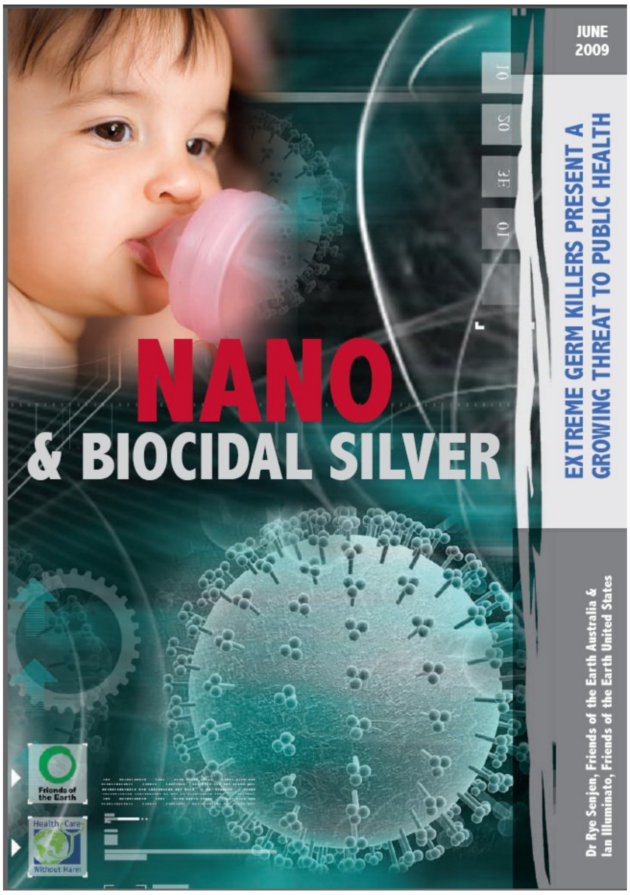

Nano and biocidal silver: extreme germ killers present a growing threat to public health

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Endorsed by

Health Care Without Harm Europe **Australia & U.S.**

Health Care Without Harm Europe (HCWHE) supports the declaration: Principles for the Oversight of Nanotechnologies and Nanomaterials, signed by 43 civil society, public interest, environmental and labour organizations in July 2007.

This report is consistent with these principles and provides valuable information for the healthcare community. HCWHE is particularly concerned about potential health risks of nanosilver and recommends a precautionary approach.

For an Electronic copy of this report, or further briefing papers from Friends of the Earth please refer to our websites:

Friends of the Earth Australia
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Executive Summary

Silver has for a long time been known to be a potent antibacterial agent and toxic to fungi and algae, but in recent years the use of silver as a biocide, either in solution, suspension and/or in nanoparticulate form has experienced a dramatic revival. Silver biocides are used in an ever increasing range of products, including fibres, washing machines, dyes/paints and varnishes, polymers, medical applications, sinks and sanitary ceramics and various 'consumer' applications such as disinfectants, cosmetics, cleaning agents, baby bottles, etc.

Widely available consumer products which contain nanosilver include food contact materials (such as cups, bowls and cutting boards), cosmetics and personal care products, children's toys and infant products and 'health' supplements.

There is clear evidence that silver, and in particular nanosilver, is toxic to aquatic and terrestrial organisms, a variety of mammalian cells *in vitro,* and may be detrimental to human health. While undoubtedly silver and nanosilver have useful applications in the medical arena (for instance as coatings for medical devices or as wound care for severe burns victims), their use needs to be strictly controlled and the dictum 'no data, no market' should always be followed.

Bacterial resistance to antibiotics is an ever increasing problem globally, and indiscrimate use of biocidal silver in numerous consumer products is not only unnecessary, but may further increase bacterial resistance to a dangerous level.

There are preliminary indications that in nanoparticle form, the toxicity of ionic silver may be increased, or that the nanoparticles may exert their own toxicity. The disposal of biocidal silver products into waste water raises a number of concerns as the resulting sewage sludge may be used on agricultural soils, disposed as solid waste in landfills or be incinerated. Biocidal silver may also disrupt the functioning of key soil microbial communities.

A 2009 international study (EMERGNANO), conducted by imminent nanotoxicologists, reviewing the evidence generated by current global research on the toxicity of nanoparticles 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."** (Aitken et al. 2009).

Friends of the Earth calls for a immediate moratorium on the commercial release of products that contain manufactured nanosilver until nanotechnology-specific regulation is introduced to protect the public, workers and the environment from their risks, and until the public is involved in decision making.

Our call is in line with recommendations from the United Kingdom's Royal Society and Royal Academy of Engineering's 2004 report on nanotechnology, which states that intentional release of nanomaterials into the environment should be prohibited until this can be proven to be safe. A precautionary approach to nanosilver technology is essential.

Nano and biocidal silver: extreme germ killers present a growing threat to public health

1. The rise of silver biocides

The fungicidal, bactericidal and algicidal properties of silver have been known to humans for a long time. Silver has for centuries been known to effectively kill harmful bacteria contaminating various commodities, including milk and water. Ancient Greeks used silver containers to store purified water and wine. In the early 1900s, families in the United States placed Silver Dollar coins into milk containers to keep it fresh. But it is in recent years that the use of silver as a biocide, either in solution, suspension and/or in nanoparticulate form has experienced a dramatic revival.

Silver biocides are used in an ever increasing range of products, including water treatment, fibres, washing machines, dyes/paints and varnishes, polymers, medical applications, sinks and sanitary ceramics and various ‘consumer’ applications such as disinfectants, cosmetics, cleaning agents, baby bottles, etc. (Hund-Rinke et al. 2008). Silver has also been incorporated as an antimicrobial agent in filters to purify drinking water and to clean swimming pool water, but we have excluded these applications from discussions as they are beyond the scope of this publication.

An increasing amount of silver used in consumer and industrial products is in the form of nanosilver. Nanoscale silver or “nanosilver” has become one of the most commonly used nanomaterials in consumer products, predominately as a bactericide. Widely available consumer products which contain nanosilver include, for instance, food contact materials (such as cups, bowls and cutting boards), cosmetics and personal care products, children’s toys and infant products and ‘health’ supplements. As of August 2008, the Project on Emerging Nanotechnologies Consumer Products Inventory (at the Woodrow Wilson International Centre for Scholars) listed 235 products (out of the 803 nanotechnology products in the inventory) as containing nanosilver (Project on Emerging Nanotechnologies 2009).

A 2009 international study (EMERGNANO), conducted by imminent nanotoxicologists, reviewing the evidence generated by current global research on the toxicity of nanoparticles found that there is

> **“indicative evidence of the harm of silver nanoparticles at low concentrations on aquatic invertebrates, which suggest that the environmental release of silver nanoparticles will be detrimental for the environment and that any industry/ institute using silver nanoparticles should consider taking the necessary steps to reduce or eliminate the potential exposure of the environment to these nanoparticles. … 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.”** (Aitken et al. 2009).

Silver is included on the U.S. Environmental Protection Agency (USEPA) 1977 priority pollutant list (still in effect) and its discharge into the aquatic environment is therefore regulated by the EPA (Luamo 2008). Indeed studies, as far back as 30 years ago, demonstrated that silver can be extremely toxic to fish (Hogstrand and Wood 1996) algae, crustaceans, some plants and fungi (Eisler 1996), especially nitrogen fixing heterotrophic and soil forming chemolithotrophic (Albright and Wilson 1974). Silver also inhibits microbial growth at concentrations far below that of other heavy metals (Braydich-Stolle et al. 2005).

While elemental silver has well known antimicrobial properties, nanoscale silver may be even more potent. Studies (Damm et al. 2007, Zeng et al. 2007) have shown that nanoscale silver embedded in polymers is twice as effective in killing *Escherichia coli* (*E. coli*) when compared to elemental silver. The same studies also showed that nanoscale silver is able to kill bacteria for longer periods of time, demonstrating the technology's potential use for long-term antimicrobial applications.

What is nanotechnology?

One nanometre (nm) is one thousandth of a micrometer (µm), one millionth of a millimetre (mm) and one billionth of a meter (m). To put the nanoscale into context: a strand of DNA is 2.5nm wide, a protein molecule is 5nm, a red blood cell 7,000 nm and a human hair is 80,000 nm wide. If one imagines that a nanometre is represented by a person, a red blood cell would be a massive 7 kilometres long!

Nanomaterials have novel properties and pose novel risks

Nanomaterials are "intentionally engineered" to take advantage of unique properties at the nano-scale. While these new properties may be desirable, changing materials at this scale can also result in the introduction of new toxicological risks. Nanoparticles have a very large surface area which typically results in greater chemical reactivity, biological activity and catalytic behaviour compared to larger particles of the same chemical composition (Garnett and Kallinteri 2006; Limbach et al 2007; Nel et al. 2006). Nanomaterials may have greater bioavailability than larger particles, resulting in greater uptake into individual cells, tissues and organs. Nanomaterials that gain access to our bodies may also more readily penetrate biological membranes and access cells, tissues, and organs. Materials which measure less than 300nm can be taken up by individual cells (Garnett and Kallinteri 2006), while nanomaterials which measure less than 70nm can even be taken up by our cells' nuclei, where they can cause major damage (Chen and Mikecz 2005; Geiser et al. 2005; Li et al. 2003).

Unfortunately, the greater chemical reactivity and bioavailability of nanomaterials may also result in greater toxicity of nanoparticles compared to the same unit of mass of larger particles (Hoet et al 2004; Oberdörster et al. 2005a; Oberdörster et al. 2005b). Other properties of nanomaterials that influence toxicity include: chemical composition, shape, surface structure, surface charge, catalytic behaviour, extent of particle aggregation or disaggregation, and the presence or absence of other groups of chemicals attached to the nanomaterial (Brunner et al. 2006; Magrez et al. 2006; Sayes et al. 2004; Sayes et al. 2006). Nanosilver particles may be engineered by a variety of methods including spark discharging, electrochemical reduction, solution irradiation and cryochemical synthesis and contain about 20-15000 silver atoms (Chen and Schluesener 2008). They may be engineered to have different shapes, including spheres, particles, rods, cubes, wires, film and coatings (Winjhoven et al. 2009).

2. Nanosilver Products Overview

Market size

The worldwide production of silver reached approximately 28,000 metric tons in 2007 (Hund-Rinke et al. 2008); approximately 500 metric tons per year are nanosilver (Mueller and Nowack 2008). The majority of silver is used in industry (38.2%), as jewellery and silverware (32.5%), and in the photographic industry (23.8%). Silver biocide use (0.5% or approximately 140 metric tons) is still very small and the remainder of the silver is used for investment and coins (5%) (Hund-Rinke et al.2008). The use of silver in the photographic industry has been declining rapidly with the introduction of digital photography, but has apparently been more than offset by the use of silver in the electronics industry as conductive pastes and solders.

In the hospital setting nanosilver is used extensively for wound management, particularly for the treatment of burns, various ulcers (rheumatoid arthritis-associated leg ulcers, diabetic ulcers, etc.), toxic epidermal necrolysis, for healing of donor sites and for meshed skin grafts (Wijnhoven et al. 2009). The wound care market alone (salves and wound dressings) was worth approximately US$3 billion in 2004 (Biogate 2008). “Acticoat” by Smith and Nephew, a silver nanoparticle based wound dressing (Nucryst, Wakefield, MA, USA), captured US$25 million in sales in 2004 alone (Wagner et al. 2006). The use of silver is predicted to continue to rise as silver is now used in textiles, plastics, and the medical industries.

Wijnhoven et al. (2009), cites several studies on the amount of silver entering terrestrial or aquatic ecosystems and concludes that probably 300,000 kg of silver waste enters ecosystems each year worldwide. The European market for silver-containing biocidal products is projected to reach 110–230 metric tons of silver by 2010 (Blaser et al. 2008). Germany alone used about 8000 kg (8 metric tons) of silver in 2007, of which 6,600 kg are used for water treatment purposes. 1100 kg are used in the treatment of surfaces and may, potentially, include nanosilver. The remainder is used in various other silver products. Water treatment mainly uses ionic silver. Silver used in textiles comes in a variety of forms including simple drenching of the cloth in silver salts and nanosilver impregnation of textiles. Nanosilver is also increasingly used in paints, lacquers and polymers and has appeared in many consumer products. It is unknown how much nanosilver is used in any of these products (Hund-Rinke et al. 2008).

According to the United States National Science Foundation, the size of the nanotechnology market is forecast to grow to $1 trillion by 2015 (Roco 2006). A 2008 nanosilver legal petition to the United States Environmental Protection Agency filed by the International Centre for Technology Assessment in Washington, DC identified more than 260 nanosilver products currently on the market, including household appliances and cleaners, clothing, cutlery, children's toys and personal care products (Kimbrell 2008).

Products using nanosilver include:

- Health’ and food supplements, food packaging/storage and food contact materials
- Household appliances e.g. fridges, washing machines, vacuum cleaners, air and water filters
- Hospital and medical applications e.g. implants, wound plasters and salves, medical devices
- Paints, lacquers and sprays for surfaces
- Surfaces in public spaces
- Textiles and shoe products
- Cosmetics and personal care products e.g. tooth brushes, soaps, hair products, deodorants, female hygiene products
- House and garden e.g. bedding, wall coverings, air and water filters, plant sprays
- Electronic articles and computers e.g. mice, keyboards
- Children’s articles

- Agricultural products e.g. seed treatment

An excellent source of information on nanosilver products is the Woodrow Wilson International Center for Scholars Project on Emerging Nanotechnologies Consumer Products Inventory (http://www.nanotechproject.org/inventories/consumer/). Rather than repeating the information available there, we have presented in Appendix 1 a selection of products readily available in shops and from online retailers in Australia, Europe and the United States.

Nanosilver Children's Products

Nanosilver products targeted towards children and infants include: strollers, toys (stuffed animals), wet wipes, mats and bedding, baby bottles, nipples and pacifiers. For instance, Baby Dream® is a large supplier of baby nanosilver products offering a wide variety of products for babies, including a baby bottle (Baby Dream 2009). Also available are stuffed animals with nanosilver treated "Memory Foam" such as Benny the Bear Plush Toy and Donny the Dog sold by Pure Plushy™ Inc. Curiously this company made claims on their website prior to February 27th 2008, which clearly indicated their use of nanosilver: "With the additive of Silver Nanoparticles, our product has been clinically proven to fight against harmful bacteria, moulds and mites." (Pure Plushy 2009). However, recently the company's website stopped highlighting their use of nanosilver. The website now claims, "Our line of plush toys has antimicrobial properties that provide protection from moulds, mites and bacteria. (Pure Plushy 2009). By not clearly identifying their product's nanoparticle content, this company and others avoid regulation by the EPA under the FIFRA Act. However they may also obstruct consumers from making informed purchases. This further confirms the need for nanosilver content to be regulated by government, to ensure that these products are safe and properly labelled.

The idea of using powerful antimicrobials in children's products is of concern. In a recent New York Times article on the benefits of dirt and certain bacteria for children, the author quotes a leading researcher, Dr. Joel V. Weinstock, the director of gastroenterology and hematology at Tufts Medical Center in Boston, who says "Children raised in an ultra clean environment, are not being exposed to organisms that help them develop appropriate immune regulatory circuits" (Brody 2009). By exposing children to increasing quantities of biocidal nanosilver, we may very well be robbing a child's need to mature his or her immune system. Nanosilver may also exert a toxic effect:

> "There are entire textbooks written on the toxicity of metals and you don't want to disturb the balance in your body. There are studies where animals have been fed nanosilver and you can detect the harmful effects on their weight and general health. I would like to see how these products are testing themselves and claiming to be safe for children. The same dose of silver would be diluted less in a child because they have less body water."(Ken Donaldson, chairman of respiratory toxicology at the University of Edinburgh, as cited by Gray 2008).

Special attention needs be given to children's interactions with nanosilver, considering their physiology is unique compared to adult bodies.

Nanosilver in dietary supplements and food related items

Food products containing nanoparticles have entered the market, mainly in the form of packaging and food contact material, which incorporate antimicrobial nanomaterials. Food and food packaging do not require labels to indicate that nanoscale materials have been added. Despite the growing number of nanotech food products on the market, consumers are left with little information on what food products they may be purchasing that contain nanoparticles.

Food supplements

A 2009 report by the Woodrow Wilson International Centre for Scholars Project on Emerging Nanotechnologies looked at nanotechnology-based dietary supplements and their regulation in the United States and found at least a dozen dietary supplements on the market which contain nanoscale silver. The report calls for the United States Congress to "adopt legislation granting the FDA [Food and Drug Administration] the authority to collect additional information about these products and to ensure that they are tested for their effects on human health" (Schultz and Barclay 2009). It is a serious concern that products on the market contain ingredients with unknown biological properties backed only by a producer's claims. Very few studies have investigated the toxicity of nanoparticle nutritional additives. The failure of governments to require comprehensive safety testing of toxicity risks in nano additives is concerning. Dr Qasim Chaudhry, leader of the nanotechnology research team at the United Kingdom's Central Science Laboratory warns that nanoparticle and nano-encapsulated food ingredients "may have unanticipated effects, far greater absorption than intended or altered uptake of other nutrients, but little, if anything, is known currently" (Parry 2006).

Food packaging/storage and food contact materials (including household appliances)

One of the earliest commercial applications of nanotechnology within the food sector is in packaging (Roach 2006). Between 400 and 500 nano packaging products are estimated to be in commercial use now, while nanotechnology is predicted to be used in the manufacturing of 25% of all food packaging within the next decade (Reynolds 2007). A key purpose of nano packaging is to deliver longer shelf life by improving the barrier functions of food packaging to reduce gas and moisture exchange and UV light exposure (Sorrentino et al. 2007). Nano packaging can also be designed to release antimicrobials, antioxidants, enzymes, flavours and nutraceuticals to extend shelf-life (LaCoste et al. 2005).

Distinct from trigger-dependent chemical release packaging, designed to release biocides in response to the growth of a microbial population, humidity or other changing conditions, other packaging and food contact materials incorporate antimicrobial nanomaterials, that are designed not to be released, so that the packaging itself acts as an antimicrobial. These products commonly use nanoparticles of silver, although some use nano zinc oxide or nano chlorine dioxide (AzoNano 2007).

Anti-bacterial nanofood packaging and nano-sensor technologies have been promoted as delivering greater food safety by detecting or eliminating bacterial and toxin contamination of food. However it is possible that nanomaterials will migrate from antibacterial food packaging into foods, presenting new health risks. This appears inevitable where nano-films or packaging are designed to release antibacterials onto the food surface in response to detected growth of bacteria, fungi or mould.

In recent years a number of 'active' food contact materials using the antimicrobial properties of nanosilver have been developed. Consumer products using these often claim that by inhibiting bacterial growth, the food material contained within will last longer. Typical examples include nano silver food containers. For a similar purpose nanosilver has also been incorporated in various inner surfaces of domestic refrigerators (LG, Samsung and Daewoo) in an apparent attempt to prevent microbial growth and maintain a clean and hygienic environment in the fridge. For instance, Daewoo Electronics offers a refrigerator that employs "Nano Silver Poly technology" that claims to be "the outcome of continuous research of Daewoo to protect your health and that of your family" (Daewoo 2009).

Other household appliances include air and water purifiers/filters, washing machines, and computer parts and hardware. Similarly antibacterial coatings containing nanosilver have been applied to kitchenware, cutting boards and tableware (see below).

There is a risk to consumers if nanosilver particles could migrate from food contact materials into food or drink and be subsequently ingested. Few studies have been done on this issue, and preliminary work by Chaudhry et al. (2008) does indeed indicate that some nanosilver particle migrate into food, but perhaps at an insignificant level. Clearly more studies need to be done on nanomaterial migration before nanopackaging products can be allowed on the market.

CASE STUDY

The use of silver in washing machines

Increasingly consumers prefer to use cold water when washing textiles, partly to reduce their energy and water consumption, but also because modern synthetic materials require it. Environmentally friendly washing powders are often preferred by consumers. The combination of these factors results in a reduction of the cleaning ability of washing machines vis-à-vis bacteria and fungi, which in turn results in biofilm. A biofilm consists of a community of micro-organisms that adheres to living or inert matter. There are a number of conventional ways to combat biofilm including a hot wash (90 C) or the addition of vinegar to the wash. An alternative, offered by Samsung (and some other washing machine manufacturers) are washing machines containing a mechanism that produces silver ions that are added during the wash. Apparently silver ions not only reduce biofilm but also impart a 'fresh' feeling to the washed cloth. The 'silver active' system as sold by Samsung contains 10g of silver (two silver plates of 5g each), which is calculated to last 15 years. Silver ions are released into the water via electrolysis. Despite initial advertising claims, apparently no nanosilver is released. According to Samsung (as cited by Hund-Rinke et al. 2008) the amount of silver released during washing is 0.05 mg/l, i.e. 2.75 mg of silver ions are released per wash (assuming 55 l of water per wash is used). According to the manufacturer about half to a third of the silver ions remain on the textiles, while the remainder (up to 2 mg) are washed off and hence end up in the sewage system (Hund-Rinke et al. 2008).

The size of the silver contribution that these washing machines might make to the overall silver burden on the environment is difficult to calculate. However Hund-Rinke calculated that up to 12.2 kg of silver in Germany alone would be washed into the water ways each year. While this may not appear much, one also needs to consider this amount is in addition to all the other nanosilver from textiles and other impregnated products.

Under pressure from various NGOs the US EPA (Environmental Protection Agency) decided to regulate what they called silver-ion generating devices such as washing machines. If the manufacturer declared that the aim of the device is to kill bacteria, the device would be considered a pesticide. The EPA was at pains to point out that this notice was not an effort to regulate nanotechnology; it was the silver’s bactericidal effect rather than its size that led to their decision (EPA 2008).

The nanosilver washing machine is still available in many countries including Australia, Germany, India, Sweden and the U.S. to name a few.

Nanosilver socks: clean feet, but dirty environment?

Our feet make us mobile and give us the freedom to walk or run around, yet they are at the base of our body and often come into contact with germs and bacteria, especially when barefoot. As an apparent remedy, companies are now selling socks impregnated with silver nanoparticles. Product claims include odorless feet, curing of Athlete's foot, and even preventing foot infections for patients with diabetes (SoleFresh 2009).

However, a study by Benn and Westerhoff (2008) found that as nanosilver socks are washed, they lose alarming amounts of nanosilver. Not only do these products become ineffective, the nanoparticles that wash out from the sock can end up in the sludge produced in waste-water treatment plants. The report authors estimate that more than half of the nanoparticles from the socks dissolve into ionic silver. These silver ions are washed out into the environment, where they may react with sulfur and eventually form silver sulfides (black tarnish that forms on silver when in contact with hydrogen sulfide, a toxic and flammable gas). The ability for nanosilver particles to find their way into the environment and cause damage is extremely disquieting and further warrants these products' proper assessment and regulation.

Or perhaps no nanosilver at all?

Then again it could also be just false advertising. When the same researchers (Benn and Westerhoff 2008) compared nanosilver content of six pairs of nanosilver socks, they observed between zero to 1.85 mg of nanosilver per sock. One pair of socks had no detectable silver whatsoever, suggesting that the manufacturer either didn't know how to bind the nanosilver to the textile (even for a short time) or had added no nanosilver.

Clothing and Textiles

Textile products containing nanosilver include: socks, pants, shorts, swimwear, shoe pads/insoles, various business wear, sportswear, jackets, slippers, intimate wear, hats, gloves, bath towels and more. Silver nanoparticles are also embedded into textiles and fabrics for furniture, beddings and mattresses and for industrial material use. Companies are claiming that the nanosilver used in their products remains in the product for the products lifetime. However, studies show otherwise. Benn and Westerhoff (2008) showed that the nanosilver contained in socks can easily be washed out (see case study below). In a report for the German Environment Ministry Hund-Rinke et al. (2008) critically queried the need for the use of antibacterial textiles, given the millions of bacteria we come into contact with on a daily basis and the fact that our immune system has evolved to deal with them.

Cosmetics and Personal Care Products
Cosmetics and personal care products containing nanosilver include: soap, toothpaste, shampoo, facial masks and creams, skin whiteners, menstrual pads, hair dryers, hair straighteners, curling irons, hair brushes, and electric razors.

A South Korean company sells soap that thanks to its nanosilver content is "highly effective as a disinfectant and guarantees protection of skin" (Natural Korea undated).. The Conair® Company claims to create its own niche in the "premium hair care appliance category" by offering hair grooming products that are coated with a layer of nanosilver (Conair 2009). There are nanosilver products on the market that come into intimate contact with our bodies, including menstrual pads and condoms. For example, Greenhealthy Australia Pty Ltd sells nanosilver menstrual pads; claiming their pads will strengthen the body's immune system and: "regulate functions by the nanosilver and aloe negative ion that strengthens body immune system." (Greenhealthy Australia 2009).

Products for Pets
The nanosilver industry has not overlooked pets in its attempt to market products. Nanosilver feeding bowls, deodorants, pet water purifiers, dog beds and pet clothing are now on the market. Saywood Inc. offers a water purifier for pets, which "serves your pet with clean & healthy water preventing … bacteria through sterilization & antibiotic effect by the Nano silver photocatalytic coating ball & photo catalytic coating" (Saywood 2009).

Paint and lacquers
The antimicrobial properties of paint and lacquer are directly dependent on the concentration of silver present, the type of silver used and whether or not the base formulation is bound within a matrix. As an antifungal, the silver concentration needs to be much stronger to be effective. To date manufacturers of paint and lacquers have only done studies proving the efficiency of their products, not the extent of the silver leaching, nor how long the products stay effective (Hundt-Rinke et al. 2008).

The market potential for silver containing paints and lacquers is currently very small and is expected to be relatively insignificant when compared to other consumer products. There are few products on the market, but examples include: silver containing biocide (TINOSAN® SDC, IRGAGUARD® by Ciba Speciality Chemicals) which can be used as a plastic additive and can be used to produce coating effects. Alfred Clouth Lackfabrik produces nanosilver containing wood lacquers (CLOUCRYL Nano-Finish ANTIBAK and WL-Nano CB ANTIBAK) and sells between 3 - 5 metric tons of these per year. The lacquers contain silver particles bound in a polymer film at a concentration of 100 - 300 ppm silver/kg lacquer. (Hund-Rinke et al. 2008).

Bioni is the only manufacturer producing antimicrobial paint containing nanosilver particles, chiefly used in hospitals (see above). Bio-Gate AG (a Spin-off of the Erlangen University) produces HyGate™ 4000, HyGate™ 9000 and HyGentic™ 4000 and 9000, as well as ingredients for antimicrobial plastics and lacquers used in medicine, consumer products and cosmetics. The nanosilver particles are 5-50 nm and act as a depot for the constant release of silver ions. According to Bio-gate (as cited by Hund-Rinke et al. 2008) the concentration of silver is below 100 ppm or 100 mg/l. Hund-Rinke et al. 2008 estimated that given the nanosilver concentration and the amount of Bioni nanosilver paint sold yearly, the nanosilver content is approximately 12 kg per year (contained in 20-30 metric tons of paint). The unresolved question is how much of this nanosilver will wash off and end up in the environment?

Hospital and Medical Applications

The use of silver for medicinal purposes has a long history. Silver has been used in wound management as early as the 18th century, during which silver nitrate ($AgNO_3$) was used in the treatment of ulcers. Silver has also been used to induce abortions, cauterize wounds and remove calluses and warts. The use of silver nitrate to induce abortion can be fatal, as a 1971 case showed. The woman died within 3 hours of having been administered a 7% solution of silver nitrate. Silver deposits were found throughout her body, including her brain (Landsdown 2007). Medical use of soluble silver compounds have included treating mental illness, epilepsy, nicotine addiction, gastroenteritis, and infectious diseases, including syphilis and gonorrhoea (Wijnhoven et al. 2009).

During the early 19th century silver ions were used for their antimicrobial properties and were approved for wound management by the US Food and Drug Administration (FDA) in the 1920s. After the introduction of penicillin in the 1940s, antibiotics replaced silver as the standard treatment for bacterial infections. The 1960s saw the re-emergence of silver for the management of burns in the form of 0.5% silver nitrate solution. In 1968 silver nitrate was combined with a sulphonamide antibiotic to produce silver sulfadiazine (SSD) cream, which acts as a broad spectrum silver-based antibacterial. This continues to be prescribed to-date chiefly for the management of burns (Chopra 2007).

In the hospital setting nanosilver is used extensively for wound management, particularly for the treatment of burns, various ulcers (rheumatoid arthritis-associated leg ulcers, diabetic ulcers, etc.), toxic epidermal necrolysis, for healing of donor sites and for meshed skin grafts (Wijnhoven et al 2009). Silver-based wound dressings claim to offer improved infection management, in the form of the stimulation of healing in indolent wounds, prophylactic use for patients at risk of contracting a wound infection, and the management of critically colonized wounds (Chopra 2007). In hospitals, silver coated catheters are also used to prevent the growth of slime-containing biofilms that encourage bacterial infection. For instance, silver-coated urinary tract catheters reduce the frequencies of urinary track infection (Silver et al. 2006).

Numerous silver nanotechnologies have been launched offering antimicrobial coatings including Bactiguard (Bactiguard AB, Sweden), HyProtect (Bio-Gate AG, Germany), Nucryst's nanocrystalline platform technology (Nucryst Pharmaceuticals Corp., USA), Spi-ArgentTM (Spire Corp. USA), Surfacine (Surfacine Development Company LLC, USA), and SylvaGard (AcryMed Inc., USA) (Wijnhoven et al 2009). These are used as medical antimicrobials in textiles and surface coating products including wall coating paints, self-sterilizing hospital gowns and bedding. Bioni Hygienic, created by the German based Bioni CS® GmbH Company (see bioni.de) is an example of a nanotech-based antimicrobial nanosilver coating frequently used in hospitals. The company claims its product will create "an antimicrobial surface which prevents the growth of mould and mildew and effectively destroys even the most resistant of hospital bacteria by the use of an entirely new combination of active agents based upon nano technology" (Bioni 2009). They claim that the 13nm sized nano silver particles are safely embedded in a matrix that permanently binds the particles to the paint (Nanovations 2009).

Advanced silver nanotechnologies are also claimed to improve battery performance in implantable medical devices. Other proposed applications of nanosilver coated/ deposited/impregnated medical devices include infusion ports, orthopaedic protruding fixation devices, endovascular stents, urological stents, endoscopes, electrodes, peritoneal dialysis devices, subcutaneous cuffs, surgical and dental instruments (see Wijnhoven et al 2009 for a full list of existing medical devices).

The potential for the widespread use of silver-based antibacterial products to result in development of bacterial resistance may be a problem (see below). And whereas, no users of these antibacterial silver devices have reported any problems so far, there is clearly some risk that long-term use may lead to toxic effects, including potentially neurological damage should sufficient exposure occur (Landsdown 2007).

Resistance to silver

The overuse of antibiotics in recent years has led to increased resistance of some bacteria to them. The UN commented that “heavy use of antibiotics in people and animals, encouraged by commercial pressures, risks causing significant antibiotic contamination of the natural environment and consequent development of resistance in communities of non-disease organisms” (United Nations System-wide Earthwatch 2009). The widespread use of nanosilver in consumer and other products may also increase the propensity for bacteria to become resistant to silver.

To date, there are 20 published reports of silver resistance in bacteria however few include data that explains the resistance mechanisms. In 1975 McHugh et al. (as cited by Chopra 2007) described the first instance of a silver-resistant strain of *Salmonella typhimurium* in a hospital burns unit. Other clinical studies identified silver resistance to members of the *Enterobacteriaceae* and *P. aeruginosa* also from burn patients (Chopra 2007).

Resistance to silver can also be induced under laboratory conditions, and “is most easily developed in bacteria with already documented resistance mechanisms to antibiotics, such as methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin- resistant *enterococci* (VRE), enterobacteria with production of extended spectrum beta lactamases (ESBL), multiresistant *Pseudomonas aeruginosa*.“ (Melhus 2007).

It is presently unclear, under clinical conditions, how severe the resistance development is to silver products. There are currently no standardized methods to determine bacterial susceptibility to silver. Additionally the wide variation in clinical silver product delivery systems and silver formulations makes it difficult to compare them. For example, silver-based dressings release different amounts of silver ions in different ways via different materials. Clearly “dressings that release low levels of silver ions are likely to be more dangerous in terms of selection for resistance, especially if the silver ion concentration is sub lethal. Faster acting dressings will inevitably present less risk because organisms are more likely to be killed, thereby eliminating possibilities for enrichment of the resistant population through growth and division, especially in the context of mutational development of resistance” (Chopra 2007). At the same time if the dose released by the dressing is too high, greater toxicity risks for the patient may be present.

3. Elemental, ionic, colloidal or nanosilver?

There is considerable confusion in non-scientific literature and amongst producers of various silver products about different types of silver, their definition and properties (especially with respect to toxicity to humans and the environment, fate in the environment, etc.). At times it is unclear whether industry's ambiguity in marketing claims about the form of silver ingredients is used to confuse and misinform consumers or whether its lack of understanding is genuine. Kulinowski (2008) provides an excellent review of the different types of silver and some of their characteristics (see table 1 for an expanded version).

Silver biocide products may contain silver in ionic, colloidal or nanoparticle form, and to complicate things further, these may either be in free or bound form. Irrespective of the form of the silver used, a major characteristic that will affect the bactericidal effect of the silver is the concentration of silver ions released. In this context nanosilver affords special consideration as it provides a reservoir for continuous silver ion release. There are also preliminary indications that nanosilver may increase the impact of the toxicity of ionic silver and/or be toxic on its own. Several mechanisms for this have been proposed, including silver nanoparticles acting as Trojan horses to enter the cell and then release silver ions to destroy cell content, or nanosilver particles clumping on the outside surface of cells and disrupting cell behaviour (Lubick 2008, Navarro et al. 2008).

Ionic silver is toxic to bacteria and to some degree to fungi and viruses – that is why it is a very effective biocide. To claim, as some producers do, that ionic silver has been used safely for this purpose for thousands of years and that its growing use in consumer products will have no detrimental effect on the environment is untrue. The scale of use of silver, and release of waste silver into the environment is increasing dramatically. An unprecedented number of nanosilver consumer products used by perhaps millions of people will leach into the environment and because of the quantity released alone cause potential damage to waterways, fish and other aquatic organisms, as well as soil organisms. Silver ions cannot distinguish between "good" and "bad" bacteria, and excessive use of silver will harm the environment, animals and humans. Finally, if sufficient quantities of silver are present in the environment, they may end up accumulating in the food chain.

Colloidal silver

Colloidal silver is a special case in point. Many extravagant, unfounded and/or dubious claims have been made regarding the properties of colloidal silver: that it protects against werewolves, guards against respiratory illnesses, and can be used to treat many illnesses including skin cancer. Some regulatory agencies (e.g. FDA in the U.S., TGA in Australia) have prohibited producers of colloidal silver products from making claims of medical effectiveness. However colloidal products still remain on sale and numerous manufacturers worldwide continue to claim medical effectiveness. Regulators have warned that apart from potentially causing a permanent blue-grey discoloration of the skin and/or deep tissues (argyria) in humans, its use especially in food-producing animals, may result in silver residues in milk and/or meat (FDA 1997). The consumption of these products may in turn be dangerous to human health. In December 2008 the European Food Safety Authority (EFSA) decided that there was insufficient evidence to determine the safety of nanosilver hydrosols used in food supplements. EFSA proclaimed that it was "unable to assess the safety of silver hydrosols for nutritional purposes as a source of silver in food supplements and the bioavailability of silver from this source." (EFSA 2008)

We believe that all over-the-counter colloidal silver products should be immediately withdrawn from the market and their sale should be banned (unless approved as a drug by the appropriate regulatory agency).

Table 1: forms of silver and their approximate size, charge

Type of silver	Approx size	Attributes
Elemental/metallic (a single atom)	0.288 nm	Not found as single atom in nature, normally found as an aggregate. Elemental silver has no oxidation state.
Silver ion (Ionic)	0.258 nm	Toxic, may dissolve in water, may have positive or negative charge.
Nanosilver	1-100nm	May release ions and/or be toxic on its own.
Colloidal	1-1000nm	A mixture of different sized particles, suspended in fluid, may contain nano particulate silver or silver ions or both.
Inorganic silver compounds/silver salts e.g. silver chloride, silver oxide	depends	Not easily dissolved, can be nanosized.
Organic silver compounds e.g. silver proteins	depends	Covalent, almost impossible to dissolve.

Source: adapted from Kulinowski 2008.

Dissolved form
- The dissolved form of silver is silver ions.
- Dissolved ionic silver is the chemically and biologically most active form of silver and is highly toxic in this form.

Bound form
- Silver can be bound to larger particle, sediment, colloidal particle, or macromolecule.

Nanosilver
- May be present in colloidal form, dissolved in water or as a suspension in the form of silver chloride.
- Nanosilver particle can be produced using physical or chemical methods.
- Because of their very small size nanosilver particles can potentially pass through biological membranes and reach more and different organs and tissues in the body.
- Nanosilver acts as a reservoir for the delivery of dissolved silver ions, which have a strong bactericidal effect.
- Nanosilver particles have also been shown to be toxic independent from released silver ions.

4. Silver nanoparticles may be toxic to a variety of organisms

The lack of studies investigating human toxicity from exposure to nanoparticles and their entry portals and interactions with the body make risk assessment for these materials challenging. Nanosilver is no exception, hence a review of studies on nanoparticle silver asks that more in-depth research be performed before “people rush to indulge into the nanosilver boom” (Chen et al. 2007).

Nanoscale silver may have access to our bodies in a number of ways, including through the respiratory tract, gastrointestinal tract, skin (dermal), and also the female genital tract, which can come into contact with nanosilver particles through women’s hygiene products available on the market. In order to confirm the long held belief that silver in very small quantities was essentially safe to humans, researchers (Ramstedt et al. 2009) investigated the hypothesis that at certain concentrations silver may be relatively safe for mammalian cells but toxic to bacteria. However they found that this ‘safe’ range is extremely small to non existent.

As with many substances at the nanoscale, the toxicity of nanosilver is greater than that of silver in bulk form; silver is comparatively more toxic than other heavy metals when in nanoparticle form (Bradich–Stolle et al. 2005). Physical characteristics of nanomaterials, such as their size, shape and surface properties, can exert a toxic effect that goes beyond that associated with their chemical composition (Brunner et al. 2006). For instance, Hussain et al. (2005) demonstrated that nanoparticles of silver produce reactive oxygen species (ROS), which may result in oxidative stress-mediated toxicity. Production of ROS, highly reactive molecules which include free radicals, can interfere with cellular metabolism, cause inflammation and damage proteins, membranes and DNA. Reactive oxygen species production is a key mechanism for nanomaterials toxicity (Nel et al. 2006).

The most common nanosilver toxicity studies focus on bacteria and to a lesser extent on complex animal species such as fish, rats, mice, and quails. *In vitro* studies demonstrate that nanosilver is toxic to mammalian liver cells (Hussain et al. 2005), stem cells (Braydich-Stolle et al. 2005) and even brain cells (Hussain et al. 2006). A study on bioluminescent bacteria showed that nanosilver particles can disrupt cell membranes resulting in cell toxicity and cell deformation (Hwang et al. 2007). Table 2 provides a summary of studies relating to animal nanosilver particle toxicity.

A number of researchers have shown that nanosilver particles can destroy the ability of bacterial DNA to replicate (Berger 2007) or can damage DNA. Ahamed et al. (2008) used two lines of mammalian embryonic cells to investigate the effect of uncoated and coated silver nanoparticles (25nm) on DNA. Irrespective of being coated or not, both types of silver nano particles induced cell death and caused DNA damage. However the polysaccharide coated particles caused more severe damage, perhaps due to different surface chemistry and decreased agglomeration.

The mechanism of (nano)silver toxicity is still unclear

All forms of silver can release silver ions, including silver compounds and silver salts. Even elemental silver has a biocidal effect, as silver ions are formed at low concentration on its surface. The higher the concentration of available silver ions (the number of silver ions in solution), the higher the reactivity and hence the biocidal effect. The actual mechanism of toxicity of (nano) silver is still unclear and may depend on the organism and the type of silver involved (see table 2). However in terms of nanosilver (Yang et al. 2009) concluded that

> **"one cannot exclude the possibility that the silver nanoparticles interact with the genetic DNA inside the cell and might also cause … higher mutation. …These results seem to be strong enough to call for a review of the long-term biohazard issues of silver nanoparticles."**

Table 2: examples of proposed mechanisms of (nano) silver toxicity

Effect of toxicity	Reference
DNA loses its ability to replicate. Brindha et al. (as cited by Yang et al. 2009) implied that replication errors in general may play a part in inducing cancer.	Feng et al. 2000, Yang et al. 2009
Proteins essential to ATP become deactivated	Yamanaka et al. 2005
Membrane bound enzymes become deactivated, leading to structural change and cell death	Sondi and Salopek-Sondi 2004
Inhibition of a respiratory enzyme, accelerates the generation of oxygen species and hence damages or kills the cell	Pal et al. 2007
Molecular mechanism: increased silver ions (even at very low concentrations) can penetrate the cell membrane because they disturb the cell wall proteins, once in the cell this leads to loss of energy and cell death.	Dibrov et al. 2002

Nanosilver toxicity may be size and shape dependent

Silver nanoparticles are typically used in the size range of 1-50nm. Nanoparticles of silver < 10 nm can penetrate the cell wall (Morones et al. 2005). A number of researchers have now shown that different sized silver nanoparticles have different toxicities (for example Carlson et al. 2008, Morones et al. 2005, Elechiguerra et al. 2005) For instance, Elechiguerra et al. (2005) showed that interaction with the HIV-I virus is highly size dependent, with silver nanoparticles in the 1-10nm range exclusively attaching to the virus and consequently inhibiting it from binding to host cells.

There are indications that the toxicity of silver nanoparticles may exceed the toxicity of the most toxic silver compound (Pal et al. 2007; Elechiguerra et. al. 2005). In their study of *E. coli* bacteria, Sondi and Salopek-Sondi (2004) found that nanosilver damaged and pitted the bacteria's cell walls and accumulated in the cell wall, leading to increased cell permeability and ultimately cell death. *E. coli* is often used as a model for gram negative bacteria, suggesting that these results could be more broadly relevant.

Silver nanoparticle toxicity may also be shape dependent. Pal et al. (2007) speculated that this may be due to the increase in effective surface areas as a result of the different flat areas that together make up the shape of the particle (also known as facet areas), even though the surface area is notionally the same. Different facet types appear to affect the reactivity of the particles. Bacterial inhibition also critically depends on the concentration of nanosilver particles present, as well as initial bacterial numbers.

Table 3: a sample of *in vitro* experiments showing toxicity of nanosilver to mammalian cells

Type of cells	Effect of nanosilver	Reference
BRL 3A rat liver cells	▪ Mitochondrial function, an indicator of energy available to the cells decreased ▪ lactic hydrogenase (LDH or) function increased significantly in cells exposed to silver nanoparticles at 5–50 µg/ml, indicating cell death and reduced cell metabolism	Hussain et al. 2005
Neuroendocrine cell lines (an *in vitro* model for brain cells)	▪ Mitochondrial activity was reduced at doses ranging from 10 to 50 lg/ml compared to untreated cells. ▪ Cells decreased in size and became irregular in shape ▪ Depleted dopamine at high and cytotoxic rates	Hussain et al. 2006
Mammalian germline stem cells	▪ Silver nanoparticles were more toxic than other metal oxides ▪ Significantly reduced mitochondrial function and interfered with cell metabolism leading to cell leakage ▪ Indicates the potential of these particles to interfere with the male reproductive system.	Braydich-Stolle et al. 2005
Rat alveolar macrophage cell lines (a model for toxicity after inhalation)	▪ After inhalation for 24 hours to hydro-carbon coated silver particles size-dependent toxicity, probably mediated through oxidative stress was confirmed	Carlson et al. 2008

Nanosilver is toxic to mammalian cells

In addition to being an effective bactericide, silver nanoparticles are also toxic to mammalian cells *in vitro* (in test tube studies), including rat liver cells (Hussain et al. 2005), cultured neuroendocrine cell lines as a model for brain cells (Hussain et al. 2006), mammalian germline stem cells (Braydich-Stolle et al. 2005), and rat alveolar macrophage cell lines used as a model for toxicity after inhalation (Carlson et al. 2008). See table 3 for more detail on these papers.

Braydich-Stolle et al. (2005) found increased toxicity of nanosilver particles to mammalian germline cells. They pointed out that while silver nanoparticles are proposed to be used as antimicrobial agents in bone cement or other implantable devices, they may in fact be toxic to the bone-lining cells and other tissues (Braydich-Stolle et al. 2005). Furthermore, the significant toxicity of silver nanoparticles to mammalian germline stem cells indicates the potential of these particles to interfere with the male reproductive system.

Silver can be toxic to humans

In vivo, silver nanoparticles can induce rat lung function changes, along with inflammation, at much lower dose concentrations when compared to standard size particles (Sung et al. 2008). But what are their effects on human bodies?

While readily absorbed into the human body through food and other means, silver is not an acknowledged trace element, but appears not to cause any major diseases. Research into the release of silver ions from medical devices (such as catheters) has shown that excess silver ions will form protein silver complexes, which are deposited into the liver, kidney, spleen, lung, brain and skin (Landsdown 2007). Agyria, grayish discoloration of the skin caused by accumulation of silver in human skin, is the most well known clinical condition resulting from the accumulation of silver in blood and tissues. A 2006 study on a 17-year old boy who had suffered burns on 30% of his body showed than nanosilver coated wound dressings caused liver toxicity and argyria-like symptoms (Trop et al. 2006). Agyria may also occur as a result of prolonged occupational exposure in particular industries e.g. metallurgy, mining photography, where blood silver levels have been observed to be twice as high as in unexposed individuals. There are some indications that in severe cases agryia is accompanied by behavior changes and neuromuscular abnormalities as well as tiredness, headaches and nervousness. Eye problems have also been identified (Landsdown 2007). Clearly workers in industries using silver or increasingly nanosilver are most vulnerable to occupational exposure and strict occupational health and safety standards must be implemented and their compliance subsequently monitored.

It is presently not known how to determine if the human central nervous system is vulnerable to silver toxicity and at what dose. While there is some evidence that silver may cross the blood brain barrier (at least in rats), the evidence is inconclusive and silver deposits do not appear to result in detectable neurological damage (Landsdowne 2007). There is at least some indication that nanoparticles can unintentionally pass from the nasal mucosa to the brain via the olfactory bulb, where they are capable of causing an inflammatory response (Oberdörster et al. 2004). Getting nanoparticles to intentionally cross the blood brain barrier for medical purposes is of course an active field of research.

Colloidal silver and silver nitrate preparations are available over the counter in many countries and used for treatment of mucus, membrane infections and infective rhinitis. They often claim to aid the recovery from many other serious and chronic diseases. However there is plenty of evidence that such preparations are dangerous, may cause argyria, have been implicated in neurological problems and may even result in death (Landsdown 2007). Table 4 provides a summary of reported cases.

Table 4: Dangers of over the counter colloidal medicine (summarized from Landsdown 2007)

Preparation used	**Disease treated**	**Observed effect**
Silver coated protein containing vasoconstrictor	Allergic rhinitis	Sever argyria
Silver containing nose drops over 2-3 years	Unknown	Death
Chronic administration of silver containing nose drops	Unknown, but possibly rhinitis	Sever argyria, silver deposits also in liver, kidney, arteries, pituitary and choroids plexus
Colloidal silver (homemade), used for 4 months	Prostate cancer	First irreversible neurological toxicity, then coma and finally death.
Silver nitrate	Tongue ulcers	Argyia, manic depression, died 6 years later from aortic aneurism
Unknown silver preparation for 18 years	Unknown	Argyia , died of cardiac failure, probably due to long-term silver consumption

5. Effects of silver and nanosilver on the environment

Fate and effect of silver in the environment

Silver does not occur commonly in the environment, but may be released into it naturally through weathering or rain. Silver may be present in a number of oxidation states from monovalent to trivalent. The latter is unstable in aquatic environments. The monovalent form of silver is normally found bound with sulphide, bicarbonate or sulphate or chlorides and sulphates complexes. Silver salts such as silver nitrate (AgNO3) and silver chloride (AgCl) are readily soluble in water (Wijnhoven et al 2009).

The background concentration of silver e.g. how much silver is naturally occurring is extremely low and are according to Louma (2008) reported in the trillion (ng/l range). Typical concentrations in open oceans are 0.03–0.1 ng/l (Ranville and Flegal 2005 as cited by Luoma 2008). In the 1970/80's this figure rose to 189 ng/l in the San Francisco Bay area, when silver pollution from industry was increased. Improved recycling and sewage facilities saw this level drop back to 2–8 mg/l (Luamo 2008).

Environmental conditions such as organic matter content, concentration of sulphide and pH play a large role in the fate of silver in the environment. Water characteristics such as hardness, natural organic matter, chloride, sulphides and sulphates all result in a lowering of silver toxicity. Mobility of silver increases under conditions of increased oxygenation and acidification. Silver may largely be immobilized as a result of sorption or binding to particles (predominantly organic matter) or when high concentrations of sulphides are present and/or precipitated in the form of silver sulphide. However while much of the free silver may bind to soil and particles, silver may also form colloids and hence be transported and dispersed.

Currently little is known about the fate of silver nanoparticles in the environment. However depending on their surface structure and shape, silver nanoparticles may have different reactivity. Silver nanoparticles also act as a reservoir of silver ions and may release Ag+-ions continuously.

Silver is after mercury the most toxic metal for aquatic organisms. The US EPA views silver in surface waters as a "priority pollutant"(Luamo 2008). In lower concentrations than that for other heavy metals (Bradich-Stolle et al. 2005), silver is toxic to fish, crabs, algae and other water plants, as well as nitrogen fixing bacteria (Albright and Wilson 1974). Of special importance may be the effect of silver on lithothrophes, organisms that play an important role in the digestion of inorganic material and creation of soils. However most scientific studies into silver toxicity have used dissolved silver (e.g. silver ions) and few conclusions can be drawn from them in regards to nanosilver toxicity.

The potential for silver toxicity in the environment revolves around its biocidal and catalytic effects on a variety of organisms (including micro organisms in the soil such as bacteria, earthworms and/ or fungi), the ability to bind to other toxic substances, toxicity effect on groundwater, air pollution, accumulation along the food chain, differential effects in saltwater versus freshwater as well as yet unknown effects.

How much nanosilver will end up in the environment?

Prior to the development of nanosilver, the source of most silver entering wastewater treatment plants was photographic, printing and plating industries (Neal 2007). In recent years, nanosilver has begun to present an increasing, but yet difficult to quantify exposure to the environment. Using a computer model, Blaser et al. (2008) analysed the risk to freshwater ecosystems of silver nanoparticles incorporated into textiles and plastics and predicted that in the future 15% of the total silver released into water in the European Union would come from biocidal plastics and textiles. Most of the silver is predicted to end up as sewage sludge and at least some of it may be spread on agricultural fields. The actual amount of silver predicted to end up in the European environment is summarized in Table 5.

Table 5: Predicted silver in the environment in Europe (assumed population of 469 million)

Location of silver	Total amount of silver	Amount of biocidal silver
Natural waters	20-130 tons	20 tons
Terrestrial ecosystems	80-190 tons	29 tons

Source: Blaser et al. 2008

While Blaser et al. (2008) were unable to perform a full risk assessment due to lack of toxicity data and uncertainty about the environmental chemistry of silver, they did not rule out a risk to freshwater ecosystems, in particular sediments. The effect of nanosilver products ending up in solid waste and landfills is also of concern, as microorganisms digesting the waste may be impaired.

Silver may affect important bacteria in sewage treatment plants

The disposal of biocidal silver products into waste water raises a number of concerns as the resulting sewage sludge may be used on agricultural soils, disposed as solid waste in landfills or incinerated. While silver applied to soils may stay in the top layer of the soil, land-filled sewage sludge may result in the silver leaching into subsoil and groundwater.

Silver toxicity in water is determined by the concentrations of silver ions. This is currently typically low in wastewater treatment systems and in the natural environment, partly due to silver's tendency to form strong binds with various ligands such as chloride, sulphide, thiosulphate, and dissolved organic carbon. Nanosilver may have a variety of fates in wastewater, including being converted into ionic form, forming a complex with other ions, molecules, or a molecular groups, agglomerating (Limbach et al. 2005; Zhang et al. 2008) or remaining in nanoparticle form (Blaser et al. 2008).

Wastewater treatment relies on heterotrophic micro-organisms for organic and nutrient removal, while autotrophic micro-organisms play an important role in nitrification. Choi et al. (2008) evaluated the effect of silver nanoparticles, silver ions and silver chloride colloids on heterotrophic and autotrophic growth and found that nitrifying bacteria are especially susceptible to inhibition by silver nanoparticles. Silver ions may inhibit the enzymes used by nitrifying bacteria (Ratte 1999), block DNA transcription and interrupt bacterial respiration and energy creation (Kumar et al. 2005).

Silver nanoparticles' inhibition of autotrophic bacterial growth was almost twice that of silver ions and colloids (Choi et al. 2008). Heterotrophic bacteria in contrast were more susceptible to silver ions versus nanosilver particles and silver chloride colloids. Choi et al. (2008) suggested that the accumulation of silver nanoparticles may have detrimental effects on the activities of micro-organisms in wastewater treatment.

> **"The results of nanosilver toxicity to environmentally sensitive nitrifying micro-organisms suggest that stringent regulations of silver nanoparticles entering Waste Water Treatment Plants are necessary. Nitrifying micro-organisms involved in nitrification are critical to biological nutrient removal in modern wastewater treatment."** (Choi et al.2008).

Both silver and nanosilver are toxic to aquatic organisms

Aquatic organisms differ significantly in their sensitivity to silver. The accumulation of silver and its toxicity depends on and varies with environmental conditions such as salinity and pH. Research into the toxicity of nanosilver to aquatic organisms is still limited and tends to focus on a small number of key species – zebra fish, invertebrates, some algae. Toxicity of silver is a result of silver ions and depends on their concentration. Silver ions reacts with thiol (a molecular group that includes a bonded sulphur and hydrogen atom (-SH) in biomolecules). For instance in fish silver ions block the active absorption of sodium and chlorine as well as causing sublethal effects (Hogstrand & Wood, 1998). In water fleas silver ions disturb ion regulation via a competitive inhibition of Na+ uptake (Bianchi & Wood, 2003).

The freshwater invertebrates *Ceriodaphnia dubia* and *Daphnia magna* are not only standard testing organisms for aquatic toxicity testing, but they are also among the most sensitive organisms to silver. Naddya et al. (2007) showed that chronic exposure of *D.magna* and *C. dubia* to silver resulted in decreased growth and reproduction (8.80 and 2.65mg dissolved silver/l), and complete mortality at higher levels.

It is well known that silver ions in the natural environment tend to form stable complexes both inorganic (e.g. chloride, thiosulphate and sulphide) and organic (monomeric thiols and natural organic matter). Silver thiosulphate was thought to be relatively inert. However Hiriart-Baer et al. (2006) showed that silver thiosulphate complexes can be transported across cell membranes in *Chlamydomonas reinhardtii* and *Pseudokirchneriella subcapitata* (two freshwater algae species), and that this leads to increased toxicity.

Navarro et al. (2008) investigated the toxicity of silver nanoparticles versus silver ions to *Chlamydomonas reinhardtii.* Based on total silver concentration the silver ions appeared to be 18 times more toxic than the nanosilver particles, however closer inspection revealed that when compared as a function of silver concentration the silver nano particles appeared more toxic than the silver ions alone. The researchers reasoned that silver nanoparticles contributed to the overall toxicity of silver to the algae by providing a continuous source of silver ions

Silver bioaccumulates strongly in saltwater

Silver can readily bioaccumulate in aquatic organisms, only mercury bioaccumulates more strongly. How much silver can accumulate in aquatic organisms depends, apart from the actual organisms, on a number of environmental factors such as salinity, water temperature, dissolved oxygen, turbidity, and presence of other compounds may have an influence on bioaccumulation. Depending on their age, size, sex, reproductive stage, general health and metabolism, oysters, gastropods (snail, slugs) and arthropods (insects, crustaceans) can all bioaccumulate silver. Algae also accumulates silver, but to a lesser extent than marine mollusks. (Wijnhoven et al. 2009).

Silver accumulates especially strongly in saltwater. Rapid uptake of silver in seawater has been observed in phytoplankton and marine invertebrates, even when few free silver ions are present. Phytoplankton (the microscopic plants at the bottom of the oceanic food web) bioconcentrate silver to an astonishing extent. Concentrations of silver in phytoplankton have been 10,000 to 70,000 times higher than the concentration of silver in the surrounding water. As many of these organisms are eaten, the silver is then passed up the food chain (Luamo 2008).

Silver ions and nanosilver are both toxic to fish

Silver ions are known to be one of the most toxic metals to freshwater fish, however their effect is often mediated by a variety of agents (e.g. chloride) present in water (Grosell et al. 2000). Silver ions are the most potent gill toxicant in freshwater fish.

Nanosilver particle toxicity appears to be independent from silver ions. Griffitt et al. (2009) found that when zebra fish were exposed to nanosilver particles rather than silver ions, the silver level in their gills increased. Gene expression proofing suggested that the silver nanoparticles interacted with the gills in a different manner than soluble silver particles and hence the observed effects were not due only to silver ions only.

Silver nanoparticles administered *in vivo* to zebra fish embryo increased deformation rates and ultimately led to death. Individual silver nanoparticles were found inside embryos at each developmental stage (Lee et al. 2007). This is one of the few available *in vivo* studies to observe passive diffusion of nanoparticles, and points to the severe consequences that the release of large amounts of silver nanoparticles may have, if the nanoparticles remain unchanged when reaching aquatic environments. A further recent study on zebra fish found that nanosilver particles can also induce altered physiology, including the degeneration of body parts and an increase in mortality and hatching delay (Ashrani et al. 2008). The research concluded that silver nanoparticles induce a dose-dependent toxicity in zebra fish embryos, which impacts normal development. They recommended that the release of untreated silver nanoparticle waste in the environment should be restricted.

Silver can disrupt key soil microbial communities

Information on the toxicity of terrestrial and sediment organisms is limited, but is slowly being investigated. Again toxicity appears to be dependent on physico-chemical soil properties and sediment properties.

There is currently very little research on the effect of silver nanoparticles on soil microbial communities *in situ*, that is, in real soils. But *in situ* studies have demonstrated that silver, even in larger particle form, inhibits microbial growth below concentrations of other heavy metals (Murata et al. 2005). It is especially toxic to heterotrophic (ammonifying/ nitrogen fixing) and chemolithotrophic bacteria. Chemolithotropic bacteria belong to the lithotropic family of microbes and consume inorganic material. These organisms liberate many crucial nutrients, and are essential in the formation of soil. Ratte (1999) showed that silver ions inhibit enzymes needed for nitrifying bacteria.

The toxic effect of silver on bacteria also appears to disrupt denitrification processes, with the potential to cause ecosystem-level disruption (Throback et al. 2007). Denitrification is a bacteria-driven process where nitrates are converted to nitrogen gas in some soils, wetlands and other wet environments. For example, denitrification bacteria play an important role in removing nitrate from water contaminated by excessive fertilizer use. Denitrification is important because excess nitrates reduce plant productivity, can result in eutrophication (an unhealthy increase in nutrients) in rivers, lakes and marine ecosystems, and are a drinking water pollutant.

Nematodes are widely found in soils and play a critical role in the soil food web. Their functions include primary production, decomposition, energy flow, and nutrient cycling. Nematode abundance also serves as a useful indicator in natural ecosystems to the presence of soil pollutants and ecological disturbances. Several toxicity tests have indeed been developed for this purpose, but Wang et al.'s (2009) study was the first to investigate the effect of metal oxide nanoparticles on nematodes (*C.elegans*). They found that both nanosilver particles and bulk silver were toxic to nematode and resulted in impaired growth and reproductive ability. Dissolved ions were not sufficient to explain the toxicity; nanoparticle dependent toxicity was observed.

The persistence of nanomaterials and their potential for bioaccumulation is poorly understood, however early studies suggest that micro-organisms and plants may be able to produce, modify and concentrate nanoparticles that can then bioaccumulate (or even biomagnify) along the food chain (Tran et al. 2005). The impact of nanomaterial exposure on plant growth remains largely uninvestigated, however high levels of exposure to nanoscale aluminium have been found to stunt root growth in five plant species (Yang and Watts 2005). No such studies have been performed on silver nanoparticles.

Soil organic matter (SOM) binds silver strongly and hence ensures limited controlling cycling, mobility, and sorption into soils. For instance, both humic and fulvic acids have been shown to retain up to 30 mg/kg of silver. While biologically available silver may only be 5% of total silver, in contaminated soils the available silver may be enough to be toxic to soil microbes (Hund-Rinke 2008). The silver content in soil varies, depending on whether it is impacted by industry contamination (2.2 mg/kg to 44 mg/kg) or not (<1 mg kg; Jacobson et al. 2005). However the state of a particular soil is not static and any changes in use, e.g. fertilizers or unseasonable rain, can result in a reduction in pH (< below 4) and hence can increase silver mobilization. Jacobson et al. (2005) showed that organic matter content is a dominant factor in silver sorption.

Silver also shows a strong reaction to anions, especially sulphides, resulting in a general immobilization of silver in wastewater streams and surface waters. However little is known about the behaviour of silver nanoparticles, especially in terms of mobility and the formation of agglomerates. An important aspect in this context is that silver Nan particles provide a reservoir of silver ions, which are continuously released.

In the context of sustainable soil protection Hund-Rinke et al. (2008) point to the fact that:

> **"…the disposal of persistent substances such as silver should be excluded, since they will not be degraded, but accumulated. Changing environmental conditions may result in undesired consequences, or adverse effects may be detected when new knowledge will be available."**

6. Regulatory issues

As with all nanomaterials, governments worldwide have been reluctant to address the regulatory gaps surrounding these new materials and technologies and to take a precautionary stance when permitting introduction of nanoproducts into the market. The general attitude, despite some lip service, has been 'no data, no problem'. This cavalier attitude, hidden under the guise of 'evidence-based' science, may not only adversely affect the end consumer, but also lead to adverse legal implications for secondary manufacturers, who may not be aware that they are using nanomaterials.

Key issues in the area of nanomaterials include the lack of data on their health impacts, potential environmental toxicity, and a continuing inability to monitor any adverse effects. The lack of technologies and protocols for environmental and health monitoring, detection, and remediation is still considerable, despite some efforts being made to address the problem. There is also a lack of coordinated, publicly available information about specific nano chemicals and materials, including where they are being produced and used, and what potential risks may be. There is virtually no labelling of nanoproducts, except for promotional purposes.

Nanosilver and silver products are increasingly available in the form of various food, consumer and medical products, indicating that human and environmental exposure to nanosilver and silver is on the increase. Little is known about the concentrations, size and form of nanosilver in these products and how much of the silver is released.

A full risk assessment of nanosilver, and data relating to exposure as well as the hazard of nanosilver, is needed. For instance, much remains unclear about the absorption of nanosilver and what type of silver is found in the blood, organs and tissues of the organisms studied so far. Future research needs to explore whether and to what extent nanosilver particles themselves enter the body, or whether silver ions originating from nanosilver are absorbed (Wijndhoven et al. 2009). In the interim and the long-term the precautionary principle should be applied and all products containing nanosilver should be removed from the market for the time being.

European Regulation

How nanomaterials should be regulated or whether current regulations cover nanomaterials is a contentious issue in European policy circles. The EU commission strongly believes that current regulation is sufficient (European Commission 2008). At the same time European NGOs and the vast majority of European Members of Parliament (MEPS) strongly disagree. An April 2009 report and subsequent motion (passed by 391 votes in favor and three against, amid four abstentions) on regulatory aspects of nanomaterials by the EU Parliament, disagreed with the commission that current legislation in principal covered nanomaterials and called on the commission to revise relevant legislation such as REACH (Registration, Evaluation and Authorisation of Chemicals), within two years to establish a no data-no market approach and to introduce mandatory labelling of nanomaterials used in consumer products, as well as a number of other suggestions (Schlyter 2009). In two other recent votes, MEPs also backed revisions of the cosmetics and novel food directives to cover nanomaterials.

There are a number of European regulations and directives that are and could in principle be relevant and applicable to the regulation of silver and in particular nanosilver products. Principally, silver and nanosilver fall under REACH (EU 1097/2006), unless another specific use is covered by another specific regulation, as is the case for a number of nanosilver uses. REACH requires all chemicals with a tonnage of greater than one ton to be registered. This may include both macro and nano-form together. Data sets must be supplied for particular uses and hence the EU could in principle demand nano specific tests, however in practice this whole area is still shrouded in uncertainty, as there are no clear guidance documents specifying when and what tests are to be used.

EU pesticide and biocide regulation needs to cover nano-formulations

Products covered by the EU Pesticides and the EU Biocides Directive (Directive 91/414, Council Directive 79/117, Regulation 396/2005 and Directive 98/8/EC, Directive 76/769/EEC) need to be assessed and authorized before use. As many pesticides are a source of surface and ground water pollution, they are also subject to the EU Water Framework Directive. However none of this legislation currently considers nanoscale products, or recognizes nanomaterials to be new substances. Friends of the Earth strongly recommends that all new pesticides and biocides and any new nano-formulations of existing products should require additional safety assessment before their authorization for commercial use.

Under the biocide directive, silver is considered a 'grandfathered' substance, which means that it can be used, as long as the product is registered and until a decision has been made about the chemical. Decisions are not expected until 2014 (originally 2010, but extended), by which time the biocide directive will apply in full.

If the intention is that the active ingredient will be used as a pesticide, i.e. an agricultural use, then the product falls under the pesticides directive (91/41 or 79/117). While these regulations make no distinction between a chemical's macro and nano-form, silver is currently not a permitted chemical for pesticidal use. A legal loop hole exists for so called "plant tonics". While they have to be registered on a national level, there are no requirements for proof of efficacy, nor a need to show what effect they may have on humans or the environment. Indeed there are examples of nanosilver tonics on the market in Germany and other European countries. It is questionable, given their purpose is to act as a pesticide, whether they should really be permitted for sale.

The cosmetics directive may cover some forms of nanomaterials

Cosmetics fall under the Cosmetics Directive (76/768 EWG). Colorants, preservatives and UV filters must be on a positive list. Other ingredients can be used as long as they are not on a negative list (e.g. ingredients which are explicitly prohibited from use in cosmetics). Silver is neither listed on the negative list, nor on one of the positive lists, meaning that under current regulation it may be used in cosmetics, unless used as preservative, UV-Filter or colorant.

However the Cosmetics Directive is currently to be converted into a regulation, meaning that it will have immediate applicability to all EU member states. In March 2009 the European Parliament adopted the new regulation in a first reading agreement. The Parliamentary decision still has to be confirmed by the European Council. However, this is regarded to be only a formality in this case, as the Council has already indicated its support for the draft adopted by the Parliament. The new regulation envisages some nanospecific directions e.g. the need to disclose nano-sized ingredients on a product's ingredients list and mandatory notification for products containing nano-engineered materials. In the case that the Commission has doubts over the safety of a specific nanomaterial, it can demand the submission of nano-specific safety data which would then be reviewed by the Commission's Scientific Committee on Consumer Safety (SCCS).
The definition for nanomaterials as "an insoluble or biopersistant" and intentionally manufactured material with one or more external dimensions, or an internal structure, on the scale from 1 to 100 [nanometers]", leaves potential room for manufacturers of certain nanomaterials to escape these rulings. However, as an insoluble nanomaterial, nanosilver should be subject to the nano-speficic provisions in the new regulation.

Nanosilver in food, food packaging and food contact materials requires regulation
The European Union regulates food and food packaging at a European Union level, and once agreed the directives and regulations are implemented on a national basis. REACH (Registration, Evaluation and Authorisation of Chemicals), the EU's chemical regulation explicitly excludes food and most food packaging, although some chemicals involved in creating packaging may come under this legislation.

The general safety article of the EU Food Law Regulation 178/2002 requires all food for consumption to be safe. As an overarching safety article, this should apply to all nanofoods and food packaging containing nanomaterials. However, as noted above, so far European regulations recognize the critical issue of particle size. If a substance has already been approved for use in bulk form, there is no regulatory trigger to require new safety assessment before a particle is used in nano-form in food ingredients, additives or packaging. This means that in practice many nanomaterials could be used as additives in foods and food packaging without legally requiring new safety assessment.

This could change with the new Novel Food Directive, which is currently under revision. In March 2009 the European Parliament voted in first reading for a draft directive that would require mandatory nano-specific safety testing and labelling of nano food products. As methods for nano-specific safety testing of food products still have to be developed, this would mean a *de facto* moratorium for nano food products. In a recent report, the British Royal Commission on Environmental Pollution (RCEP) estimated that it might take up to 15 year to develop test protocols for the safety assessment of nanomaterials (RCEP 2008). The draft novel food directive favoured by the Parliament will now be discussed in the Council before going into a second reading, which is likely to take place in late 2009.

EU food packaging regulation
EU Food Packaging Regulation (EC 1935/2004) covers all materials that come into contact with food such as a packaging, bottles (plastic and glass), cutlery, domestic appliances and even adhesives and inks for printing labels. Similarly to the regulation on novel foods, it requires the establishment of a positive list of authorized food contact materials, and an assessment of their potential toxicity or safety. However its weakness is that once again, the failure to identify nanomaterials as new substances means that nanomaterials of substances which are already authorized in bulk form for use in food contact materials will not be subject to new safety assessments.

This regulation also requires that authorized food contact materials must be traceable. The Institute of Food Science and Technology (IFST), the leading European independent professional qualifying body for food scientists and technologists, have argued that "traceability should include a specific reference to the presence of nanoparticles and should, ultimately, enable the relevant safety dossiers for these materials to be accessed" (IFST 2006).

EU labelling laws need to cover nanomaterials and ingredients
EU food labelling laws require the names of most ingredients to be listed on product labels, and in some specified cases their physical condition or treatment they have undergone. To ensure the capacity for informed consumer choice, the label should indicate if nanomaterials have been used in the food or in the food packaging. Friends of the Earth recommends regulatory amendments to ensure that consumers can establish if nanosilver or other nanomaterials have been added to food packaging or food contact materials, as this is envisaged by the draft novel food directive as it was adopted by the EU Parliament in first reading, but may still be subject to amendments.

Australian regulation leaves many nano-products effectively unregulated

As with the EU and US systems, Australian regulations are primarily focused on "new" chemicals. To date, Australian legislation fails to recognize that nanoparticles present new and often greater toxicity risks than larger particles of the same chemical composition (Bowman and Hodge 2006).

Australia has four national chemicals assessment and registration schemes which cover food, industrial chemicals, pharmaceuticals and agricultural and veterinary chemicals. All of these regulatory agencies may be responsible for products containing silver or nanosilver. The use of industrial chemicals is also regulated at the state and territory level by a range of agencies, including those concerning OHS, environmental, public health, and transport. Additionally the Australian Competition and Consumer Commission (ACCC) is responsible for product labelling in accordance with the Trade Practices Act (see table 6 for a summary).

NICNAS regulates industrial chemicals. If the chemical is included in the Australian Inventory of Chemical Substances (AICS) and the product using the chemical is intended for consumer use then no further product registration is required (unless of course it falls into the jurisdiction of another agency). Silver and various forms of silver are included in the AICS. Fifty eight silver containing chemicals are currently registered with AICS; forms of nanosilver are not mentioned specifically.

Despite most of the above regulatory authorities showing an active interest in nanotechnology and its impact on human health and environment, the Australian government response has been to pretend that current regulations cover all nanotechnological regulatory possibilities. This is despite a government funded regulatory report (Ludlow et al 2007) finding that there are at least six gaping holes in current government regulations regarding nanotechnologies. To give a few pertinent examples of these regulatory holes, NICNAS does not consider nanoscale reformulated existing chemicals as new chemicals. The current threshold for triggering regulatory oversight in relation to new chemicals may be too high and the risk assessment protocols are based on conventional methods and hence may not be suitable. Although FSANZ has introduced some new requirements in relation to nanomaterial food additives, Friends of the Earth believes that these are grossly inadequate to deliver confidence in safety assessment.

In Australia colloidal silver products making therapeutic claims must be registered, but they are widely still available

Since December 2002 colloidal silver products making therapeutic claims must be approved by the TGA. So far no such product has been approved by the TGA. The TGA has on occasion taken action to stop the sale of unapproved colloidal silver products which make therapeutic claims. Water purification substances containing colloidal silver that do not make therapeutic claims are permitted. The TGA made this decision because of the risk of silver toxicity to consumers, the lack of evidence to support therapeutic claims and the risk of bacterial resistance developing (TGA 2009).

Unfortunately despite the TGA tightening rules in 2002, the products are still widely available (often still making therapeutic claims) in health food shops, and misinformation about their (in our opinion) dubious value is published and believed widely. Clearly regulations surrounding these products need to be further tightened and in the opinion of Friends of the Earth they should not be permitted for sale (unless registered properly).

Table 6: Australian regulatory agencies (and associated regulatory acts) with responsibility for nanosilver products

Regulatory Agency	Relevant Act	Comment
Comcare	▪ Occupational Health and Safety Act 1991 ▪ Safety, Rehabilitation and Compensation Act 1998	Workplace safety issues
NICNAS	▪ Industrial Chemicals (Notification and Assessment) Act 1989	Industrial chemicals, including cosmetics
TGA	▪ Therapeutic Goods Act 1989	Therapeutic goods including medicines and medical products
APVMA	▪ Agricultural and Veterinary Chemicals(Code) Act 1994 ▪ Agricultural and Veterinary Chemicals Administration Act 1994	Pesticides and veterinary medicines
FZANS	▪ Food Standards Code	Food and food safety
ACCC	▪ Trade Practices Act	Product labelling
Department of Environment and Heritage	▪ Environment Protection and Biodiversity Conservation Act 1999	Environmental protection e.g. life cycle assessments, bioaccumulation; water, air and land exposure and toxicity, environmental release

Source: adapted from Bowman and Hodge 2006

The U.S. is doing too little to increase nanomaterial oversight

Like the EU, regulation in the United States continues to languish far behind the commercialization curve. While U.S. federal agencies have held public meetings, tried voluntary data programs and published white papers, they yet to engage in any meaningful regulatory activity. Nano-product manufacturers are still not required to identify nanoparticle ingredients on product labels, to conduct nano-specific safety tests on these ingredients, or to submit their products for approval prior to commercialization. No U.S. law or regulation is specifically designed or has been amended to regulate nanotechnology and nanomaterials. The National Nanotechnology Initiative (NNI), the U.S. government's current hub for coordinating federal agencies' nanotechnology research and development funding, has no oversight authority (National Nanotechnology Initiative undated).

Nanotechnology and the already extremely broad swath of commercialized nanomaterials implicate numerous U.S. federal agencies' jurisdiction, including the Environmental Protection Agency (EPA), the Food and Drug Administration (FDA), the Consumer Product Safety Commission (CPSC), and the Occupational Safety and Health Administration (OSHA). A number of laws provide some basis for regulatory oversight of some aspects of nanotechnology's effects on the environment and human health. Nanomaterials like nanosilver products could fall under a number of agency's jurisdictions. See Table 7 for a summary of agencies and laws potentially applying to nanosilver products.

Table 7: US regulatory agencies and regulatory acts with responsibility for nanosilver products

Federal Agency	**Relevant Act**	**Comment**
Environmental Protection Agency (EPA)	▪ Clean Air Act (CAA), ▪ Clean Water Act (CWA), ▪ Toxic Substances Control Act (TSCA), and the ▪ Federal Insecticide, Fungicide, & Rodenticide Act (FIFRA, i.e., the pesticide law)	To protect the environment and also regulate pesticide use
Food and Drug Administration (FDA)	▪ Federal Food, Drug, and Cosmetic Act	The impacts of many nanomaterial products, including drugs, food and food packaging, dietary supplements, medical devices, and cosmetics.
Consumer Product Safety Commission (CPSC)	▪ Consumer Product Safety Improvement Act	Oversees many types of consumer products, but in practice has very little pre-market authority and even less funding
Occupational Safety and Health Administration (OSHA)	▪ Occupational Safety and Health Act	Has in principal authority over workplace health and safety issues, including the manufacturing of nanomaterials and nanoproducts

U.S. government action has been inadequate
Both the EPA and FDA have demonstrated their interest in creating solutions to the current gaps in the regulation and oversight of nanomaterials, but their actions thus far have been wholly inadequate. In 2007 EPA published a nanotechnology "white paper" (EPA 2007a) which was a good summary of nanotechnology's scientific and regulatory challenges but fell short of providing any policy guidance. Then there was EPA's voluntary program adventure under the general chemical law, TSCA. In the summer of 2005, EPA's Office of Pollution Prevention and Toxics (OPPT) began discussions regarding a potential voluntary pilot program for nanomaterials under TSCA, and proposed a voluntary program that fall (EPA 2005). The program would request that manufacturers of nanomaterials submit to EPA basic materials data. Given the then already advancing state of nanomaterial development and commercialization, the EPA voluntary program was sharply criticized by a coalition of consumer and environmental advocacy groups (including Friends of the Earth and the International Centre for Technology Assessment) as "inadequate and inappropriate" for the regulation of nanomaterials (ICTA et al. 2005), who warned that it would only forestall needed mandatory measures. EPA delayed over two years, before in summer 2007 proposing to finally choosing to begin the program, without addressing the concerns raised by the NGO community, who again warned that the program lacked incentives or deadlines for industry participation and that mandatory oversight was urgently needed (ICTA and FoE 2007). The program was finally launched in January 2008 and as predicted the participation was sparse: there were only 29 "basic" submissions, representing less than 10% of the unique nanomaterials EPA estimates are already available, and only four companies indicated they were willing to undertake any additional nano-specific testing (EPA 2009).

With the voluntary program an unmitigated failure, it now appears the new Obama EPA is willing to follow Canada's lead and make its nano-chemical data program mandatory (Pearl 2009). Even if the TSCA program is made mandatory, without further statutory or regulatory change the amount of oversight EPA can provide is limited due to the inherent weaknesses and outdated nature of that law (Davies undated).

The U.S. FDA has followed a similar path of "all talk, no action." FDA held its first public meeting on nanotechnology in the northern hemisphere Fall 2006 (FDA 2006). FDA created an internal task force that drafted a report and recommendations similar to EPA's white paper (FDA 2007). The report provided a good summary of the known science and recognized the fundamentally different challenges and uncertainty that nanomaterials present but failed to recommend any meaningful policy or oversight measures (ICTA 2007). In 2008 FDA held another public meeting on nanotechnology (FDA 2008). FDA also recently promised a new nanotechnology initiative in early 2009 (FDA 2009). This initiative would see the agency collaborating with Texas-based universities to take a closer look at the risks of nanoparticles and what behaviours they demonstrate. While meetings and initiatives are welcomed, at a time when new nano-products are arriving on the market every day, FDA's failure to take concurrent oversight action demonstrates the agency's lack of urgency in protecting the public from the potential health and environmental risks of nanomaterials. In the interim manufacturers are able to bring to market nano-products in many sectors without any pre-market assessment, testing, data or approval by FDA.

No data = no problem = consumer bears the risks
In the US nano-product manufacturers are still not required to identify nanoparticle ingredients on product labels or conduct nano-specific safety tests on these ingredients, or submit their products for approval prior to commercialization.

One of the problems with US food and agrochemicals regulation is that it rests on the principle that an absence of evidence of chemical or product harm, even if very little research has been conducted into its safety, means that the product is considered safe. This has been called the 'no safety data, no problem' approach. This approach places a burden on the community to demonstrate that a nano-product is harmful, before regulators will control its release, for example by requiring manufacturers to conduct new safety testing. This reversal of the burden of proof not only undermines the precautionary principle, it also acts as a disincentive for companies to engage in comprehensive product safety testing.

A further and very serious weakness is that US regulators often focus on the marketing claims of product manufacturers, rather than the actual content of foods, packaging, pesticides, etc. Despite the authority of regulators to regulate products' content, if a manufacturer chooses not to make marketing claims about its product's nano content, there is a real possibility that a product could be treated as nano-free.

US food and food packaging regulation leaves many nano-products unregulated
Food additives and new dietary ingredients in food supplements require "premarket authorization" from the FDA. For this authorization to be granted the FDA requires companies provide their own safety testing data, from which the FDA also specifies the conditions for its use. However manufacturers of food additives can legally market a product if the chemicals have already been approved for commercial use (US Food and Drug Administration 2007). If they have already been approved for use in larger particle form, nanoparticles do not legally require any additional authorization or trigger new safety testing, despite the fact that many may introduce new toxicity risks.

The EPA appears reluctant to use its powers to regulate nano-agrochemicals
The EPA has legal powers to compel nano-agrochemicals manufacturers to provide toxicity data and demonstrate product safety and hence places the burden of proof on the manufacturers (Davies 2007). However the EPA is yet to decide whether or not nano-agrochemicals warrant new safety testing. To date it has not required manufacturers introducing nano-formulations of existing pesticides to submit their products to nanotechnology-specific safety testing.

In early 2007 the EPA announced its intention to regulate as biocides (i.e. a chemicals used to kill micro-organisms) all nano-products, including food packaging and other food contact materials, which contain nano silver and whose manufacturers make claims of antimicrobial action (Acello 2007). However in September 2007 the EPA disappointed many observers when it said it would only regulate the silver ions released from washing machines, and was taking no action to manage the risks posed by the growing number of other consumer products which contain silver nanoparticles (EPA 2007).

US agencies are hampered by limited and often joint authority over products
Nanomaterials like nanosilver products could fall under a number of agency's jurisdictions. For example, with regard to nanomaterial food packaging like nanosilver containers, FDA has joint authority with EPA because of the product's pesticidial properties: FDA regulates the container, EPA the pesticide ingredient itself.

Like EPA, in some cases, FDA is hampered by limited authority. Dietary supplements are one such area. A 2009 report by the Woodrow Wilson International Centre for Scholars Project on

Emerging Nanotechnologies (PEN) looked at nanotechnology-based dietary supplements and their regulation in the United States. PEN found at least a dozen dietary supplements on the market that contain nanoscale silver. The report calls for the United States Congress to “adopt legislation granting the FDA [Food and Drug Administration] the authority to collect additional information about these products and to ensure that they are tested for their effects on human health” (Schultz and Barclay 2009).

Another report from the Woodrow Wilson International Centre for Scholars Project on Emerging Nanotechnologies, entitled *EPA and Nanotechnology: Oversight for the 21st Century*, explains how the U.S. Government is currently incapable of providing necessary oversight regulation for nanotechnology. According to the report, the legal frameworks within which the EPA and the FDA operate and which could potentially used for regulating nanotechnology are deficient and incapable of doing so. The report outlines numerous steps that Government has yet to take in order to protect the public, workers, and the environment from potentially hazardous nanotechnology (Davies 2007).

NGOs are demanding action on nanosilver products

In 2008 a non-profit coalition, lead by ICTA, submitted a legal petition (ICTA 2007), to the EPA, on the health and environmental risks of nanosilver products (ICTA 2008). The 100-page petition for rulemaking and 500-page supporting administrative record requested that the EPA regulate nanoscale silver as a pesticide under its pesticide authority, which would require nanosilver products to undergo pre-market approval by EPA (ICTA 2008). Using this authority EPA can also require manufacturers to submit nano-specific testing data. No products can be approved unless they are found by the agency not to create an unreasonable risk to the environment. If any products are approved they must be labelled and can be limited in use approval. The petition also demanded EPA assess the health and environmental impacts of these materials under other health and environmental laws, such as the Food Quality Protection Act (FQPA), the National Environmental Policy Act (NEPA) and the Endangered Species Act (ESA). The petition included a product appendix of nearly 300 nanosilver products currently on available in the U.S. (ICTA 2008). Finally the petition demanded EPA immediately stop the sale of those products currently available until and unless it approved them as pesticides.

EPA opened a public comment period on the nanosilver legal petition in the northern hemisphere Fall 2008 (EPA 2008), then extended the comment period to March 2009 (EPA 2009). Over 15,000 public comments were filed in support of the petition. EPA has yet to make a decision, but initial indications are that the agency will grant the petition and regulate at least some nanosilver products as new pesticides. If so, it would be the first regulatory action for nanomaterials in the U.S. and bring needed oversight to the current largest sector of nanomaterial commercialization.

7. The rise of silver biocides: a cultural and economic response?

It is well established that silver and nanosilver are toxic to aquatic and soil organisms and that they are persistent and will accumulate under certain conditions. Knowledge about the latter is still patchy and information regarding which organisms are especially at risk is also largely lacking (Luoma 2008). There are many unanswered questions, especially regarding the remobilization of bound silver and the bioavailability of silver to organisms.

It is hence not at all surprising that a recent international study, reviewing the evidence generated by current global research on the toxicity of nanoparticles 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.**" (Aitken et al. 2009).

While this is a clear wakeup call in regards to the environmental release and effects of nanosilver, there are indications that silver may also have adverse health effects on humans, especially as its use has dramatically risen in the last few years. Apart from the obvious spectre of development of bacterial resistance to silver, Hollinger (1996, as cited by Luamo 2008), suggested that silver bandages may delay wound healing—the potential for silver's accumulation in specific organs need to be further investigated.

While undoubtedly silver and nanosilver have useful applications in the medical arena (for instance as coatings for medical devices or as wound care for burn victims), their use needs to be strictly controlled and the dictum 'no data, no market' should always be followed. In contrast, the indiscriminate sale of silver impregnated bandages and plasters for home use should be stopped.

One of the unanswered questions is, 'why has silver suddenly become so popular'? By extension, we must also ask 'why are we so afraid of bacteria and dirt?'. Tomes (2009) points out that our current obsessions with germs has parallels with a similar period of intense anxiety about disease causing agents between 1900 and 1940. It is her contention that this 'new' fear of germs reflects our anxieties about globalization, the environment, suspicions of governmental authority, and distrust of expert knowledge.

From an economic point of view, with the demise of the photographic industry, silver producers were desperate need to find new markets for silver. It appears this quest has been successful, industrial and electronic applications of silver, along with the ever increasing uses for silver biocide have easily made up for this loss (Wijnhoven 2009).

In many respects, the increasing use of nanosilver is a typical example of what Gould (2005) has called "the technological treadmill of production." The purpose of this treadmill is growth in the form of an increased corporate profitability at the expense of workers and the environment and it "depends directly on technological innovation to replace human labour with capital and to increase the capacity for the transformation of natural resources into commodities." In doing so the treadmill increases profits and environmental threats while reducing the generation of social benefits (employment, wages, etc.), "ensuring constant increases in social and environmental inequality." (Gould 2005). A hallmark of the technological treadmill of production is that, despite claims to the contrary, the economic benefits of any form of nanotechnology will accrue to corporations as well as governments, while the economic costs will be born by the citizens and the environment.

The need for extreme germ killers: Why are we afraid of dirt?
A recent article in the New York Times highlighted scientific research which showed bacteria found in common dirt are good for you (even essential), especially for children developing their immune system (Brody 2009). Other studies also suggest that exposure to certain orofecal and food borne microbes may make people less susceptible to respiratory allergies (Matricardi et al. 2000). These studies, along with epidemiological observations, provide an intriguing hypothesis that immune system disorders like multiple sclerosis, Type 1 diabetes, inflammatory bowel disease, asthma and allergies may have risen significantly in the United States and other developed countries because of our recent 'war on bacteria' (Matricardi et Al. 2000).

8. What needs to be done & what you can do

We call for an immediate moratorium on silver nanotechnology products

Friends of the Earth calls for a immediate moratorium on the commercial release of products that contain manufactured nanosilver until nanotechnology-specific regulation is introduced to protect the public, workers and the environment from their risks, and until the public is involved in decision making. In line with recommendations from the United Kingdom's Royal Society and Royal Academy of Engineering's 2004 report on nanotechnology, intentional release of nanomaterials into the environment should be prohibited until this can be proven to be safe. A precautionary approach to nanosilver technology is essential.

The United Kingdom's Royal Commission on Environmental Pollution, in a November 2008 report on nanotechnology, strongly recommended the regulation of nanomaterials. The Commission recommends that relevant government authorities should "focus specifically on the properties and functionalities of nanomaterials rather than size. Since these properties and functionalities will often differ substantially from those of the bulk material, strict chemical equivalence does not preclude the need for a separate risk assessment" (Royal Commission on Environmental Pollution 2008). The Commission also states its concern for nanosilver, which it believes "exhibits quite different toxicity to the bulk metallic form." Friends of the Earth agrees with these recommendations. Furthermore, we demand that government authorities assess nanosilver as a new chemical, and enact regulation that focuses on nanosilver properties rather than claims made by marketers and producers. Silver nanoparticles must be classified as hazardous waste and the use of silver nanoparticles in consumer products should be subject to thorough new safety tests.

Friends of the Earth United States and Australia have furthermore called for the recall of Samsung's silver appliance range (washing machine, vacuum cleaner, refrigerator, air conditioner, etc.) until publicly available, peer reviewed studies can demonstrate their safety for the environment and human health. We believe similar measures should be enacted for clothing and other products that contain nanosilver.

United States EPA nanosilver petition
Friends of the Earth also requests the United States Environmental Protection Agency grant in full the recent petition for rulemaking requesting that the EPA regulate nanoscale silver as a pesticide. The EPA must assess the human health and environmental risks presented by nanomaterials in consumer products and immediately remove all nanosilver products from the market and prohibit their sale until a proper safety assessment of these products is carried out.

The EPA should also analyze the potential human health and environmental risks of nanoscale silver, take regulatory actions under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) against existing products that contain nanoscale silver, and take other regulatory actions under FIFRA as appropriate for nanoscale silver products. Furthermore, products containing nanosilver must be labelled as such to support consumer choice and awareness.

What governments must do globally:

- **Establish comprehensive and precautionary legislation to manage the risks associated with nanotechnology in general and nanosilver technology in particular.**
- **All nanomaterials must be subject to new safety assessments as new substances, even where the properties of larger scale counterparts are well-known.**

Assessment

- All manufactured nanomaterials must be subject to nano-specific health and environmental impact assessment and must be demonstrated to be safe prior to approval for commercial use.
- Assessments must be based on the precautionary principle and the onus must be on manufacturers to comprehensively demonstrate the safety of their product. No data, no market.
- Safety assessment must be based on the nano content of products, not marketing claims.
- Safety assessment must include the product's entire life cycle.

Transparency

- All relevant data related to safety assessments, and the methodologies used to obtain them, must be placed in the public domain.
- All manufactured nano-ingredients must be clearly indicated on product labels to allow members of the public to make an informed choice about product use.

Public involvement in decision making

- The public, including all stakeholder groups affected, must be involved in all aspects of decision making regarding the use of nanotechnology

What industry must do:

Producers and retailers of nanosilver and nanosilver products must respect people's right to safe products, and to make informed purchases. Producers and retailers of nanosilver and nanosilver products must stop selling nanosilver products until nanotechnology-specific regulation is introduced to protect the public, workers and the environment from potential new risks associated with nanotoxicity.

Assessment

Manufacturers must work with regulators to ensure that their products have undergone appropriate safety testing, and must provide the relevant data regarding the health and environmental safety of their product. No data, no market.

Transparency

- All relevant data related to safety assessments, and the methodologies used to obtain them, must be placed in the public domain.
- All food and agricultural products which include manufactured nanomaterials must be clearly labelled to allow members of the public and farmers to make an informed choice.

What concerned individuals and organizations can do:

Hold government and industry to account over nanosilver!

- Write to your local members of state, federal and regional parliaments, requesting their support for a moratorium on the use of nanosilver
- Demand that governments regulate and label products that contain manufactured nanosilver, before allowing any further commercial sales.
- Insist that governments and industry take seriously the risks of occupational exposure to nanomaterials in your work place, talk with your colleagues or your union representative about opportunities for collective action to secure a safe work place.
- Contact civil society organizations you think may be interested in taking action to ensure precautionary management of the use of nanosilver

Appendix 1: examples of nanosilver products readily available in shops and from major online retailers

United States

Note: all products were viewed on the 1st of May 2009

Product Type	Nanosilver claim	Product & Manufacturer	Purchased or viewed at
Hair Styling	"The advanced technologies of ionic steam infuses hairi with healthy moisture, tourmaline coating provides radiant shine, nano silver particles for clean, healthy-looking hair, ceramic provides uniform heat-no hot spots."	Conair Infiniti Nano Silver 1 1/2" Steam Straightener	http://www.walmart.com/catalog/product.do?product_id=10055577#ProductDetail
Hair Styling	"Nano-Silver technology has anti-bacterial properties."	Andis 1" Nano-Silver Tourmaline Wet or Dry Ceramic Flat Iron	http://www.walmart.com/catalog/product.do?product_id=10780591
Hair Styling	"… clean, shiny, healthy-looking hair with less damage. Ionic technology and infrared energy protect hair's natural luster."	INFINITI INFINITI NANO SILVER 1 3/4" STRAIGHTENER	http://www.walmart.com/catalog/product.do?product_id=9854673
Hair Styling	"… dry and styles hair quickly, minimizing heat damage and leaving hair less frizzy and more manageable."	INFINITI NANO SILVER TOURMALINE CERAMIC FOLDING HANDLE HAIR DRYER	http://www.walmart.com/catalog/product.do?product_id=9854676
Hair Styling	"The TStudio Nano Silver Professional Dryer offers professional styling power backed by 1,875 watts. Easy-on-the-eyes silver and white design matches its easy-to-hold handle."	Remington TStudio Nano-Silver Professional Dryer 1875W	http://www.walmart.com/catalog/product.do?product_id=5934611
Hair Styling	"…minimizing heat damage and leaving hair less frizzy and more manageable."	INFINITI NANO SILVER TOURMALINE HAIRSETTERS	http://www.walmart.com/catalog/product.do?product_id=5155919
Food container	"Joycook container is the freshest airtight container applied to Nano-silver technology."	Joycook Nano Silver Square Plastic Container 23 OZ	http://www.amazon.com/Joycook-Silver-Square-Plastic-Container/dp/B0014E8UCQ/ref=sr_1_7?ie=UTF8&s=home-garden&qid=1241468897&sr=8-7
Door opener	"Constructed with nano silvers that inhibit the growth of bacteria, mold, fungi and more, for the life of the product"	The Handler open doors, flush toilets and more	http://www.amazon.com/Handler-The/dp/B000NUJ6V6/ref=sr_1_16?ie=UTF8&s=shoes&qid=124146889

			7&sr=8-16
Hand Cleaner	"Cyclic Cleanser is a scientifically balanced blend of Nano Silver and natural ingredients. By penetrating into pores, Cyclic's special formula cleanses deep into the skin s surface."	Cyclic Nano Silver-Pink Cleanser 0.53 oz	http://www.amazon.com/Cyclic-Nano-Silver-Pink-Cleanser/dp/B000KG8OBQ/ref=sr_1_20?ie=UTF8&s=hpc&qid=1241469251&sr=8-20
Hand Cleaner	"NANO 153 Cleanser does not have exfoliating effect unlike other similar cleansers' claims. As matter of fact, nano silver particles used in the cleansers do not have exfoliating effect at all. It might be soaps' other additives or strong lavation which might cause serious skin damages for some peoples. Be cautious! "	NANO 153 Silver Soap Cleanser - 60g Dry to Normal	http://www.amazon.com/NANO-153-Silver-Soap-Cleanser/dp/B000YAOL3I/ref=sr_1_41?ie=UTF8&s=hpc&qid=1241469392&sr=8-41
Humidifier	"… stop mold and bacteria from growing in the tank so you can humidify clean water for a healthier breathing environment."	Germ Guardian Table Top Ultrasonic Humidifier	http://www.sears.com/shc/s/p_10153_12605_03279121000P?keyword=nano-silver#descriptionAnchor
Air cleaner	"… releases positive and negative ions, creating clusters which attack odors and organic particles."	Kenmore EnviroSense™ True HEPA Air Cleaner	http://www.sears.com/shc/s/p_10153_12605_03285500000P?keyword=nano-silver
Hand vacuum cleaner	".. help fight the growth of odor-causing bacteria and mold."	Germ Guardian Germ Defense Germ Guardian Clean 2 Hand Vac with UV-C Technology	http://www.sears.com/shc/s/search_10153_12605?keyword=nano-silver
Hand vacuum cleaner	"Small nano-silver particles have been imbedded into the dirt cup to help fight the growth of odor-causing bacteria and mold."	Germ Guardian 2 in 1 Upright Vacum	http://www.sears.com/shc/s/search_10153_12605?keyword=nano-silver
Shaving equipment	"Features Hygienic Nanosilver Coated Replacement Foils and Pop-up Trimmer."	Spectrum Men'sRazor	http://www.kmart.com/shc/s/p_10151_10104_038W852692110001P?keyword=nano-silver&sid=K-on-Sx20k061224x0000002

Australia

Product Type	Nanosilver or silver claim	Manufacturer	Purchased or viewed at
Socks	"Silver fabric eliminates bacteria and odour. .. keeping you cool in summer and warm in winter …silvertech is safe and natural and will last for the life of the product"	Outdoor expedition silver tech hiking socks	Rays Tent City
Underwear	"Silver fabric is moisture repellant and dries quickly, antimicrobial"	Wild workwear thermal bottom/top	Rays Tent City
Hair styling	"Clean beautiful shine. Nanosilver technology"	Remington Tstudio hot rollers	
Band-aids	"Kills harmful germs for optimal healing. Silver ions are continually released…"	Elastoplast	Pulse Chemist
Mattress fabric	"Anti static – reduces electrostatic discharges. Thermodynamic- regulates temperature - Cool in summer, warm in winter .Anti microbial- inhibits growth of fungi and bacteria .Hypo allergenic – reduces allergies …Natural "	Interlude mattress fabric	Mattress Resources Australia http://www.mattressresources.com.au/index.php?option=com_content&task=view&id=35&Itemid=127
Children's playmatt	"Nano-silver is: Highly effective, Fast acting, Non Poisonous, Non toxic, Non allergic"	Bubba-mat (LG Chem)	http://www.softmats.com.au/TechnicalSpec.aspx
Refrigerator	"Cool air from the duct circulates environmentally friendly silver particles to every compartment of the fridge to reinforce antibiotic sterilisation."	Daewoo Refrigerator	http://www.daewooelectronics.com.au/docs/FR-291W_brochure.pdf
Footwear sanitizer	"Nano Silver ions … are blasted around the chamber by an inbuilt fan."	Klenz Sanitizer	http://www.klenz.com.au/index_files/page0002.htm
Face spray	"With superior antibacterial benefits to keep your skin germ-free, deionized water maintains optimal hydration without interfering with the activity of nano-silver."	Beaubelle Face spray	http://www.beaubelleaustralia.com.au/beaubelle_products.php?cat_id=&subcat=30
Colloidal silver	"The natural antimicrobial. Safe for human consumption"	Fulhealth Industries Silver colloid	Northcote Plaze Healthfood shop
Colloidal silver	"Quality , reliability, trust"	Silvex Solutions Colloidal silver	Northcote Plaze Healthfood shop
Colloidal silver	"Non allergenic"	Natures Treasures Colloidal Silver (Australian Health Research	Northcote Plaze Healthfood shop

Note: products similar to those available in the United States and Australia are also widely available in Europe.

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