAL PROTECTION AGENCY INAPPROPRIATELY GRANTED CONDITIONAL REGISTRATION TO NANOSILVER FOR USE IN TEXTILES

Nanosilver—particles of silver that are in the nanometer size range—is claimed to kill bacteria, and therefore must be registered as a pesticide by the EPA.

Nanosilver is different from conventional silver because of its small size. This difference raises many concerns, particularly considering the ability of nanosilver to travel through the body and damage cells in the brain, liver, stomach, testes, and other organs, as well as pass from mother to fetus.

47
Ag
Silver
107.8682

Conventional silver has long been known to be an effective germ killer and has been registered since the 1950s as an antimicrobial pesticide used to inhibit bacteria growth in water filters and to control algae in swimming pools.[7] Although conventional silver is not very harmful to humans, it is highly toxic to microbes and aquatic organisms, and the toxic silver ions (Ag+) are persistent in the environment. Nanosilver particles share these properties with conventional silver, making it an effective antimicrobial agent that kills harmful microorganisms, like germs, as well as beneficial microorganisms, such as daphnia and algae, that are critical in the food web.

Although sharing many hazardous properties with conventional silver, nanosilver particles raise the additional concern that the smaller size means the nanoparticle and its ions can access places that conventional silver cannot. Laboratory rodent studies suggest that if breathed or swallowed, for example, by workers using nanosilver powders to treat fabrics or families using sterilizing sprays and nanosilver air fresheners, the particles could travel throughout the body, ending up in the testes, liver, kidney, lungs, brain, stomach, and other organs, where they may damage cells and compromise organ function.[8]

In 2008, Swiss company HeiQ Materials Ag applied to the EPA to register nanosilver as a preservative in textiles such as clothing, bed sheets, pillowcases, and blankets. This application represented the first pesticide to be registered as a nano-size chemical. Other consumer products use nanosilver unlawfully because they have not gone through the legally-required registration process.[9] The EPA determined that nanosilver is different from silver, meaning that HeiQ needed to go through a full registration process and submit data on the toxicity of nanosilver, rather than applying under the existing registration of conventional silver.[10] Since HeiQ had not yet conducted many of the necessary studies, the EPA granted the company a conditional registration in 2011, allowing the product onto the market while HeiQ undertook the research. Among the absent studies required as a condition of the registration were those looking at reproductive and developmental toxicity, inhalation toxicity, dermal toxicity, and chromosomal damage.

PHOTO: GRIBLEY/FLICKR

In granting a conditional registration for nanosilver in textiles, the EPA acknowledged that people will be in direct contact with nanosilver from these textiles, including workers who make the clothing, consumers who use and wear it, and infants and babies who lay against it, and suck or chew their parents' treated clothing. (Nanosilver leaches from clothing into wash water and has been shown to go from treated clothing onto skin in laboratory tests using artificial skin.[11])

The EPA claimed that allowing this product onto the market while awaiting the toxicity studies would benefit the public interest by reducing the overall environmental load of silver because of its smaller size. However, nanosilver is not only replacing conventional silver uses, but also being sold for new and expanded markets, resulting in the release of far more nanosilver and toxic silver ions into sewage and water treatment systems, and ultimately into rivers, streams, and other receiving waters. Consumers can now buy pillows and shirts that contain nanosilver without any warning labels about toxicity concerns. Furthermore, if nanosilver proves to be much more toxic than conventional silver, the smaller quantities released will not necessarily cause less harm.

THE ENVIRONMENTAL PROTECTION AGENCY ALLOWS CONTINUED USE OF CLOTHIANIDIN DESPITE FLAWED STUDIES

Pollinators, including bees, bats, and butterflies, contribute approximately $15 billion to the economy through the pollination of more than 130 cash crops, which make up approximately one-quarter of all the foods in the human diet, including almonds, cherries, pumpkins, and apples.[12] Unfortunately, beekeepers have been suffering dramatic bee colony losses of about 30 percent annually since 2007, likely from a combination of environmental stressors, parasites, pathogens, and pesticide residues in bee hives.[13]

Clothianidin is one in a family of neonicotinoid pesticides that are key suspects in these losses because they are systemic (taken up and distributed throughout the plant tissue, including its pollen and nectar), long-lasting, and highly toxic to honey bees.[14] Bayer CropScience was granted a conditional registration in 2003 for clothianidin to treat corn seed and canola seed. The registration was conditioned upon, among other things, the submission of a field study of the effects on bees by 2004. Bayer not only conducted a defective study but also submitted findings three years late.

The EPA had required the pollinator field test to include a complete worker-bee life cycle study and an evaluation of the exposure to and effects of clothianidin on the queen bee. The study, submitted in 2007, was so poorly undertaken that the EPA considered it to be invalid (though it later slightly upgraded it to "supplemental" because of some limited redeeming information it provided).[15]

Bayer's study concluded that clothianidin had no effect on bee mortality. The study had numerous flaws; the most egregious ones noted by the EPA reviewers state that 1) the treated and control (no pesticide) fields were too close together, and bees likely foraged among all fields, resulting in cross-contamination of treated and control hives; and 2) the study likely undercounted dead bees by using a faulty "sheet method" instead of the EPA-recommended, more accurate bee trap. Because of these and other flaws, both treated and control fields had significant bee deaths.[16] Because Bayer failed to provide its raw data, the EPA could not conduct a statistical reanalysis of the study results, meaning that the EPA and the public must rely on the data analysis provided by Bayer rather than being able to scrutinize the data using alternate assumptions and approaches.[17] In fact, Health Canada, the Canadian agency that regulates pesticides, found that "mortality in worker bees was obviously higher in clothianidin-treated colonies" when only dead-bee traps data were used in the analysis.[18] Design flaws make it almost impossible to determine the risks from clothianidin to bee survival.[19] Despite these issues, in April 2010 clothianidin's registration was switched from conditional to fully registered. A November 2010 EPA memo determined that Bayer's field study was deficient, but clothianidin remains fully registered today.

The EPA had conditioned clothianidin's registration on an informative final study, which never materialized. Moreover, the public never had a chance to comment on the study or the EPA's conditional registration decision. Yet the insecticide remains registered and on the market, thanks to the use of the conditional registration loophole.

PHOTO: HITTHATSWITCH/FLICKR

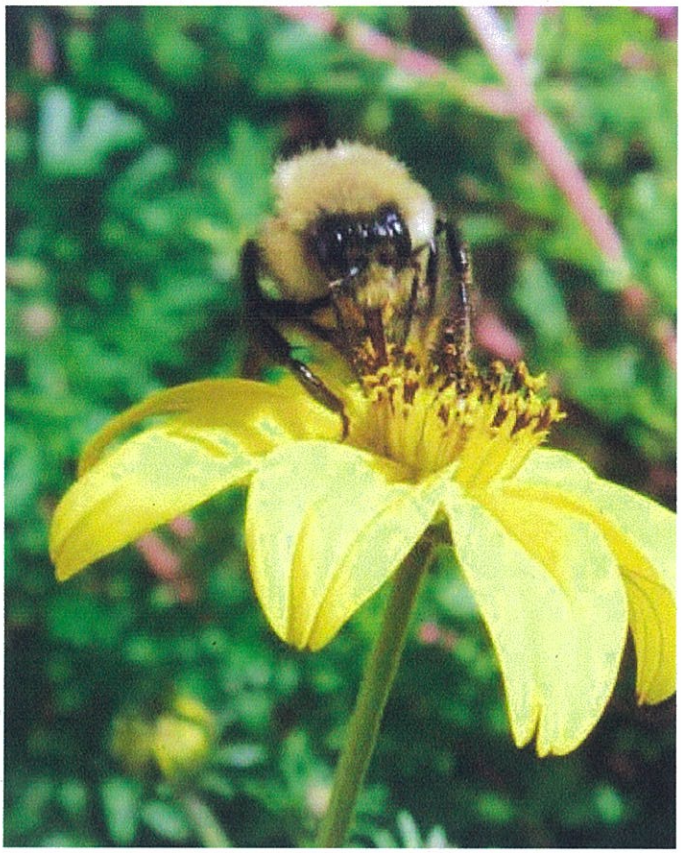
RECOMMENDATIONS

The EPA is conditionally registering pesticides with inadequate or absent data. Further, subsequent EPA determinations about whether the conditions imposed on registrants have been satisfied are made in private without any opportunity for the public to comment. Ultimately, conditional registration of pesticides is not a temporary and rare occurrence as Congress intended, but a wide loophole that pesticide manufacturers use to get many products onto the market before they are proven safe to the public. The EPA's own website acknowledges that it needs improved registration tracking and staff training to avoid continued misuse and overuse of the conditional registration provision.[20]

NRDC recommends that the EPA take the following steps to respond to and improve its grievously flawed practices in pesticide registration:

1. **Review all previously conditionally registered pesticides and bring them into compliance with the law and with the recommendations of this report.** In the course of its review of conditional registrations triggered by NRDC's inquiries, it appears the EPA has never received data for some of the conditional registrations.

2. **Immediately cancel pesticide registrations with overdue studies or those that are out of compliance for any other reason.** The EPA should immediately cancel the registrations for clothianidin and nanosilver.
3. **Properly document conditional registration actions.** One of the most fundamental problems identified in the NRDC study and by the EPA is that the agency does not have systematic tracking and management systems for conditional registrations.[21] Addressing this should be an immediate priority for the EPA, so it can provide a credible and transparent program to the public.
4. **Establish a process where the public can comment on new data received to support a conditional registration.** Currently, once a pesticide is conditionally registered, the public is no longer afforded any opportunity to either track or comment on subsequent data submissions. Lack of data or potential flaws in the follow-up studies are hidden from public scrutiny, depriving the EPA of the insights of scientific experts in the field, and forcing the public to blindly trust the EPA's determinations.
5. **Place all submitted data into a publicly accessible, updated database.** To show that required studies are being submitted for conditional registrations, the EPA should establish a publicly accessible, electronically searchable database that identifies all the actions taken under the agency's conditional registration authority, and the status of those registrations. The database should clearly identify for each conditionally registered pesticide
    - the conditions upon which registration was based
    - the EPA's authority for issuing the conditional registration
    - the time line for the registrant to submit the data
    - the date that the EPA received the required data
    - the Data Evaluation Record or the EPA's summary assessment of the data
    - how the EPA addressed the results of submitted studies in the registration decision



6. **Use the conditional registration process only in the limited and rare circumstances described by Congress.** Congress gave the EPA the authority to limit or even prevent the use of a pesticide where there are scientific uncertainties and data gaps, with the understanding that these chemicals are harmful by design. The EPA must use its authority to protect people, pollinators, and other wildlife, in accordance with its stated mission and obligation as a public health agency.

Endnotes

1 The active ingredient is the chemical in a pesticide product that kills, controls, or repels pests. The same active ingredient may be found in hundreds of pesticide products with different names; Conditional registrations can also be granted to applications for a new end-use product on an already registered pesticide or for a pesticide product that is identical or substantially similar to one that has already been registered. There are fewer requirements to be conditionally registered for these two types of applications.

2 Federal Insecticide, Fungicide, and Rodenticide Act. 7 U.S.C. §136a(c)(7)(C); 42 C.F.R. § 152.114.

3 Sass J, Wu M. Letter to U.S. Environmental Protection Agency. Comments from the NRDC on the proposed conditional registration of a pesticide product HeiQ AGS-20, containing nanosilver. Sept 10, 2010. Federal Docket ID # EPA-HQ-OPP-2009-1012-0061

4 U.S. Environmental Protection Agency, *Conditional Registration—Evaluating Program Use of Conditional Registrations*, April 25, 2011, http://www.epa.gov/pesticides/regulating/conditional-registration.html#evaluating (accessed September 8, 2011).

5 Ibid.

6 Ibid.

7 U.S. Environmental Protection Agency. *Reregistration Eligibility Document Facts: Silver*. EPA-738-F-93-005. U.S. Environmental Protection Agency. June 1993. http://www.epa.gov/oppsrrd1/REDs/factsheets/4082fact.pdf (accessed September 8, 2011).

8 U.S. Environmental Protection Agency, *US EPA Response to Comments Received on Proposed Decision Document for the Registration of HeiQ AGS-20 as a Materials Preservative in Textiles*, December 1, 2011, 34. Federal Docket ID# EPA-HQ-OPP-2009-1012-0065; U.S. Environmental Protection Agency. EPA Decision Document. *Conditional Registration of HeiQ AGS-20 as a Materials Preservative in Textiles*, December 1, 2011. Federal Docket ID# EPA-HQ-OPP-2009-1012-0064; J. H. Sung, Ji, J.H., Park, J.D. et al., "Subchronic Inhalation Toxicity of Silver Nanoparticles," *Toxicological Sciences*, April 2009; 108(2):452-61. doi: 10.1093/toxsci/kfn246; U.S. Environmental Protection Agency, External Review Draft Nanomaterial Case Study: Nanoscale Silver in Disinfectant Spray, August 13, 2010. EPA/600/R-10/081. ; J. H. Sung, Ji, J.H., Song, K.S., Lee, J.H., Choi, K.H., Lee, S.H., Yu, I.J., "Acute Inhalation Toxicity of Silver Nanoparticles," *Toxicology and Industrial Health*, March 2011,; 27(2):149-54. J. H. Ji, Jung, J.H., Kim, S.S., Yoon, J.U., Park, J.D., Choi, B.S., Chung, Y.H., Kwon, I.H., Jeong, J., Han, B.S., Shin, J.H., Sung, J.H., Song, K.S., Yu, I.J., "Twenty-eight Day Inhalation Toxicity Study of Silver Nanoparticles in Sprague-Dawley Rats," *Inhalation Toxicology*, August 2007; 19(10):857-71. M. van der Zande, Vandebriel, R.J., Van Doren, E., Kramer, E., Herrera Rivera, Z., Serrano-Rojero, C.S., Gremmer, E.R., Mast, J., Peters, R.J., Hollman, P.C., Hendriksen, P.J., Marvin, H.J., Peijnenburg, A.A., Bouwmeester, H., "Distribution, Elimination, and Toxicity of Silver Nanoparticles and Silver Ions in Rats After 28-Day Oral Exposure," *ACS Nano*, August 28, 2012; 6(8):7427-42.

9 U.S. Environmental Protection Agency. *Proposed Decision Document for the Registration of HeiQ AGS-20 as a Materials Preservative in Textiles*. 12 August 2010. Federal Docket ID# EPA-HQ-OPP-2009-1012-0020.

10 U.S. Environmental Protection Agency FIFRA Scientific Advisory Panel. Meeting Minutes November 3-5, 2009: Evaluation of Hazard and Exposure Associated with Nanosilver and Other Nanometal Pesticide Products. 26 January 2010. Page 7. http://www.epa.gov/scipoly/sap/meetings/2009/november/110309ameetingminutes.pdf ; U.S. Environmental Protection Agency. Proposed Decision Document for the Registration of HeiQ AGS-20 as a Materials Preservative in Textiles. 12 August 2010. Federal Docket ID# EPA-HQ-OPP-2009-1012-0020.

11 Westerhoff P, Benn TM. "Nanoparticle Silver Released into Water from Commercially Available Sock Fabrics." *Environmental Science & Technology*. 2008;42(11):4133-4139. doi: 10.1021/es7032718; Kulthong, K, Srisung S, Boonpavanitchakul K, Kangwansupamonkon W and Maniratanachote R. "Determination of Silver Nanoparticle Release from Antibacterial Fabrics into Artificial Sweat." *Particle and Fibre Toxicology*. 2010;7(1):8. doi: 10.1186/1743-8977-7-8.

12 Agricultural Research Service. "Questions and Answers: Colony Collapse Disorder." U.S. Department of Agriculture. http://www.ars.usda.gov/News/docs.htm?docid=15572 Updated December 17, 2010. (accessed September 8, 2011).

13 Colony Collapse Disorder Steering Committee, Agricultural Research Service, *Colony Collapse Disorder* Progress Report, June 2010, http://www.ars.usda.gov/is/br/ccd/ ccdprogressreport2010.pdf (accessed September 8, 2011).

14 R. Johnson, *Honey Bee Colony Collapse Disorder*, Congressional Research Service 7-5700, January 7, 2010, http://www.fas.org/sgp/crs/misc/RL33938.pdf. Charles Abel, "Bee Concerns Pose Threat to OSR Viability," *Farmers Weekly*, January 3, 2013, http://www.fwi.co.uk/Articles/03/01/2013/136998/bee-concerns-pose-threat-to-osr-viability.htm (accessed January 4, 2013).

15 EPA memo from J DeCant to K Davis. "Revised assessment for clothianidin registration of Prosper T400 seed treatment on mustard seed (oilseed and condiment) and Poncho/Votivo seed treatment on cotton." 3 December 2010; EPA memo from A Pease to K Davis. "Reclassification of MRID 46907801/46907802 data package 336888 for clothianidin, PC Code 044309." December 22, 2010.

16 The bee trap works by trapping the dead bees as they are expelled from the colony and holding them for counting, whereas the sheet method catches dead bees that fall onto a sheet placed on the ground at the entrance of the hive. The sheet method undercounts dead bees because it loses the dead bees that blow away or get eaten by insects or other animals before someone can get out to the field to count them, a highly likely event since Bayer scientists only counted dead bees once per week instead of daily as EPA had recommended.

17 Email from W Hou, Health Canada to K McCormack, EPA and J DeCant, EPA. "Clothianidin field study." 10 December 2010 (with attachment).

18 "Data Evaluation Record for honey bee field testing for pollinators." Reviewed by EPA: CE Padova, 18 September 2007; TS Myers, 26 September 2007; A Pease, 22 December 2010; T Steeger, 22 December 2010. http://www.epa.gov/pesticides/chemical/foia/cleared-reviews/reviews/044309/044309-090201-113501-079801-2010-12-22a.pdf (accessed September 8, 2011).

19 The study redeemed itself somewhat in that it proved that clothianidin from seed-treatments had contaminated honey, nectar, and pollen in the beehive, meaning bees can be exposed to clothianidin through these contaminated food sources. "Data Evaluation Record for honey bee field testing for pollinators." Reviewed by EPA: CE Padova, 18 September 2007; TS Myers, 26 September 2007; A Pease, 22 December 2010; T Steeger, 22 December 2010. http://www.epa.gov/pesticides/chemical/foia/cleared-reviews/reviews/044309/044309-090201-113501-079801-2010-12-22a.pdf (accessed September 8, 2011).

20 U.S. Environmental Protection Agency, *Conditional Registration*, September 25, 2012, http://www.epa.gov/pesticides/regulating/conditional-registration.html.

21 U.S. Environmental Protection Agency, *Conditional Registration—Issues with Tracking Conditional Registrations*, April 25, 2011, http://www.epa.gov/pesticides/regulating/conditionalregistration.html#issues (accessed September 8, 2011).

APPENDIX B

GreenScreen™ Rating: Conventional Silver was assigned a Benchmark Score of **1 based on combined very High Persistence coupled with very High Ecotoxicity, as determined in standardized tests.**

Route	GreenScreen™Hazard Ratings: Conventional (low-solubility, non-nanoscale) silver																			
	Group I Human					Group II and II Human									Ecotox		Fate		Physical	
	C	M	R	D	E	AT	ST		N		SnS	SnR	IrS	IrE	AA	CA	P	B	RX	F
							Single	Repeated	Single	Repeated										
o	DG	L	DG	DG	DG	**L**	DG	DG	DG	DG	*L*	DG	**L**	**L**	**vH**	**vH**	**vH**	**L**	**L**	**L**
d	DG		DG	DG		**L**	DG	DG	DG	DG										
i	DG		DG	DG		DG	DG	DG	DG	DG										

GreenScreen™ Rating: Nanosilver was assigned a Benchmark Score of **1** based on very High Persistence coupled with High systemic toxicity and very High Ecotoxicity.

Route	GreenScreen™Hazard Ratings: Nanosilver, metallic																			
	Group I Human					Group II and II Human									Ecotox		Fate		Physical	
	C	M	R	D	E	AT	ST		N		SnS	SnR	IrS	IrE	AA	CA	P	B	RX	F
							Single	Repeated	Single	Repeated										
o	DG	L	DG	DG	DG	L	DG	**M**	DG	DG	**L**	DG	**L**	**L**	**vH**	**vH**	**vH**	**L**	DG	DG
d	DG		DG	DG		L	DG	DG	DG	DG										
i	DG		DG	DG		**vH**	DG	**H**	DG	DG										

GreenScreen™ Rating: AGS-20 was assigned a Benchmark Score of U. Numerous datagaps exist for AGS-20, which earns a BM score of U (Unspecified).

Route	GreenScreen™Hazard Ratings: AGS-20 (silver-silica nanocomposite containing 19.3% silver nanoparticles imbedded in a matrix of amorphous silicon dioxide)																			
	Group I Human					Group II and II Human									Ecotox		Fate		Physical	
	C	M	R	D	E	AT	ST		N		SnS	SnR	IrS	IrE	AA	CA	P	B	RX	F
							Single	Repeated	Single	Repeated										
o	DG	DG	DG	DG	DG	**L**	DG	DG	DG	DG	**L**	DG	**L**	**M**	DG	DG	**vH**	DG	*L*	*L*
d	DG		DG	DG		**L**	DG	DG	DG	DG										
i	DG		DG	DG		**M**	DG	DG	DG	DG										

Note: Exposure routes include Oral (o), Dermal (d), and Inhalation (i). Hazard levels are Very High (vH), High (H), Moderate (M), Low (L), and Very Low (vL)). *Italics* reflects estimated values and lower confidence, as with data gaps (DG), whereas **BOLD** font reflects values based on test data (see guidance). Endpoints include Carcinogenicity (C), Mutagenicity / Genotoxicity (M), Reproductive Toxicity (R), Developmental and/or Neurodevelopmental Toxicity (D), Endocrine Activity (E), Acute Mammalian Toxicity (AT), Systemic Toxicity – Single Exposure (ST-single) or Repeated Exposure (ST-Repeated), Neurotoxicity – Single Exposure (N-single) or Repeated Exposure (N-Repeated), Skin Sensitization (SnS), Respiratory Sensitization (SnR), Irritation/Corrosivity – Skin (IrS), Irritation/Corrosivity – Eyes (IrE), Acute Aquatic Toxicity (AA), Chronic Aquatic Toxicity (CA), Persistence (P), Bioaccumulation (B), Reactivity (Rx), and Flammability (F).