RISK ANALYSIS OF NANOTECHNOLOGY THROUGH EXPERT ELICITATION: A SILVER NANOTECHNOLOGY CASE STUDY

A Thesis
Presented to
the faculty of Engineering and Applied Sciences
University of Virginia

In Partial Fulfillment

of the requirements for the Degree

Masters of Science Electrical Engineering

by

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August 2008

APPROVAL SHEET

The thesis is submitted in partial fulfillment of the

requirements for the degree of

Master of Science Electrical Engineering

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August 2008

Abstract

A practical approach is needed to analyze and assess quickly emerging technologies, such as nanotechnologies, where there exist uncertainty and undefined risk. The method presented here utilizes expert elicitation of a pre-selected panel of experts to determine Risk Triggers, which are essential in evaluating a technology, as well as to define exposure scenarios, knowledge gaps and regulatory issues. To illustrate this method, a case study was undertaken on silver nanotechnology in which the research team created a Silver Nanotechnology Consumer Inventory (SNCI), the interactional expert elicited a sample of eleven experts and the research team performed an analysis on the above-mentioned criteria. The interactional expert is key to oversee the elicitation process and the use of Trading Zones among various specializations. Overall this method proved to be very successful in assessing and analyzing the risk of an emerging technology because of the breadth of the expertise elicited, the expedited analysis and the ability to direct research funds where they will be most effective.

Acknowledgements

I would like to thank all the people who took time out of their busy schedules to contribute their expertise to this method and to all those who helped make this thesis possible. Thank you.

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Introduction

Statement of Purpose

This report presents a method to aid in the analysis and assessment of emerging technologies, such as nanotechnology, in which there is much uncertainty and the risk is undefined. The method involves the creation of an interactional expert who, through the use of expert elicitation, provides an in depth look into what is needed to evaluate that new technology. To illustrate how this method is applied, a case study on silver nanotechnology was performed.

Technology Needs Better Guidance

Emerging technologies have always presented the promise of a better world, one where we can exceed our potential and remedy our mistakes. Electricity fundamentally changed the way we lived and worked. The personal computer continues to shape our minds and shrink the distances between people, bringing the world closer together. More recently, Genetically Modified Organisms (GMOs) promised to eradicate world hunger and enhance the quality of our food.[1] Now nanotechnology promises to make faster computers, smarter drugs, enhanced materials, and improve our environment, essentially transforming the way we design and create our world. These technologies, however, do not always live up to the “holy grail” images we create of them.

Technology is not removed from the society that creates it and it is shaped by the demands we place on it. Chauncey Starr (1969), a respected pioneer in physics and nuclear engineering said in his well known paper ‘Social Benefit versus Technological Risk’,

> “If we understand quantitatively the causal relationships between specific technological developments and societal values, both positive and negative, we might deliberately guide and regulate technological developments so as to achieve maximum social benefit at minimum social cost. Unfortunately, we have not as yet developed such a predictive system analysis. As a result, our society historically has arrived at acceptable balances of technological benefit and social cost empirically-by trial, error, and subsequent corrective steps.”[2]

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[1] Gorman, M. E., Hertz, M., Nieusma, D., & Mead, J. (2004). *Monsanto and Intellectual Property (UVA-E-0216).* Charlottesville, VA: University of Virginia Darden School Foundation.
[2] Starr, Chauncey. (1969). Social Benefit versus Technological Risk. *Science*, 165, 1232-1238.

This can be demonstrated by looking at our regulatory system. As new technologies are coming along, they are regulated based on old models, and if a problem arises in the future, the government takes corrective action to regulate or ban the harmful product or substance. Asbestos is a perfect example. Asbestos became a popular building material in the 19th century because of its resistance to heat and electricity. Asbestos, however, is not one type of chemical, but a classification of many fibers, some more toxic than others. It was discovered in the 1980's that asbestos was toxic and in 1989 the EPA issued a final rule banning most asbestos-containing products. This created a national scare and the result was millions of dollars spent in litigation and corrective action. If we could have taken action like Chauncey Starr suggested to "deliberately guide and regulate the technological developments as to achieve maximum social benefit at minimum social cost," perhaps both lives and money could have been saved.

Speed of Technological Advancement is Increasing

Another significant challenge we face today with emerging technologies is the speed of technological development. In "The Age of Spiritual Machines" Ray Kurzweil (1999) states,

> "Like the evolution of life-forms, the pace of technology has greatly accelerated over time. The progress of technology in the nineteenth century, for example, greatly exceeded that of earlier centuries, with the building of canals and great ships, the advent of paved roads, the spread of the railroad, the development of the telegraph, and the invention of photography, the bicycle, sewing machine, typewriter, telephone, phonograph, motion picture, automobile, and of course Thomas Edison's light bulb. The continued exponential growth of technology in the first two decades of the twentieth century matched that of the entire nineteenth century. Today, we have major transformations in just a few year's time."[3]

If the evolution of technology is moving at an accelerated rate the question becomes what and who is guiding its development. It could be argued that in a free capitalist market such as in the United States, the "what" is the drive to make products which make money and the "who" is both industry and academia. With the "bottom line" being the guiding factor of an emerging technology such as nanotechnology, the problem then becomes that these technologies are thrown on the

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[3] Kurzweil, R. (1999). The Age of Spiritual Machines. New York, NY: Viking. (pp. 15).

market before the implications of those technologies have time to be absorbed in the psyche of both the inventor and the society. Rosalyn Berne, a trained ethicist from the University of Virginia, had the opportunity to study those inventors, the people developing nanotechnology's potential. She had a five-year grant in which she spent discovering who is the driver of this technology and how ethical thought was incorporated into its development. Her major concern at the end of her study was the pressure on those scientists; with so much invested in nanotechnology both in industry and in academia, there is an overwhelming push to win the "race" and not to be reflective of the implications of those new technologies.[4]

So we have put ourselves in a precarious position: we are in a marathon, blindfolded and running with a knife. This pressure to win approval and profits placed alongside our current governmental method of regulation where we find a problem and then take corrective action, is dangerous. Nanotechnology is already being used and incorporated into hundreds of products. The Project on Emerging Nanotechnologies last had a count of 610 consumer products available on the market.[5] That does not count the various other uses of nanotechnology such as catalysts and the incorporation of nanomaterials.

A Solution Though Adaptive Management & Anticipatory Governance

The United States political system is unable to quickly adapt to an increasingly complicated world. The current regulatory system allows for the use and distribution of products whose effects are not well-defined. There appears to be an ever-increasing need to evaluate quickly an emerging technology. A psychologist of science at the University of Virginia, Mike Gorman has suggested that strategies of both adaptive management and anticipatory governance must be utilized. Each of these proactive practices involves the use of trading zones, where multiple stakeholders "exchang[e] ideas, resources, and solutions across different communities and interests." FN Adaptive management requires constant communication among

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[4] Berne, Rosalyn. "Ethics, Meaning, and Belief in Nanotechnology Development." University of Virginia, Virginia Festival of The Book Lecture. Charlottesville, VA. 30 March, 2008.

[5] Woodrow Wilson International Center for Scholars, The Project on Emerging Nanotechnologies. (June, 2008). Consumer Product Inventory. http://www.nanotechproject.org (accessed June , 2008).

the stakeholders and the system they are managing, having the flexibility to adapt new strategies to new situations. With anticipatory governance, policy institutions must be included in the group of stakeholders. Overall Gorman et. al. (2008) concludes that, "[r]egulatory systems need to be more anticipatory and adaptive, steering a course between the precautionary principle and reactive risk management. Expert elicitation is one method for implementing adaptive management and anticipatory governance."[6] Here we suggest that expert elicitation can be a tool to evaluate quickly an emerging technology such as nanotechnology. This evaluation process is not meant to replace the much-needed lab work of hard science such as toxicology studies and geochemical cycling analysis. Considering that each of those methods takes years to complete, Expert Elicitation utilizes the experience of experts to help ask the right questions now about these new technologies and guide informed decisions about technologies that are already affecting peoples everyday lives. It is a scientific approach that reaches into an area of knowledge that remains untapped.

This report displays a method of systematically evaluating information to attain a risk assessment of an emerging nanotechnology through structured expert elicitation and its rigorous evaluation using silver nanotechnology as an example. The challenges in assessing nanotechnology in this manner are discussed herein as well as certain regulatory issues that are specific to the use of nano-sized silver or nanosilver.

It could be said that the social acceptance of risk is a function of pubic perceptions or awareness of the benefits of an activity.

Social Acceptance of Risk = f(Public Awareness of the Benefits of an Activity**)**[7]

In the case of asbestos, after the EPA ban, the perceived risk outweighed those benefits that the technology had delivered. Nanotechnology presents an even greater challenge to the public, industry and government. In looking at nanotechnology,

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[6] Gorman, M., Ahson, W., Fauss, E., & Swami, N. (2008). A framework for using nanotechnology to improve water quality. In Savage, N. (Ed.), *Nanotechnology Applications: Solutions for Improving Water Quality*. Manuscript submitted for publication.
[7] Starr, Chauncey. (1969).

> "the characteristics that make nanomaterials of such interest to materials scientists and others, namely, that their physical, chemical, and biological properties are fundamentally different from those of individual atoms or bulk materials, also make it difficult to predict their effects on human health or the environment based on prior knowledge of the materials in their bulk forms."[8]

In other words, those special characteristics specific to nanotechnology also present unique challenges in defining how they interact in the human body, in the environment and any other microenvironment that they come in contact with.

What is Nanotechnology?

Nanotechnology involves the characterization, manipulation and fabrication of materials and devices at the "nano" scale (1 nanometer is equal to one billionth (10^{-9}) of a meter). The rough estimate for defining nanotechnology is the measurement of a material or device at one or more dimensions in the range of 1-100nm. To put this into perspective, "a human hair is approximately 80,000nm wide, and a red blood cell approximately 7000nm wide."[9] Nanotechnology and nanoscale materials are not entirely new. There have always been nanoscale materials in the environment, and it could be argued that many biological substances such as DNA (strands which have a 2nm diameter) are a form of nanotechnology. Humans inadvertently have even made use of nanotechnology's wonderful properties. The Damascus Sabre from the seventeenth century has been shown to contain carbon nanotubes and cementite nanowires which help give the blade "extraordinary mechanical properties and an exceptionally sharp cutting edge."[10] The difference is, today, we are gaining the ability to create nanomaterials and nanotechnologies to our own specifications; creating new devices that have new and novel properties.

The notion that there is "plenty of room at the bottom," meaning that there is lots of research and potential for innovation when working in the nanoscale, was presented in a lecture

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[8] Woodrow Wilson International Center for Scholars, The Project on Emerging Nanotechnologies. (2007, July). *Where does the Nano Go? End-of-Life Regulation of Nanotechnologies* (PEN 10). Washington, DC: Linda K Breggin & John Pendergrass.

[9] The Royal Society. (2004, July). *Nanoscience and nanotechnologies: opportunities and uncertainties.* Retrieved June 23, 2008, from http://www.nanotec.org.uk/finalReport.htm

[10] Reibold, M., Paufler, P., Levin, A. A., Kochmann, W., Pätzke, N., & Meyer, D. C. (2006). Materials: Carbon nanotubes in an ancient Damascus sabre. *Nature*, *444*, 286.

in 1959 by Richard Feynman.[11] As tools have improved, such as the transmission electron microscope (TEM) and the scanning electron microscope (SEM), Feynman's vision of a world where micromachines can exist has become more of a reality than a dream. Scientist across various disciplines, ranging from chemistry to physics and electrical engineering to medicine, have been approaching nanotechnology from different perspectives and methods. The results, to name a few, have been faster and smaller electronics, enhanced materials that provide better thermal, electrical and mechanical properties, cancer drugs that specifically target cancer cells, and small sensors that can be used to monitor environmental or workplace contamination.

Due to the wide array of materials used and the fields that do work in this area it should be noted that there is not one nanotechnology but many nanotechnologies. An important distinction is that no two nanotechnologies look or act the same; not only can the properties of individual materials change with size, but the methods of fabrication and application can vary tremendously. To give an example, the fabrication of nano materials and devices can begin by being built from the atom up using wet chemistry self assembly methods or a top down approach could be taken, where a surface is modified by nanoscale etching techniques.

Unique Properties make Nanotechnologies Hard to Quantify

Our entire regulatory system is defined by regulating chemicals and substances by amounts and concentrations. The majority of these nano-characteristics, however, cannot be simply defined by measuring chemical concentrations, but rather a whole list of factors must be considered and measured. Environmental Defense and Dupont partnered to develop a Nano Risk Framework that would aid in companies better defining and cataloging their nanotechnologies. In this framework they provide a list of minimum physical and chemical properties that need to be recorded to classify a nanomaterial.

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[11] Feynman, R. P. (1959, December 29). *Plenty of Room at the Bottom.* Annual meeting of the American Physical Society. Retrieved June 23, 2008, from http://www.zyvex.com/nanotech/feynman.html

Table 1: Environmental Defense and Dupont Physical and Chemical Properties List for Nanomaterials[12]

Chemical Composition (including surface coating)	Dispersibility
Molecular Structure	Bulk Density
Crystal Structure	Agglomeration State
Physical Form/ Shape (at room temperature and pressure)	Porosity
Particle Size, Size Distribution and Surface Area	Surface Charge
Particle Density	Surface Reactivity
Solubility (in water and biological relevant fluids)	

Defining these factors is not a small task. This list demonstrates that evaluating each individual nanotechnology is a huge undertaking in itself. Even measuring concentration presents a problem since sufficient tools have not been developed to measure exposure of nanomaterials within the environment. Even if regulations are created that state maximum exposure limits, currently there is no practical way to enforce those limits.

Public Awareness of Nanotechnology

There is also the problem of "Public Awareness." According to a Woodrow Wilson International Center for Scholars Project on Emerging Nanotechnologies study conducted from May to June 2005, approximately 54% of its sample knew nothing about nanotechnology. If half of the population does not even know what a technology is, how can it be aware of the technology's benefits and make a rational judgment on acceptable risk? There are examples in recent history of technologies that have been restricted because of uninformed public reaction to negligible risks, such as the aforementioned GMOs.[13]

[12] Environmental Defense & Dupont Nano Partnership. (2007, June). *Nano Risk Framework.* Washington, DC.
[13] Gorman, M. E., Hertz, M., Nieusma, D., & Mead, J. (2004).

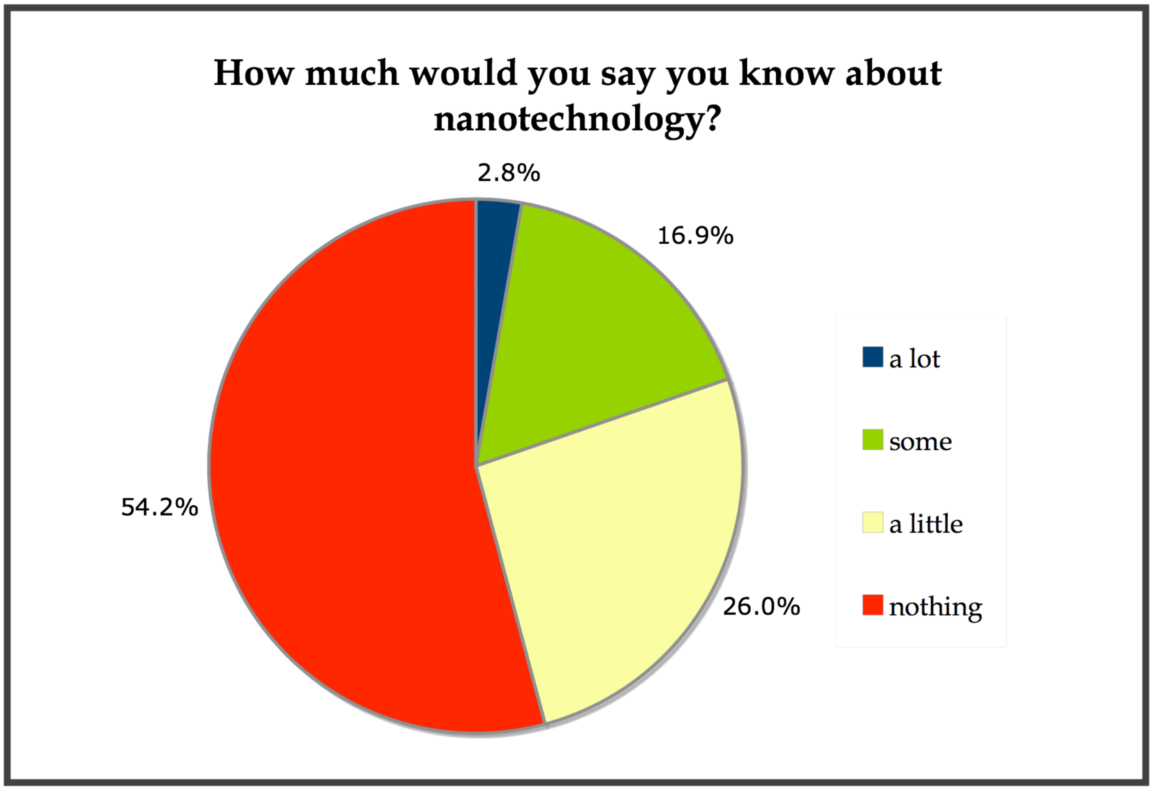

Figure 1. 2005 Poll on Public Awareness of Nanotechnology[14]

The Woodrow Wilson Center has written many publications on different aspects of nanotechnology including the aforementioned public perceptions and regulatory gaps. They can be accessed at (www.nanotechproject.org).

Type of Knowledge Accessed through Expert Elicitation

To better understand expert elicitation one must understand what type of knowledge is being elicited. In Bilal M. Ayyub's 2001 book, *Expert Opinions for Uncertainty and Risk*, he reviews the evolution of knowledge. In the 18th century Kant divided knowledge into three types, combining both empiricism and rationalism: "(1) an *analytical priori,* which is exact and certain, but also uninformative because it makes clear only what is contained in definitions; (2) a *synthetic posteriori,* which conveys information about the world learned from experience but is subject to the errors of the senses; and (3) a *synthetic priori,* which is discovered by pure intuition and is

[14] Woodrow Wilson International Center for Scholars, The Project on Emerging Nanotechnologies. (2006, January). *Informed Public Perceptions of Nanotechnology and Trust in Government* (PEN 1). Washington, DC: Jane Macoubrie.

both exact and certain, for it expresses the necessary conditions that the mind imposes on all objects of experience."[15] While it was debated as whether the third type of knowledge existed, it is clear that expert elicitation falls under the *synthetic posteriori*, and as such, the interactional expert must be aware of the "error of the senses," or the problems that arise from using such a source.

There are two sources of error, which can arise from the interpretation of data. First, facts or factual knowledge, which are exact and certain come from historical records. Predictions on future events based on facts hold certain assumptions that can be suspect. This can lead to predictions that are false due to misguided or incorrect assumptions. Second, experimental setups and experiment results interpretations are based on the paradigm of the scientist. Therefore, experimental results that might be accepted as fact in a expert's mind might have little validity in respect to a new paradigm.

In the Reliability of Theory of Knowledge, knowledge is divided into four parts: *episteme* otherwise known as "cognitive knowledge," *dianoi* "correct reasoning from hypotheses," *pistis* the "intellectual and/ or emotional acceptance of a proposition" and *eikasia* "in which knowledge is based on inference, theorization, or prediction based on incomplete or reliable evidences."[16] Ayyub (2001) writes,

> "The pistis and eikasia categories are based on expert judgment and opinions regarding system issues of interest. Although the pistis and eikasia knowledge categories might by marred with uncertainty, they are a certainty sought after in many engineering disciplines and the sciences, especially by decision and policy makers. . . . Opinions rendered by experts, that are based on information and existing knowledge, can be defined as preliminary propositions with claims that are not fully justified or that are justified with adequate reliability but are not necessarily infallible."[17]

In performing an expert elicitation study, one finds that experts do not make the distinction to separate their belief or assumption (*pitis*) from the judgment or opinion (*eikasia*). In other words, experts have the tendency to make a judgment or form an opinion based on a set of assumptions or beliefs. In this expert elicitation process both judgment and assumptions are important in the

[15] Ayyub, B. M. (2001). *Elicitation of Expert Opinions for Uncertainty and Risk*. Washington D.C.: CRC Press. (pp. 32).
[16] Ayyub, B. M. (2001). (pp. 38).
[17] Ayyub, B. M. (2001). (pp. 38-39).

evaluation of the emergent technology. The justifications of certain opinions provide valuable insight into issues surrounding the technology. For example, one expert will make the judgment that it is highly hazardous to have dermal exposure of a product coated with nanosilver. This stems from the assumption that the coating will flake off and, because of its size, migrate to different regions of the body such as the liver, brain and other organs where it has the potential to cause problems. The reasoning behind the judgment proves to be far richer knowledge than the judgment itself.

Difficulties with Expert Elicitation and Risk Analysis

There are some inherent challenges which are posed by expert elicitation. Error can arise from uncertainty and biases both from the expert and the interactional expert. The elicitation process is affected both by the ability of the interactional expert to elicit a comprehensive story of the emergent technology and by the knowledge the experts' possess. As Ayyub (2001) puts it, "[a]lmost all of our commonsense beliefs are based on evidence that is not infallible eventhough some may have overwhelming reliability."[18] For the interactional expert to perform effectively, the words used to describe what the experts say becomes especially important for consistency in comparison. The following section describes the holarchy of belief to opinion.

Uncertainty

Uncertainty is inherently found in any experiment. There is no perfect system in any discipline. The result is uncertainty must be acknowledged when interpreting any experimental data. Uncertainty can be classified under two types, aleatory and epistemic. "Aleatory uncertainties are described as arising from inherent variabilities or randomness in the systems, whereas epistemic uncertainties are due to imperfect knowledge. . . [of the researcher, or analyst.]"[19]

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[18] Ayyub, B. M. (2001). (pp. 38-39).
[19] O'Hagan, A., & Oakley, J. E. (2004). Probability is perfect, but we can't elicit it perfectly. *Reliability Engineering and System Safety*, 85, 239-248.

Within an experiment there exists epistemic model inadequacy, the epistemic analyst's uncertainty, epistemic parameter uncertainty and residual variability which "might appear to be inherently aleatory. In reality there are two sources of uncertainty combined in one. The process itself may be inherently unpredictable and stochastic, in which case we can regard the variable as aleatory; but it may also be that this variation would be eliminated (or at least reduced) if the analyst was able to recognize and to specify within the model some more conditions."[20]

Bias

In dealing with any system which involves humans, there exists the element of bias. There are biases held by all parties involved: the decisionmakers, the group which designs the experiment and selects the experts, the interactional expert, the experts themselves, the individuals coding the interviews and the interpreters who read this report. A major problem with biases is, even if they can be distinguished, it is not always possible to adjust for them. There should be an attempt to mitigate biases where possible at each stage of he elicitation.

The first level of bias is introduced in the decisionmaker's selection of experts and the inherent determination of equivalency of these experts to be consulted. When presented with two sources of data, *A* and *B*, a judgment is made by the decision maker which of those sources is more reliable. More weight may be assigned to source *A* because they present the better data, however this would be the ideal case. *A* might carry more weight because they come from a more renowned institution, have a better presentation carried out by a charismatic individual or are back by more resources. Equivalency between sources cannot always be easily categorized but it is a factor that must be acknowledged. Even within this method, it was decided which experts would be selected. There is a level of equivalency where it was decided that these individuals had enough expertise to be considered experts.

Unintentional bias also is a factor with which the interactional expert and the coders must deal. Forester, et. al. (2004) list a number of unintentional biases.

[20] O'Hagan, A., & Oakley, J. E. (2004).

"Evaluators often:

- ignore uncertainty (this is a simplification mechanism); uncertainty is uncomfortable and complicating, and beyond most people's training.
- lack an understanding of the impact of sample size on uncertainty. Domain experts often give more credit to their experience than it deserves (e.g. if they have not seen it happen in 20 years, they may assume it cannot happen or that it is much more unlikely to happen or that it is much more unlikely than once in 20 years.)
- lack an understanding or fail to think hard enough about independence and dependence.
- have a need to structure the situation, which leads people to imagine patterns, even when there are none.
- are fairly accurate at judging central tendency, especially the mode, but tend to significantly underestimate the range of uncertainty (e.g. in half the cases, people's estimates of the 98% intervals fail to include the true values).
- are influenced by beliefs of colleagues and by preconceptions and emotions"[21]

The best defense against these biases for the research group and the interactional expert is to be aware that they exist and to review results in light of these influences at each step of the method. In the case of the individuals who coded the interviews, the coder's subjective weighting of the experts can be remedied by removing the audio component of the interview and by allowing the coders to review the transcript without identification of the particular expert. In this way the coders can only base coding on the content of the expert's interview.

<u>Holarchy of Belief to Opinion</u>

To perform the role of the interactional expert properly, the individual must detach himself from personal judgment and observe the experts. By creating a trading zone the interactional expert can assess the experts' worldview and broker information based on objective criteria such as the Risk Triggers. In the analysis, critical thinking must then be applied to the collected data. The more consistent and detached the research group is in evaluating the content, the more objective the weighting of the information will be.

[21] Forester, J., Bley, D., Cooper, S., Lois, E., Siu, N., Kolaczkowski, A., et. al. (2004).

It is critical that in this type of analysis that the vocabulary used to describe what the experts say be clearly defined. With precision of word use in describing the elicited information, specific content can be distinguished from interpretations.

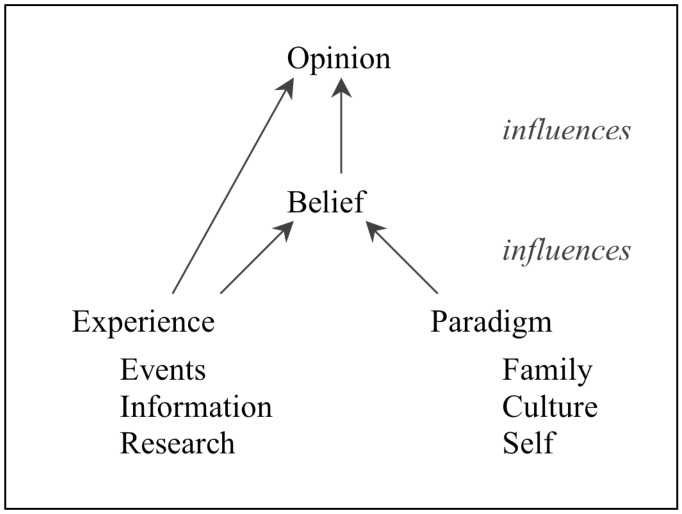

Figure 2. Holarch of Belief to Opinion

In this thesis it is important make the distinction between an expert's belief and his opinion. For the purposes of this report, *belief* is defined as justifications for a particular viewpoint that are more firmly rooted in an individual's paradigm or worldview. These can be defended and influenced by one's experiences. An *opinion* is a conclusion drawn primarily from experiences including specific research, but always influenced by one's foundational belief system that involves an internalized hierarchy of beliefs. An individual is less attached to his opinion and with the introduction of new information, an opinion can be more easily changed than a belief. The figure above illustrates this holarchy of how experiences and paradigms influence belief and then, in turn, evolve into opinions.

A question which emerges during analysis of these interviews is "should more weight or importance be assigned to belief or opinion?" It may appear that a belief should be given more weight because it is often defended with more conviction. Such an assumption should be approached with caution. Belief systems have two downfalls: the potential to incorporate divergent fundamental beliefs of the expert and the danger that new information might be automatically disregarded if it does not fit into that expert's particular paradigm. It is not possible in this method for the interactional expert to have access to the expert's foundational belief system. It is therefore important that analysis and assigned weights to certain criterion be based on the justifications or reasoning provided by the experts rather than the conversational nuances of the interviews. It is also important that a consistent use of these terms is made by the research team and that an individual who then interprets the final analysis be aware of the distinction between belief and opinion.

Parameters to Control for Bias in Expert Elicitation

Expert Elicitation methods are not as simple to define as traditional experimental methods. In designing an expert elicitation study there are many factors that need to be considered such as dependence between experts, sources of error, bias and uncertainty. Forester, Bley, Cooper, Lois, Siu, Kolaczkowski, Wreathall (2004) present a list of desirable criteria for an expert elicitation process:

- Considers all elements of context
- Considers all aspects of uncertainty
- Incorporates all relevant information (including data)
- Ensures intra- and inter-rater reliability
- Provides traceability
- Guards against bias.[22]

Each of these criteria is key in controlling the sources of error that can come from expert elicitation methods and have been addressed in this analysis. A thorough literature review was performed before the creation of the database and the expert elicitation study to insure the consideration of elements that were vital in the discussion of silver nanotechnology. There was also room provided within the interview process to the experts to add their thoughts and opinions on what were important factors to consider with the use of nanosilver.

[22] Forester, J., Bley, D., Cooper, S., Lois, E., Siu, N., Kolaczkowski, A., et. al. (2004). Expert elicitation approach for performing ATHENA quantification. *Reliability Engineering and System Safety*, 83, 207-220.

Risk Assessment

The purpose of risk assessment is to assess the particular risk of an event. Policy is then based on taking making a judgment on what level of risk is acceptable. There are four lines of investigation into risk that are described by Lowrance (1976):

1. Define the conditions of exposure;
2. Identify the adverse effects;
3. Related exposure with effects;
4. Estimate overall risk.[23]

Measurements are taken to determine the above criteria. In this study risk is divided into two components, exposure and hazard. In investigating exposure or "defining the conditions of exposure" many factors are explored: who is exposed? are there any susceptible populations? what are they exposed to? does the material change under different circumstances? what are the exposure scenarios? and how long are they exposed?

Risk = f(Exposure & Hazard**)**

In looking at hazard, the "adverse effects" are examined. The questions that are posed involve: what are the material hazards in terms of physical properties, reactivity and toxicology? What is the danger for a particular type of exposure?

Silver Nanotechnology, A Case Study

A Brief History of Silver

Silver is a naturally occurring element. Humans have used silver for thousands of years. It has been used as a precious metal in jewelry and in currency. The ancients even discovered an antimicrobial if silver vessels were used to store water and wine, they would not spoil.[24] Before the emergence of antibiotics, silver and silver compounds were commonly used in medicine to treat a wide assortment of ailments. Metallic silver was used to treat surgical prosthesis, splints,

[23] Lowrance, W. W. (1976). *Of acceptable risk*. Los Altos, CA: William Kaufmann, Inc.
[24] Russell, A. D., & Russell, N. J. (1995). Biocides: Activity, Action and Resistance. In Hunter, P. A., Darby G. K. & Russell N. J. (Eds.), *Fifty Years of Antimicrobials: Past Perspectives and Future Trends.* (pp. 327-365). Cambridge: Cambridge University Press

and fungicides, while soluble silver compounds have been used to treat "mental illness, epilepsy, nicotine addiction, gastroenteritis, and infectious diseases, including syphilis and gonorrhea."[25] Silver sulfadiazine was a common use of silver to treat burn wounds. Colloidal silver is still used today as a homeopathic remedy to treat a wide variety of problems ranging from the common cold to irritated skin.

Toxicology of Silver

Has silver been shown to be toxic to humans? Drake and Hazelwood (2005) express that "[s]everal factors influence the ability of a metal to produce toxic effects on the body; these include the solubility of the metal, the ability of the metal to bind to biological sites, and the degree to which the metal complexes formed are sequestered or metabolized and excreted."[26] Below is a table that summarizes the known effects of different forms of silver.

Table 2. Human Health Effects of Silver[27]

Silver nitrate	Acute symptoms of overexposure include a decrease in blood pressure, diarrhea, stomach irritation and decreased respiration.
Silver Salts	Chronic symptoms from prolonged intake of low doses cause fatty degeneration to the liver and kidneys and changes in blood cells.
Soluble silver or Colloidal silver	Long-term inhalation or ingestion may cause argyria and/or argyrosis. They can also accumulate in small amounts in the brain and muscles
All forms of Silver	**Non-toxic** to the immune, cardiovascular, nervous, or reproductive systems. It is **not** carcinogenic.

The most commonly known health effect of silver is silver poisoning or argyria: a permanent blue discoloration of the skin and/or argyrosis, a permanent blue discoloration of the eyes. This generally occurs when there is prolonged exposure to silver such as with homeopathic use or occupational exposure. It has been noted that "argyria can be considered a mechanism to detoxify silver by sequestering it in the tissues as harmless silver protein complexes or silver

[25] Drake, P. L. & Hazelwood, K. J. (2005). Exposure-Related Health Effects of Silver and Silver Compounds: A Review. *Annals of Occupational Hygiene. 49,* 575-585
[26] Drake, P. L. & Hazelwood, K. J. (2005).
[27] Drake, P. L. & Hazelwood, K. J. (2005).

sulfide."[28] Generally it is only the soluble silver compounds, not metallic or insoluble silver compounds that are readily absorbed by the body. It is suspected that as the body takes up the silver compounds, "they form complexes primarily with proteins, but also with RNA and DNA."[29]

Silver has a high affinity for sulfur and thiol groups. In the creation of silver nanoparticles through electrostatic or steric stabilization techniques, this property is often exploited. This capping or protective component "not only protects the nanoparticles from precipitation but also plays a critical role in the size, size distribution, morphology and the biocompatibility of the resulting nanoparticles."[30] In terms of human health, silver ions have been shown to bind to thiol groups in the liver and bind to reduced glutathione which is then transported into the bile. This depletes the overall amount of reduced glutathione for biochemical pathways, which "plays an important role in maintaining proper structure and function of red blood cells, as well as eliminating organic peroxides."[31]

The US department of Labor Occupational Safety and Health Administration (OSHA) and the National Institute for Occupational Safety and Health (NIOSH) regulate silver in regards to human exposure in the workplace. This includes forms of exposure such as dermal absorption, ingestion, inhalation and chronic effects. OSHA has a Permissible Exposure Limit (PEL) of 0.01 mg/m^3 TWA (8hr total weight average) for silver metal and soluble compounds for general industry.[32] NIOSH has the same limit of 0.01 mg/m^3 TWA for their Recommended Exposure Limit (REL) for silver metal dust and soluble compounds. NIOSH also lists the Immediate Dangerous to Life or Health Concentrations (IDLH) level as 10 mg/m^3.[33]

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[28] Drake, P. L. & Hazelwood, K. J. (2005).
[29] Drake, P. L. & Hazelwood, K. J. (2005).
[30] Nair, L. S. & Laurencin, C. T. (2007). Silver nanoparticles: Synthesis and Therapeutic Applications. *Journal of Biomedical Nanotechnology. 3(4)*, 301-316.
[31] Drake, P. L. & Hazelwood, K. J. (2005).
[32] U.S. Department of Labor Occupational Safety & Health Administration. (2006, August 5). *Silver, Metal & Soluble Compounds (as Ag).* Retrieve June 23, 2008, from Chemical Sampling Information Online, from http://www.osha.gov/dts/chemicalsampling/data/CH_267300.html
[33] National Institute for Occupational Safety and Health. (2005, September). *Silver (metal dust and soluble compounds, as Ag).* Retrieved June 23, 2008, from NIOSH Pocket Guide to Chemical Hazards Online, from http://www.cdc.gov/niosh/npg/npgd0557.html

Table 3. OSHA & NIOSH Exposure Limits for Silver Metal and Soluble Compounds[34]

OSHA Permissible Exposure Limit	TWA 0.01 mg/m^3
NIOSH Recommended Exposure Limit	TWA 0.01 mg/m^3

TWA is the total weight average over an 8hr period.

The EPA also regulates the amount of silver. For drinking water the EPA has silver listed under secondary standards, which are non-enforceable guidelines that regulate contaminants that can cause cosmetic effects. The Clean Water Act (CWA) regulates the discharge of materials to the sewer through the EPA's Effluent Guidelines. And it is also regulated under the hazardous waste program in conjunction with the Resource Conservation and Recovery Act (RCRA).[35]

Table 4. EPA Exposure Limits on Silver

National Secondary Drinking Water Regulations[36]	0.1 mg/L	
Current National Recommended Water Quality Criteria, Priority Pollutants Criteria Maximum Concentration[37]	Freshwater	3.2 μg/L
	Saltwater	1.9 μg/L
Effluent Limitations Guidelines for the Centralized Waste Treatment Point Source Category[38]	Daily maximum	0.12 mg/L (ppm)
	Monthly maximum average	0.0351 mg/L (ppm)

The National Recommended Quality Criteria lists silver as a "Priority Pollutant" the above limits are determined for the "Criteria Maximum Concentration" (CMC) which is an estimate of the amount of silver in the surface water to which an aquatic community can be exposed briefly without resulting in an unacceptable effect. The EPA also lists "Criterion Continuous

[34] National Institute for Occupational Safety and Health. (2005, September).
[35] U.S. Environmental Protection Agency. (1986, June 26). *Silver in Wastes and in Sewer Discharges from the Photo-finishing Industry* (RCRA Online No. 12674). Retrieved June 23, 2008, from RCRA Online Access: http://www.epa.gov/rcraonline/
[36] U.S. Environmental Protection Agency. (n.d.). *Drinking Water Contaminants.* Retrieved June 23, 2008, from http://www.epa.gov/safewater/contaminents/index.html
[37] U.S. Environmental Protection Agency. (n.d.). *Current National Recommended Water Quality Criteria.* Retrieved June 23, 2008, from http://www.epa.gov/waterscience/criteria/wqctable/#cmc
[38] U.S. Environmental Protection Agency (2000, December 22). *Effluent Limitations Guidelines, Pretreatment Standards, and New Source Performance Standards for the Centralized Waste Treatment Point Source Category.* (Volume 65, No. 247, DOCID:fr22de00-25). Retrieved June 27, 2008, from Federal Register Online via GPO Access: http://www.gpoaccess.gov/index.html

Concentration" (CCC) for various pollutants, which is the highest concentration of a material that an aquatic community can be exposed indefinitely without resulting in an unacceptable effect. They do not provide a CCC concentration for silver.[39]

Finally, the EPA provides guidelines for effluent levels of silver for centralized waste treatment centers. These regulations would be applied to sewage treatment plants that would treat wastewater. The daily and monthly maximums are listed under what is known as Best Practicable Technology (BPT) limitations or the best available technology for pollution control at a reasonable cost for implementation and operation under normal conditions.

It is not entirely clear what effect silver nanoparticles will have on the human body. There are some unique properties that have been demonstrated with the use of nanosilver in the medical field.

The majority of the nanosilver products use silver because of silver's antibacterial properties. Antibacterials, which are a form of pesticide, fall under the regulation of the EPA's Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). There is an important distinction when talking about products that contain pesticides: only products providing antibacterial protection that make a <u>claim</u> of being antibacterial must be regulated. This is a loophole which, many companies are using to avoid registering their products. Pesticides used to "protect" a product, not provide antibacterial benefit through use and "devices," do not have to be regulated through FIFRA. In September 2007 the EPA clarified its stance on ion generating products such as the Samsung washing machine that is designed to kill bacteria on clothing by releasing silver ions. It stated, "a product that uses only physical or mechanical means to trap, destroy, repel, or mitigate a pest (including microbial pests) is a device and is not required to be registered (though its production and labeling are regulated). However, if the product incorporates a substance or mixture of substances intended to prevent, destroy, repel, or mitigate pests, then it is considered to be a pesticide and is required to be registered."[40] This should place many of the products

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[39] U.S. Environmental Protection Agency. (n.d.). *Current National Recommended Water Quality Criteria.*
[40] U.S. Environmental Protection Agency (2007, September 21). *Pesticide Registration: Clarification for Ion Generating Equipment.* Retrieved June 28, 2008, from http://www.epa.gov/oppad001/ion_gen_equip.htm

currently on the market under the regulations pertaining to FIFRA if an antibacterial claim is made, however, very few if any of these products have been registered.

In November 2006 the Natural Resources Defense Council (NRDC) sent a letter to the EPA calling for the immediate registration and regulation of nanosilver as a pesticide under FIFRA. They made reference to over 40 consumer products that were on the marketplace and unregulated. Their main concern was for the toxic effect of nanosilver on the aquatic ecosystem.[41] The EPA responded in 2007 with the aforementioned notice on products that use ions as antibacterials. Then in March 2008 the EPA took action against one company, ATEN Technology, Inc. fining them $208,000 for making 'nano coating' pesticide claims on computer peripherals sold by their subsidiary IOGEAR. An EPA representative, Katherine Taylor, was quoted as saying, "[w]e're seeing far too many unregistered products that assert unsubstantiated antimicrobial properties."[42] This action, however, was only against one company and a handful of products out of hundreds.

In May 2008 the International Center for Technology Assessment (CTA) and a coalition of consumer, health and environmental groups submitted a legal petition to the EPA demanding the EPA stop the sale of 260 potentially dangerous nano-silver products. They cite the hazard of bulk silver to the environment and the unknown effects of nanosilver on both human health and the environment. Some of the major concerns were with the pervasive use of antibacterials that will spur the emergence of resistant strains and the ability of nanosilver to effect wastewater beneficial bacteria populations. One important factor they would like the EPA to deal with is

> "to clarify that nano-pesticides, such as nano-silver products, are new pesticide substances that require new pesticide registrations, with nano-specific toxicity data requirements, testing and risk assessments. Nano-silver must be classified as a separate substance than macro-silver based on the nanomaterial's capacity for fundamentally unique and different properties and because nano-silver many new antimicrobial uses are not previously registered silver uses.[43]

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[41] Sass, J. & Wu, M. C. (2006, December 22). *Registration of Nanosilver as a Pesticide under FIFRA (*Natural Resource Defense Council). Retrieved June 29, 2008, from www.nrdc.org/media/docs/061127.pdf

[42] Environmental Protection Agency. (2008, March 5). *U.S. EPA fines Southern California technology company $208,000 for "nano coating" pesticide claims on computer peripherals.* Retrieved June 29,2008, from http://yosemite.epa.gov/opa/admpress.nsf/2008%20Press%20Releases?OpenView

[43] International Center for Technology Assessment. (2008, May 1). *Executive Summary: Legal Petition Challenges EPA's Failure to Regulate Environmental and Health Threats from Nano-Silver.* Retrieved June 29, 2008, from http://www.icta.org/global/actions.cfm?page=15&type=364&topic=8

This is an important distinction because as of now, nanosilver is regulated just as bulk silver is, under the same concentration levels. Testing for EPA pesticide registration depends a lot on the uses of that product. If a company made a product that would end up in bodies of water, toxicology studies on aquatic organisms would be required during the registration process. The EPA bases the testing of a substance on the most toxic form of that substance. For the case of silver, the silver ion is considered the most hazardous. The current levels of silver in the regulations are based off of tests done with silver nitrate, which easily dissociates into silver ions when placed in water.

These “unique” properties that nanosilver have may be drastically varied by the size of the particle and water composition as shown in this following risk analysis study. Some of the questions that this report raises but does not resolve are: “Can governmental organizations adapt quickly to these emerging technologies such as silver nanotechnology? Do they have the tools to assess these new products and make informed decisions on the appropriate allocation of research funds and enforcement resources?” This is where the use of expert elicitation in adaptive management and anticipatory government can be useful. The following method demonstrates how expert elicitation can help to assess silver nanotechnology in the exposure scenarios, the risk triggers, and the benefits, and help to identify the knowledge gaps, regulatory issues and areas of needed research.

Methods

In this project a practical approach was taken to eliciting expert *opinion* to provide an accurate risk assessment of silver nanotechnology as it exists today. This method is divided into five stages: *contribution,* a source of data that the interactional expert brings to the trading zone to help frame the problem and focus the discussion; *elicitation,* the process by which the experts are interviewed and data is collected; *synthesis*, where the interviews are reviewed and critical criteria are defined and justified; *ranking* the process where particular criteria are ranked according to expert judgments; and *analysis* of the combined scores as well as the consideration of non-ranked factors including expert rationales.

Table 5. Method Overview

Contribution	Data that is brought by the interactional expert to the trading zone.
Elicitation	Experts are interviewed and data is collected.
Synthesis	Interviews are reviewed and criteria are defined and justified.
Ranking	Criteria are coded and ranked.
Analysis	Data is compiled and non-ranked factors are included.

In the particular case of silver nanotechnology, a technology that is one of the most prominent uses of nanotechnology on the consumer market, it was decided that a good first step would be to access the current uses of the technology. This was carried out through the creation of a Silver Nano Commercial Inventory (SNCI) that would help frame where silver nanotechnology was and where it is going. Data from this type of study would also be helpful in incorporating real-world information into isolated research initiatives, which then become *a contribution* the interactional expert can make to a broader conversation with the experts.

The next stage, after developing and filling the database, was to develop an appropriate elicitation model. Due to the investigative nature of the study and the use of experts across various disciplines, it was decided that the best approach would be to use a non-restrictive interview format. This allowed for each expert to expand on the areas most closely associated with their expertise. Using the data from the SNCI, an interview format was set, experts were selected and interviews were held.

In the third stage, *synthesis*, using a set of exposure scenarios and Risk Triggers (RT) defined in the previous work of Shilpa Deshpande for nanotechnology and the interviews, a table of exposure scenarios and Risk Triggers were reworked for the case of silver nanotechnology.[44]

The final two stages, *ranking* and *analysis*, involved organizing the data from the interviews, ranking the appropriate exposure scenarios and Risk Triggers and analyzing them. The key factor in both of these stages was not to lose valuable information contained within the experts rationales.

Contribution: The Silver Nano Commercial Inventory (SNCI)

A Silver Nano Commercial Inventory (SNCI) was created in the summer of 2007. This was a project conducted in conjunction with the Project on Emerging Nanotechnologies at the Woodrow Wilson International Center for Scholars in Washington D.C. The purpose of this database was not only to evaluate nanosilver products currently on the market and aid in understanding what information companies were and were not providing, but it was intended be the foundation for our expert elicitation study by providing the experts with current up-to-date data on how silver nanotechnology was being utilized. It was important that the interactional expert could approach the interviews with an overview of what information companies were making available and understand product trends.

A full copy of the is provided in the Appendix. The database can be accessed at the Project on Emerging Nanotechnologies website found at (www.nanotechproject.org).

In the original database twenty different fields were created for each product. The fields used were decided upon by a group at the Project on Emerging Nanotechnologies, primarily

[44] Deshpande, S. (2007). *A framework to identify risks from nanotechnology-enabled products..* Unpublished masters thesis, The University of Virginia, Charlottesville, Virginia, The United States.

based on both what information was deemed important and what information was out there as discovered in preliminary searches. This included basic information such as: product name, company, country, and product website, and more detailed information such as category, type/form, size, concentration of nanosilver, rate of Ag+ release, expected product lifetime, precursor product (Y/N)*, dispersive (Y/N), number of similar product models, structure of particle and/or substrate, synthesis method, application (how the nanotechnology is used), manufacturers recommended uses, antibacterial claims, regulation information and product testing information. Together, these gave an overview of what the company was producing, where it would be used and what claims were being made.

*Precursor products represent products that are used in the fabrication/production process of a separate end product.

The database was entered over the summer of 2007. The total number of products compiled came to 240, out of which 214 were general commercial products and 26 were precursor products. Products ranged from household cleaners, personal hygiene items and ant-odor clothing to antibacterial coatings for hardware and office supplies. A total of 65 companies were involved in the design and manufacturing of the commercial products listed, representing eleven countries: China, Germany, Iran, Japan, New Zealand, Singapore, Korea, Taiwan, Thailand, the United Kingdom and the United States of America.

To give a brief overview of what trends emerged; displayed below are four of the graphs from the analysis report. These can be found in the analysis of the SNCI at the Project on Emerging Nanotechnologies website (www.nanotechproject.org).

In the first figure the products are divided by type/form. This is the classification scheme that was predominately referred to when interviewing the experts. In this case, each product is only counted once and the commercial products have been separated from the precursor products.

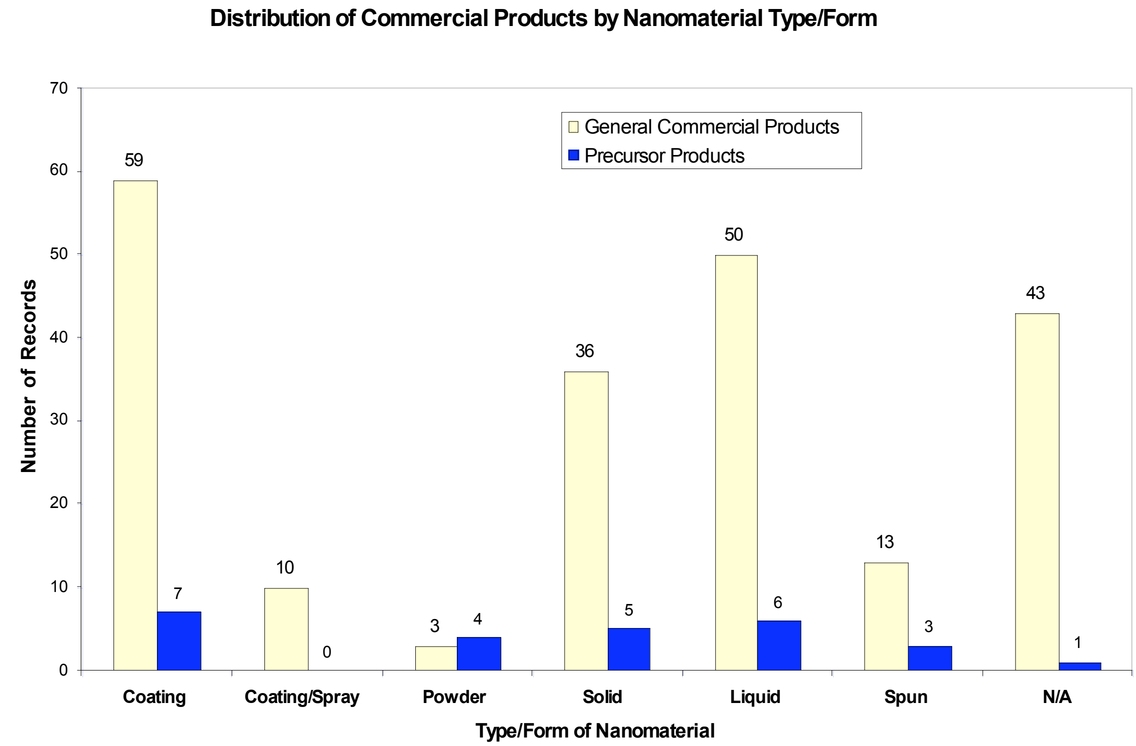

Figure 3. Distribution of Commercial Products by Nanomaterial Form[45]

As it is shown, the coating product type is the most common with the liquid form or colloid based products come in at a close second. The less frequent items are those within the powder and coating/spray type. The coating/spray type are those products that are in spray form and are used to create coatings. Spun is an application of nanosilver on fabrics, the exact method of application is unclear.

The second figure displays the division of the 240 products by category. In this case, products can be listed under more than one category such as a colloidal silver supplement which is recommended as a daily supplement (Food & Beverage) and as a skin treatment (Health & Fitness). Health and Fitness is the overall largest group and consists of the four subcategories: personal care, sporting goods, clothing and cosmetics.

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[45] Fauss, E. (in press). Silver Nanotechnology Commercial Inventory Analysis. Washington, DC: Woodrow Wilson International Center for Scholars Project on Emerging Nanotechnologies.

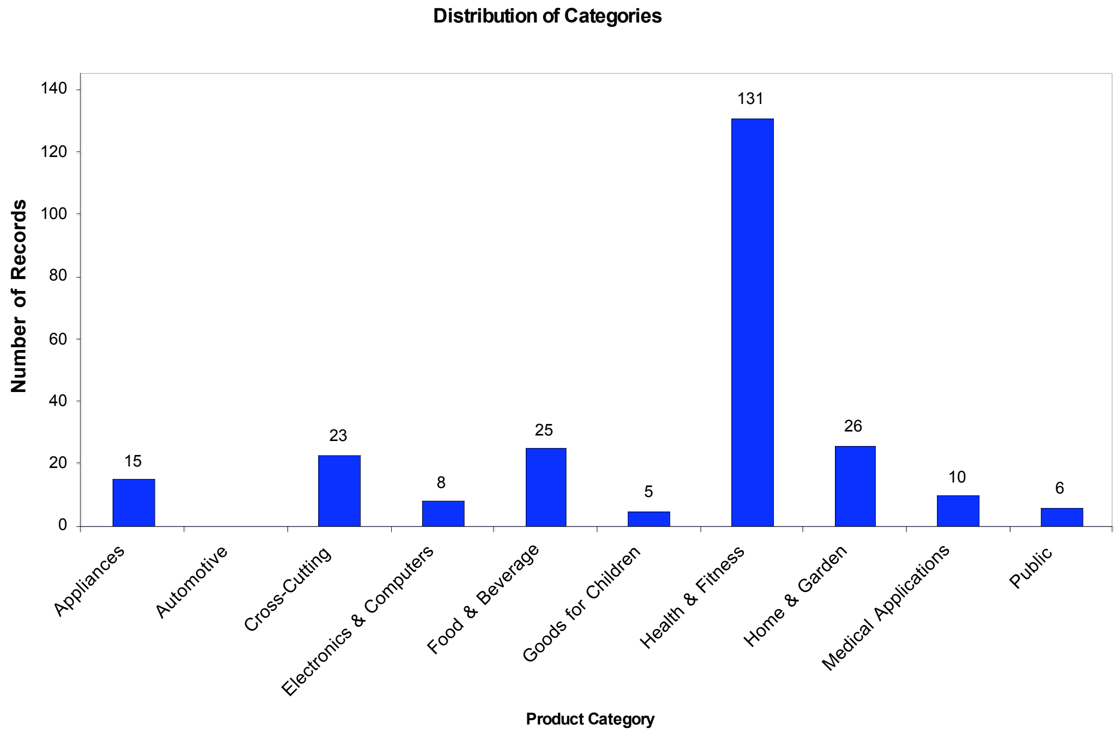

Figure 4. Distribution of Product Categories[46]

In this following figure, products were divided by the company's country of origin. The expert elicitation primarily was focused on investigating silver nanotechnology within the United States which happens to produce the majority of silver nanotechnology products (117). It should be noted that this bias could be due to the nature of the internet searches that were English based.

[46] Fauss, E. (in press).

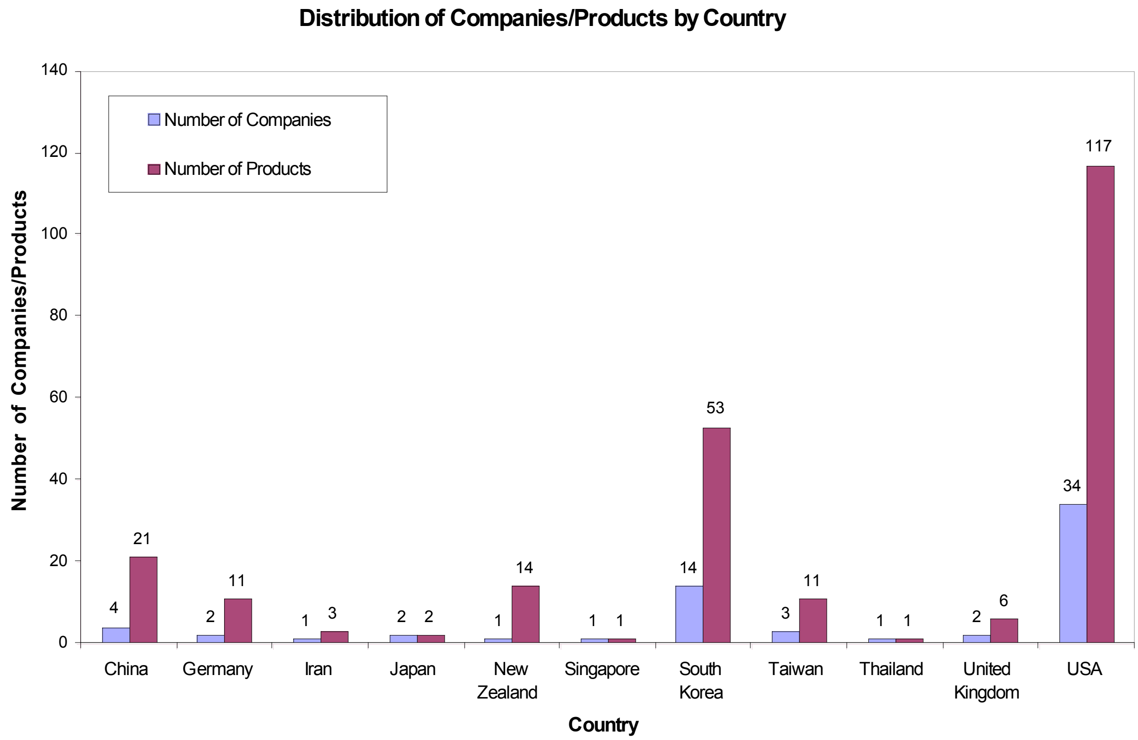

Figure 5. Distribution of Commercial Products by Country[47]

This final figure from the SNCI analysis gives an overall view of what types of information the companies were and were not providing. Percentages of data available are displayed next to each search criteria. Data for a particular criterion such as product testing could be anything ranging from a reference to a company that performed certain toxicology tests to a full report, results included, on a particular product.

Some important highlights of this figure have to do with antimicrobial claims and number of dispersive products. It can be seen that 88% of the companies made antimicrobial claims. Specifically in the United States 108 of 117 or 92% made antimicrobial claims. Those are claims that would suggest the majority of those products should be regulated under FIFRA.

[47] Fauss, E. (in press).

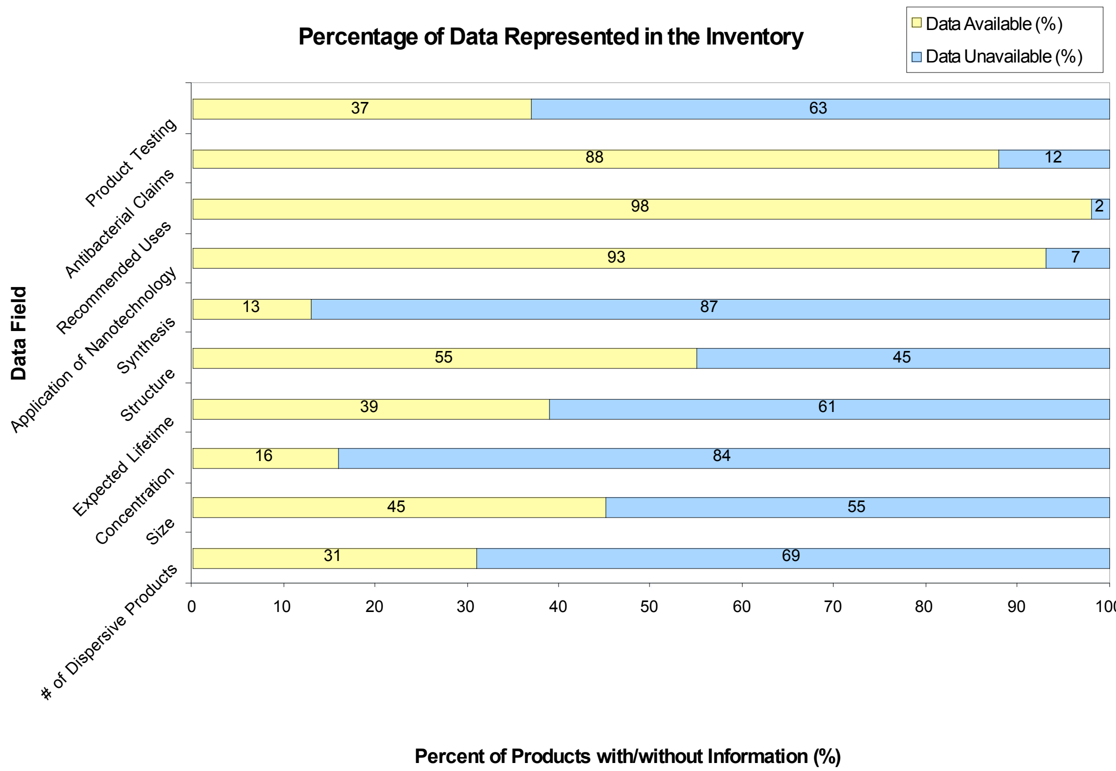

Figure 6. Percentage of Data Represented in the Inventory[48]

Overall the SNCI proved to be a useful illustration of silver nanotechnologies currently on the market. The full analysis document of the inventory can be found on the website for Project on Emerging Nanotechnologies (www.nanotechproject.org). In addition to the results listed in the analysis there were three general observations developed during the creation of the inventory. They were an acknowledgement of a compounding effect or various non-point source contaminations, a lack of scientific definitional clarity within the industry and a low level of transparency to the consumer. These are further discussed in the appendix section "SNCI Independent Conclusions."

[48] Fauss, E. (in press).

Elicitation

Pre-Elicitation

A handout was developed to inform the expert about both the nature and structure of the interview. It was given to each of the experts before the interview and an opportunity for asking questions about the handout was provided. This document shows the linking thread that connects each of the interviews. It helped standardize the elicitation method by providing the same information to each expert. The handout consisted of four parts, the interview outline accompanied by a brief memo, broad cases of nano silver applications, a real world example of each of those cases and finally a list of example exposure scenarios and Risk Triggers.

The interview outline as presented to the experts is shown below. Flexibility was incorporated into the elicitation model. This was done by presenting an interview format that allowed the interactional expert to focus the direction of the interview upon the experts specific area of expertise. For instance, if an expert had specific experience with the geochemical cycling of nanoparticles in the environment, the interactional expert would direct the conversation towards the exposure scenarios and Risk Triggers associated with nanosilver in the environment.

Table 6: Interview Outline

1) EXPERTISE: I will ask you to briefly describe, on tape, what your area of expertise is and what, if any, experiences you have had with nanotechnology, silver or silver nanotechnology.
2) EXPOSURE, HAZARD & RISK TRIGGERS We will then review a list of scenarios of silver nanotechnology. (See attached list of scenarios and example products) We will explore different methods of use ("exposure") and disposal ("hazard") and review a list of Risk Triggers. To give you an overview of the information we will be seeking in our conversation, two excel pages are provided at the end of the document which contain a selection of possible topics. Not all of these topics will be covered due to time constraints, but any expert advice or insight that you can provide will be welcome.
3) REGULATIONS, KNOWLEDGE GAPS & RESEARCH In the final portion of the interview I would like to hear your opinion on what types of regulations might come in to play or influence the technologies we will have discussed and what information might be pertinent in the regulation of these technologies. I would also like to hear where you think "knowledge gaps" lie and, if you could, where you would recommend research funds be directed.

Once the interactional expert had finished reviewing the expert's area of expertise, associated exposure scenarios and Risk Triggers, the experts were asked to contribute other areas of knowledge and experience. This was presented in an open ended manner. Experts were asked if they knew any regulatory issues that should be considered, if there were any critical knowledge gaps that would be important in evaluating silver nanotechnology and finally, what area if any would they recommend research in. While silver nanotechnology benefits were not listed on the interview outline, each expert was asked what, if any, are beneficial uses of silver nanotechnology? This concluding section of the interview was designed to allow the expert to contribute any key pieces of knowledge or insight into the risk analysis of silver nanotechnology.

The second part of the handout dealt with providing database information to the expert. In the SNCI one of the ways to classify products was by type/ form. As mentioned before these categories were: coating, liquid, solid, spun, coating/spray, and powder (in order of most to least common as seen in Figure 3. Distribution of Commercial Products by Nanomaterial Form) For the information packet more specific cases were presented: coatings incorporating nanotechnology, colloidal silver, homeopathic nanosilver applications, spun nanosilver applications, solid nanosilver applications and nanosilver powder. A description, its prevalence, uses and an example was given for each case. These cases were designed to capture a sample of what the SNCI analysis stated, such as what types of products were out there, and what types of information the companies were providing about their products.

An example of each of these cases were chosen from the database and presented in the handout. Products were selected to help demonstrate the breadth and variety of the commercial products that contain silver nanotechnology.

As mentioned before, the tables provided at the end of the handout were adapted versions of tables develop by a previous University of Virginia Masters student, Shilpa Deshpande. The for exposure scenario considered: inhalation, skin absorption, ingestion, fresh water entrainment, salt water entrainment, and air release for both use and disposal scenarios.

The risk trigger table listed a few criteria such as: coating/matrix stability, multiple disposal pathways, dispersibility, toxicology, particle size, and susceptible population to list a few.

<u>Selection of the Experts</u>

A list of 25 experts was drawn up divided into groups from government, industry, and academics. The selection was based on references provided from contacts at the Woodrow Wilson International Center of Scholars, contacts from the research group at the University of Virginia and selected experts from articles written on silver nanotechnology. When selecting experts from limited sources it is important to realize the element of dependence that can occur between experts. Hammitt and Shlyakhter (1999) commented on dependence between experts,

> "Dependence among experts is both central to proper combination of expert judgments and difficult to evaluate. Judgments of multiple experts about a parameter can be extremely informative when those judgments are probabilistically independent, conditional on the 'true' value. If, as is often the case, experts share much of the knowledge relevant to estimating a parameter value (e.g., a common scientific literature), the information contained in the union of multiple experts' judgments may be little more than that contained in a single multiple expert's judgment (in effect, each expert may report an idiosyncratic perception of a consensus)."[49]

In this case, dependence was not taken into account when calculating final scores. Due to the nature of silver nanotechnology such that there is little literature in general it would be hard to discern levels of dependence. It could be said that four of the final experts had a high level of dependence. However, even with this dependence, they did not always agree.

The experts were approached with an introductory letter of inquiry as to whether or not they would be interested in participating in the study. If the expert responded in an affirmative manner, the handout was sent followed up by a phone call in which the study was further explained and questions were answered. From this point an interview date was set and then confirmed.

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[49] Hammitt, J. K., & Shlyakhter, A. I. (1999). The Expected Value of Information and the Probability of Surprise. *Society for Risk Analysis*, 19(1), 135-152.

A total of 24 experts were approached with only 10 responding in an affirmative manner. Two experts were used as preliminary test subjects for the elicitation method. They responded positively to the method. They were included in the final analysis because no major changes were made to the handout or interview method. The following two tables list the experience and education of the 10 experts used in this study. It should be noted that the tables do not correspond directly, in other words, the individual who works at the EPA does not necessarily have a degree in biology.

Table 7. Sample of Experts: Experience

Experience
Government
- EPA Office of Pesticides
Industry
- photography industry ~30 years
Non-Profit
- monitor regulation of pesticides
Research
- crystallography, mineralogy, geochemistry, biogeochemistry
- biological and chemical oceanography, biogeochemical cycling
- aquatic toxicology of silver and various silver compounds
- acute and chronic mechanism of toxicology of silver in fish
- water purification using colloidal silver
- vascular cell biology, with an interest in nanopatterned and nanostructured surfaces
- surface modification of polymers and metals at the nano level

Table 8. Sample of Experts: Education

Education
- Bioengineering
- Biologist (x2)
- Chemistry, polymer chemistry and biomaterials
- Civil and environmental engineering
- Earth science, geological and environmental sciences
- Fish physiologist and toxicologist
- Molecular eco-toxicologist
- Neurotoxicology, metal and heavy metal toxicology
- (training not given)

The final step in preparation for the interviews involved reviewing the expert's background and preparing specific questions that would pull from the experts experience. Various news and journal articles as well as institutional webpages were investigated to help the interactional expert understand the context from which the expert was coming from. This helped to avoid gaps in the conversation and helped guide the interviews in a constructive manner.

The Interviews

The elicitation portion of this risk assessment was conducted in most cases (except for 3) over the phone. The interactional expert was present along with the interviewee and occasionally another member of the research team. The interviews ran no longer than one hour and were guided by the interactional expert. Each interview followed the method as outlined in the handout where the order of topics covered included: the expert areas of expertise, the exposure, hazards and Risk Triggers and finally any regulatory issues, knowledge gaps or areas of future research. The interviews were performed in a discussion format where the experts were encouraged to share as much experience and knowledge as possible on the mentioned topics.

To encourage the experts to talk more freely, each interview was confidential. The experts were assured that all identifying information would be removed from examples from the interviews and records of what had been disclosed would stay within the research group.

For data collection purposes and scoring, each of the interviews were recorded and then transcribed. When the study is complete these records, identifying experts with their comments will be destroyed.

Synthesis

Once the data had been collected, both the interactional expert and another member of the research group, Jennifer Seage, reviewed each transcript forming a list of identified exposure scenarios, Risk Triggers both exposure and hazard related, knowledge gaps, proposed research, regulation issues and benefits. From this, a refined table of general exposure scenarios and Risk

Triggers was created. The following tables display first what was presented to the experts in the handout, and then the general tables that were derived from the interviews.

Table 9. Exposure Scenarios Presented in Handout

Exposure Scenario
Inhalation
Skin absorption
Ingestion
Fresh Water Entrainment
Salt Water Entrainment
Air Release

The handout suggested the above exposure scenarios for both a use and disposal case for each product group. It was discovered that two other general exposure scenarios arose within the interview process and those were chronic exposure and the ability for nanosilver to migrate though the food chain. This reflects the types of experts that were involved in the interview process. The air release scenario was removed because it was captured within the inhalation scenario.

Table 10. General Exposure Scenarios Derived from Interviews

Exposure Scenario
Absorption (dermal) - The level of risk of exposure to nanosilver through dermal absorption.
Inhalation/ Absorption (lung) - The level of risk of exposure to nanosilver through inhalation or absorption through the lung.
Ingestion - The level of risk of exposure to nanosilver through ingestion. This can include ingestion from a food source or from the use of the product.
NS release into aquatic environment - The level of risk of exposure that nanosilver is released into the aquatic environment.
NS migrate through the food chain - The level of risk that nanosilver will migrate though the food chain through bioaccumulation across species.
Chronic exposure - The level of risk of chronic exposure to nanosilver. This includes the potential for chronic exposure in the environment and the risk of exposure from multiple consumer products.

Table 11. Risk Triggers Presented in Handout

Exposure Related Risk Triggers
Coating/Matrix stability - Are there scenarios where the nanoparticle is freed from the polymer matrix/the coating?
Media dependent property - Does the material behave differently in water, air etc?
Free nanoparticles - Would there be scenarios where the nanoparticles could be biologically available within the product lifecycle?
Used with other products - The effect of the nanomaterial would probably be different if the product is used with other products.
Multiple Disposal Pathways - Is the product disposed in different ways, each with a different degree of effect on the environment? Recycling would have the least effect.
Dispersibility - Does the material disintegrate into free nanoparticles in water? A hydrophobic coating would probably make it less dispersible?
Hazard Related Risk Triggers
Toxicology - Is there enough toxicology information currently available?
Particle size < 100nm
High aspect ratio - does the shape enhance transport?
New product - Is the product itself a new nano-application or is the nano material used only for performance enhancement?
Catalytic Property - Does silver catalyze anything?
Susceptible population - Are there scenarios during the product use where significant number of people would be more susceptible to have a higher degree of effects?
Antibacterial - Does the nanomaterial kill/harm useful bacteria in the environment or the human body?

In regard to the Risk Triggers, many of the RTs presented to the experts remained, however there were a couple, the “media dependent property” and “new product,” that simply did not apply to the use of nanosilver in the products presented. Media dependent property was transformed into exposure route dependent because the only thing that appears to change when silver is in different environments is its level of antimicrobial action. As for the new product RT, silver as demonstrated in the database is used primarily as an antimicrobial or as a supplement. As for the use as an antimicrobial, it is not a new novel use and it is meant to improve product performance. “Susceptible Population” was covered in each interview and will be reviewed later in the Results section.

Table 12. General Exposure Related Risk Triggers Derived from Interviews

Exposure Related Risk Triggers
Bioavailability - Could the nanosilver display bioavailability characteristics? Bioavailability is the ability of a substance to be absorbed and used by the body. (This has to do with migration of nanosilver into an organism. The more bioavailable it is, the more organism have the chance to be exposed. This incorporates sizes as a factor.)
Rate of Ag+ release - Is the rate of silver ion release an important factor in evaluating exposure? (This factor is important because silver ions are considered one of the most toxic forms of silver. If the experts acknowledge this factor as being important, it could be key in determining a products overall risk. Also, in terms of different silver applications, how does this exposure change? This could be media dependent)
Rate of agglomeration - Is the rate of particle agglomeration (from nano to not nano) an important factor in evaluating exposure? (There is a dispute as to whether particle agglomeration renders a particle non toxic, but if this is the case, then the rate of agglomeration will be an important factor in determining exposure scenarios.
Coating/ Matrix stability - Are there scenarios where the particle is freed from the coating / matrix? (The issue as to whether coating / matrix stability is an important factor in evaluating a product was addressed here. While many experts could not directly comment on individual products they were asked to comment on possible coating / matrix scenarios.)
Multiple disposal pathways - Does the product disposed in different ways contribute to different patterns of exposure, each with a different effect on the environment? (This factor focuses on the issue of disposal / end of life treatment of a product. This addresses the multiple disposal pathways, asking the expert to list them and identify the areas of concern such as sewage treatment.)
Exposure route dependent - Does the route of a product help determine its exposure? (Can environmental factors such as water quality or soil content effect the overall exposure to nanosilver? Silver ions are highly reactive and will bind quickly with sulfur groups, especially in organic matter, minimizing their ability to cause harm, however it is unclear as to whether the same applies with these new applications of silver nanotechnology.)

In regards to silver, the rate of Ag+ or silver ion release is a critical factor when determining exposure.Silver ions as mentioned before are the most toxic form of silver. As reviewed later in the material reactivity, the release of silver ions is one of the main mechanisms of antibacterial action of nanosilver.

Table 13. Hazard Related Risk Triggers (Material Properties) Derived from Interviews

Hazard Related Risk Triggers: Material Properties
Particle size <100nm* - Does the particle size factor into the hazard of the nanosilver application? (Nanotechnology is generally considered arbitrarily from 1-100nm. The experts were asked how size played a part in the hazard of nanosilver.) *contained within the bioavailability factor in exposure related Risk Triggers.
Particle shape - Does the particle shape factor into the hazard of the nanosilver application? (Does the nanosilver display different reactivity characteristics due to shape?)
Aggregated nanoparticles - Are the properties of the free silver nanoparticles different from the aggregated forms of the nanoparticle? (This asks the experts to consider the hazard of free nanosilver vs. the aggregated form of the nanoparticles.)

Table 14. Hazard Related Risk Triggers (Material Reactivity) Derived from Interviews

Hazard Related Risk Triggers: Material Reactivity
Catalytic action - Is catalytic action a factor in nanosilver antibacterial action? (In some cases it is thought that silver reacts with oxygen to produce antimicrobial activated oxygen.)
Ag^+ release - What is the hazard of nanosilver releasing silver ions in the environment? (Before we looked at the exposure side of these particles releasing silver ions, here we are looking at that associated hazard due to release. While Ag^+ on their own are not considered a large threat in the environment (due to their fast reactivity), do silver nanoparticles pose an environmental hazard through Ag^+ release? This may be dependent on the media to which the particle is exposed.)

In the exposure scenario section, the expert's opinions are elicited on the level of risk of exposure. Here in the hazard-related risk trigger section, the expert's opinions are elicited on the hazard level of a particular form of exposure.

Table 15. Hazard Related Risk Triggers (Material Toxicity) Derived from Interviews

Hazard Related Risk Triggers: Material Toxicity
Dermal toxicity - Hazard level due to dermal toxicity. (How dangerous is nanosilver in dermal contact?)
Toxicity in lung - Hazard level of nanosilver through entry into the lung. (How dangerous is nanosilver if absorbed in the lung or gill?)
Toxicity from chronic exposure - Hazard level for chronic exposure to nanosilver. (How dangerous is it to be chronically exposed to nanosilver, even at a low dose?)
Toxicity from ingestion - Hazard level for ingestion of nanosilver. (How dangerous is nanosilver is ingested, either through diet or another means?)
Toxicity in Salt Water - Hazard level of nanosilver in a marine environment. (How dangerous is nanosilver in salt water? Why is it less or more toxic than in fresh water?)
Toxicity in Fresh Water - Hazard level of nanosilver in a freshwater environment. (How dangerous is nanosilver in fresh water? Why is it less or more toxic than in salt water?)

Ranking

After carefully defining the exposure scenarios and Risk Triggers, it was necessary to code the interviews to help establish what were the greatest risk for exposure and greatest hazards. Both the interactional expert and another member of the research team coded the interviews giving a ranking of 1-5, one being no risk of exposure or no hazard and five being high risk of exposure or high hazard, or non-applicable if the expert did not comment on that particular criteria.

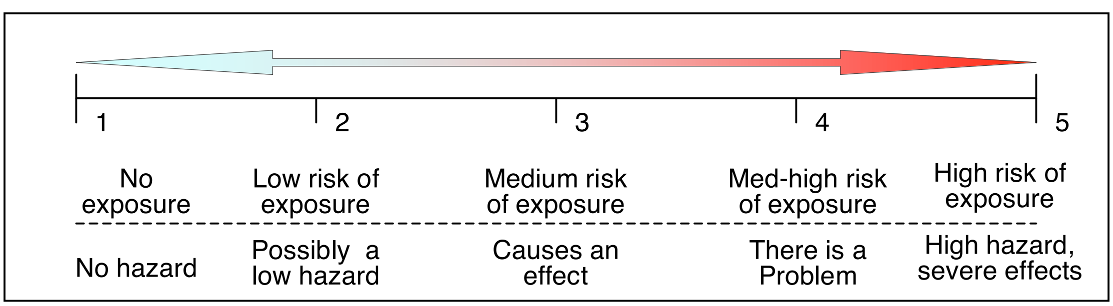


Figure 6. Coding Scale

Due to the discussion format of the interviews, the experts were not specifically asked to rank a scenario or hazard on a 1-5 scale. The coders determined each ranking based on quotes from the interviews. If there was a disagreement between rankings, it was discussed and a final ranking was selected by the interactional expert.

There are difficulties that are naturally inherent to coding expert opinion and belief. Going back to the Reliability of theory of Knowledge, the two types of knowledge that are dealt with in expert elicitation are *pistis* the “intellectual and/ or emotional acceptance of a proposition” and *eikasia* “in which knowledge is based on inference, theorization, or prediction based on incomplete or reliable evidences.”[50] This can be seen in the fact that experts often have a belief (*pistis*) and then make a judgment or opinion off of that belief (*eikasia*). The expert rarely makes the distinction between the their opinion and the foundation of their assumptions. For example in a quote, “Silver nanoparticles, a lot of it might get in the environment but in most environments it may never reach concentration levels that will dramatically effect the ecosystem or human health,” there exists an assumption that there will not be significant exposure of nanosilver to the environment, and a judgment that this amount will not effect the ecosystem or human health. It was decided that in this elicitation, the combination of the expert’s assumptions and judgments were both important.

There were two stages of coding. At first each expert was ranked separately by two coders.* Scores within subsections such as exposure scenarios were cross checked to check for appropriate scaling. After a break and some distance from the interviews, the transcripts were revisited. This time the rankings for each criteria, such as ingestion, were reviewed between the various experts to check for consistency in ranking. The interactional expert determined the final official ranking after reviewing results with the research team.

[50] Ayyub, B. M. (2001). (pp. 38).

Table 16. Stages of Coding

First Coding: Compare between exposure scenarios	Second Coding: Compare each criteria between experts
Expert 1	Ingestion
Absorption (dermal)	Expert 1
Inhalation / Absorption (lung)	Expert 2
Ingestion	Expert 4
NS release into aquatic environment	Expert 6
NS migrate through the food chain	Expert 7
NS chronic exposure	Expert 10

*One expert was interviewed in Spring 2008, this expert did not get ranked by the second coder. Ranking for this individual was reviewed twice by the interactional expert.

The next step after the general ranking of each criterion was to infer rankings to three product types, colloids, coatings and powder. This was done by reviewing each interview separately and investigating the specific concerns that were raised for each product type, exposure scenario and hazard related Risk Triggers. For instance, if an expert said “fine powder, you are absorbing it, high risk through use and disposal” the powder product category would be ranked as high for all exposure scenarios. The ranking scale of 1-5 for these inferred rankings are High (5), Medium (3) or Low (1), a less sensitive scale. Product rankings are never higher than the general rankings unless there was a specific concern raised by the expert for that particular product category.

Originally in the handout, there were six product categories that were based on the products found within the SNCI, coatings, colloidal silver as an additive, colloidal silver in homeopathic applications, spun, solid and powder nanosilver applications. In the interviews the product categories that were focused on were the colloids, coatings and powder. This is why they were chosen as the product categories to rank. Colloidal silver as an additive and as a homeopathic remedy were lumped together. There was little interest in solid applications and the Spun category seemed to lack the necessary clarification. This in part is due to the nature of the category, not many companies would specify how the nanosilver was adhered to the fabrics. The spun category in the interviews was often treated as a coating application by the experts.

Analysis

In the case of combining scores for each criteria, Clemen and Winkler (1999) said, "[w]hen little information is available about the relative quality of and dependence among the experts' probabilities, a simple rule such as a simple average is recommended."[51] So a simple average for each criterion was calculated. If a particular expert did not comment on that topic they were not factored into that average. The result is that each criterion has a different sample of experts. Standard deviations were calculated for each. The Data Tables and Calculations can be found in the Appendix.

[51] Clemen, R. T., & Winkler, R. L. (1999).

Results

Exposure Scenarios

One of the most significant issues concerning the use of silver nanotechnology does not stem from any one product; it comes from the compounding effect of using nanosilver in a wide array of applications. Silver nanoparticles as a Prof. at Virginia Tech, Michael Hochella (personal communication, May 7, 2008) who specializes in nano-geosciences points out in a casual conversation, “I am not aware that silver occurs naturally as a nano material. It may but to my knowledge it’s never been reported in the literature and I have never seen it. So when one talks of nanosilver, one is talking about man made material.” Exposure to nanosilver will originate not only from specific point sources such as industrial effluent but also from various non-point sources. In this section different exposure scenarios were explored with the experts. The following section reviews the number of experts that responded to each criterion, the average scores and their standard deviations from the mean. A sampling of quotes is provided for each of the ranking schemes. These help demonstrate the justification behind the scores that were assigned to the experts. A more detailed analysis of each criterion is discussed after each set of quotes.

When the experts were shown the various product types, they were asked to imagine what exposure scenarios might exist with nanosilver and what was the associated level of risk which came with that type of exposure. Below is a chart which displays the average ranking of each exposure scenario denoted by the black rectangle, one standard deviation away from the mean represented by the black line and the number of experts who responded to that scenario shown with the blue bar. (See Appendix: Data Tables and Calculations for the calculations of standard deviation)

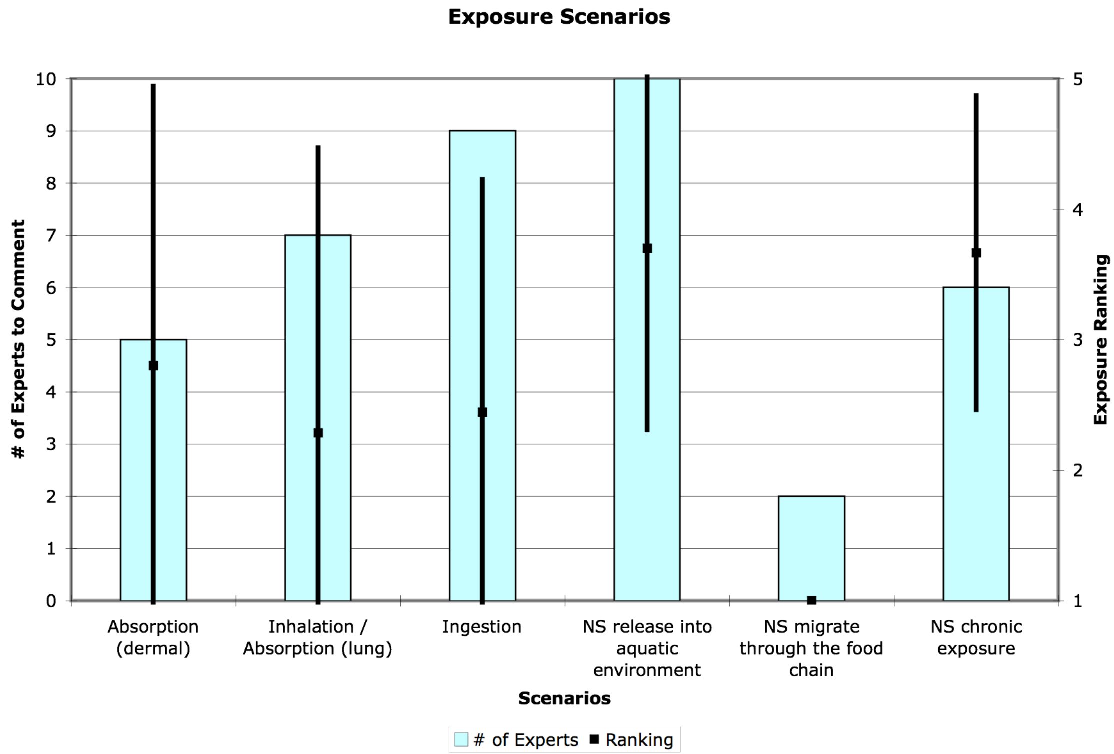
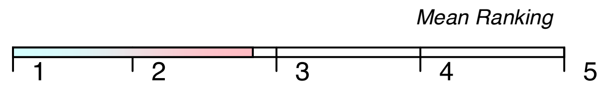


Figure 7. Exposure Scenario Rankings

This table shows the combined scores of each of the individual expert-ranked exposure scenarios. If an expert did not talk about that particular scenario, they were not included in the calculation of the mean or standard deviation. (See Appendix Data Tables and Calculations for Individual Scores)

The exposure scenario which displayed the highest level of risk of exposure to nanosilver was the release into aquatic environments followed by chronic exposure, dermal absorption, ingestion, inhalation/ absorption into the lung and migrating through the food chain. The standard deviation for dermal absorption, inhalation / absorption into the lung and ingestion were very large. In two cases this was due to a disagreement between the experts, which resulted with groupings of experts at either end of the spectrum. The reasons behind such divides will be discussed in the following subsections.

Absorption (dermal)



The level of risk of exposure to nanosilver through dermal absorption.

High – "Shampoo or liquid detergent: skin absorption or ingestion" (Bioengineer); "The socks application, fine powder, you are absorbing it, high risk through use and disposal." (Bioengineer)

HM – "Secondary concern is human exposure with products that have direct contact with individuals, dermal absorption, pillows and clothing." (Neurotoxicologist)

Med. – none

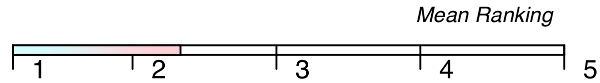
ML – "Silver nanoparticles, a lot of it might get in the environment but in most environments it may never reach concentration levels that will dramatically effect the ecosystem or human health." (Earth Scientist)

Low – "Silver is generally not a big problem for human health… the dermal toxicity of silver is low." (Fish physiologist and toxicologist)

Five experts responded directly to human dermal exposure in their interviews. Two of the five referred to possible exposure scenarios by spun, colloids, coatings and powder nanosilver products. Three of the five expressed direct concern for human exposure from silver enhanced products as provided in the handout. Their concern ranged from slight to severe. Overall dermal absorption was given a ranking of 2.8 of 5 for the level of risk of exposure to nanosilver.

Specific concerns included the potential for nanosilver to be transported out of a solid phase although flakes from coatings were not a concern for dermal exposure. One example is the prevalent use of nanosilver in wound care with individuals who have severe burns.

The large standard deviation in the category comes from two experts taking a cautious stance and the other three not considering it to be a problem. This lack of concern may stem from the belief that there will not be large amounts of exposure to nanosilver because of its size and concentration in products. In the case of the two experts who show concern, one is looking at dermal exposure in medical applications such as wound care where exposure is more concentrated and the other stated even small amounts of exposure are an important factor to consider.



Inhalation / Absorption (lung)

The level of risk of exposure to nanosilver through inhalation or absorption through the lung.

High – "Baby powder worried about inhalation, depends on bulk liquid phase or an aerosol or powder…. Powder dishwashing detergent, spill and cloud, worried about things along with silver nanoparticles" (Bioengineer)

HM – "Secondary concern is human exposure with products that have direct contact with individuals…. If it is a powder she is worried about inhalation." (Neurotoxicologist)

Med. – none

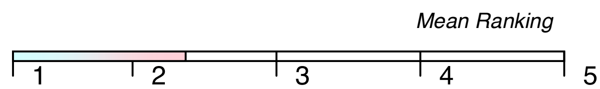
ML – "The fish have a directly exposed surface, it is basically irritated by any irritant added to the water. You get mucus production which leads to poorer oxygen uptake… this does happen with nanoparticles…. Not sure if this could ever happen in the environment, but it has the potential of causing that effect." (Molecular eco-toxicologist);

Low – "Silver is generally not a big problem for human health." (Fish physiologist and toxicologist); "The most concerning product for me was the dust. Environmental exposure will be limited, but human exposure needs to be considered." (Industry expert)

Seven experts commented on inhalation / absorption of nanosilver. Three out of the seven refer to specific problems with dust and aerosol product use. In many cases these are products that are meant for frequent use and therefore greater periods for exposure. One example was given of using a powder dish detergent which could produce a cloud if spilled, another would be a cleaning spray which is used to disinfect within the home.

Low rankings were given for different reasons including: fabrication techniques generally involve wet chemistry methods and therefore there would be little exposure to factory workers. Along with the fact that silver has been deemed "non toxic" to humans and the belief that the overall environmental exposure will be limited.

The factors as mentioned above played into the large standard deviation calculated for this criterion. High marks were given by experts who were looking at specific exposure scenarios within the home and with the application of the product and low scores were given by experts based on other scenarios. There is the conflict on whether exposure amounts are an important factor with regard to humans. Two experts saw cause for concern and said that the regular use of the mentioned products might cause a problem while one expert believed any exposure to humans was not important due to silver not being a known toxin for humans. One expert thought dilution within the environment and competition for aggregation would also minimize the exposure to forms nanosilver.



<u>Ingestion</u>

The level of risk of exposure to nanosilver through ingestion. This can include from a food source or from use of the product.

High – "Scenarios and exposure routes, exposure viva getting in the body depends on adhesions to underlying material which will never be perfect…. Particles are being used in some existing coating application, most of them will flake off with wear and tear. There is a concern for both use and disposal for flaking…. End product route is important to consider, shampoo or liquid detergent… ingestion." (Expert experienced with nanopatterned and nanostructured surfaces)

HM – "Secondary concern is human exposure with products that have direct contact with individuals…. Ingestion, babies sucking on fabrics" (Neurotoxicologist)

Med. – "Silver is assimilated a bit but not effectively. So you see greater enrichment of silver at the bottom of the food chain compared to the top of the food chain…. It is concentrated very effectively by the cytoplasm….. In polluted environments might have a subleathal effect which interferes with population success." (Biogeochemical cycling expert)

ML – "You do have homeopathic applications, they have high concentration. They claim effects, and those effects have to come from somewhere." (Molecular eco-toxicologist)

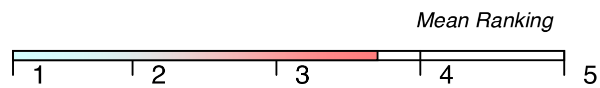
Low – [When algae is the food source] "In the fresh water systems you will have a lots of competition for uptake, more than just algae It does not mean that it will not happen, we just don't have enough information." (Industry expert)

Nine experts discussed issues concerning ingestion of nanosilver. Three of the nine experts focused on homeopathic use while four out of nine mentioned examples of accidental exposure. This included a concern for nanosilver-treated fabrics that infants might suck on, coating flakes that might be ingested and migration of nanosilver from food packaging.

Five of the nine experts made reference to the environment and dietary exposure, which might occur there. One expert had the opinion that ingestion of silver would only be a problem in industrial countries due to the increased number of products that use nanosilver. Another mentioned that in the environment there will be lots of competition for the uptake of silver, so there will be an overall decrease in silver available for ingestion.

While the standard deviation in this case was large, there was not an overall split in expert opinion. There were many examples presented of ingestion-type exposure and their ranking was evenly split across the board. There seemed to be more weight towards the low end of the scale due to environmental exposure scenarios, which involved a lot of competition for agglomeration.

<u>NS release into aquatic environments</u>



The level of risk of exposure that nanosilver is released into the environment.

High – "Primary concern is the release into the aquatic environment…. You should not buy them, it is the worst use of antibiotics. It is low level chronic use… creates resistance all over your house." (Neurotoxicologist)

HM – [Silver nano in the waste water] "More concern in the industrial nation, discharge… to wastewater plant may be the bigger concern." (Environmental Engineer)

Med. – [Lots unregistered products] "There are a lot of people out there that make antimicrobial claims that do that without registration." (Biologist); "Probably true for things like fish, they probably will not be exposed to concentration of silver where it would cause a problem, but then you get to talking to animals, invertebrates that live in the sediment, they eat the sediment and will have toxic effects." (Expert experienced with acute and chronic mechanisms of toxicology of silver in fish)

ML – "Where the silver goes through the waste water treatment. It sits for 4-6 hours and much of it is removed In the bio-solids." (Industry expert)

Low – none

Ten out of ten experts discussed concern for aquatic environment exposure. Four out of ten experts focused on problems related to wastewater and its treatment. Issues such as effecting wastewater treatment beneficial bacteria populations were discussed as well as the opinion that much of the silver will be removed in the biosolids during that treatment. These biosolids used as fertilizers on farms, however, could create high concentrations of nanosilver in soils. Leaching from both farms and landfills were mentioned as concerns but not elaborated on due to either the complexity of soil analysis or the fact that the expert was not worried about this form of exposure.

In general this type of exposure ranked the highest, especially with regards to colloids and colloid-related products. Not only did experts express concern about various non-point sources of nanosilver into wastewater systems, but also mentioned ways that nanosilver might go directly into aquatic environments such as in use on boats and discharge into lakes. Increased exposure might be seen due to multiple products used. Because of the particles size there may be a longer duration of exposure. A unique nano-feature can be seen in nanoparticles as observed in the environment, they can stay in the water column due to the effects of Brownian motion and be transported hundreds of thousands of kilometers eventually ending in the ocean.

Mean Ranking

<u>NS migrate through the food chain</u> 1 2 3 4 5

The level of risk that nanosilver will migrate through the food chain through bioaccumulation across species.

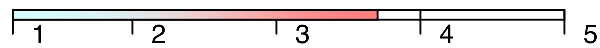
High – none HM – none Med. – none ML – none Low – “Silver is not one of the substances that bioaccumulates up the food chain.” (Fish physiologist and toxicologist)

Two out of ten experts talked about the migration of silver up through the food chain. In both cases these two experts had experience in bioaccumulation. While their work did not specifically deal with looking at the bioaccumulation of nanosilver, they seem to have no reason to suspect that nanosilver would behave differently, although concerns did exist for those organisms at the bottom of the food chain such as animals that dwell in the sediment or are in a fishes diet.

One expert pointed out that there is greater enrichment or bioaccumulation of silver at the bottom of the food chain such as in phytoplankton based on his specific research. He reported that dissolved silver (< 1nm) is effectively concentrated by a cell’s cytoplasm. Even if an herbivore eats a fairly large amount of phytoplankton, a direct transfer is not seen directly up the food chain. In zooplankton a sub-lethal effect is demonstrated which interferes with population success. Therefore fish could be indirectly affected through their diet.

Mean Ranking

NS chronic exposure



The level of risk of chronic exposure to nanosilver. This includes the potential for chronic exposure in the environment and the risk of exposure from multiple consumer products.

High – "Problem, most of the major issues for concern with silver nanoparticles revolve around chronic use. Example, medicines, implants, or supplements." (Chemistry, polymer chemistry and biomaterials expert)

HM – "You should not buy them, it is the worst use of antibiotics. It is low level chronic use… creates resistance all over your house." [This was not the primary concern.] (Non profit, monitor regulation of pesticides)

Med. – "It is not so much that we have toxic asbestos in the air or maybe toxic nanoparticles in the air, but it is the level of and duration of exposure that one gets that may or may not make it a problem." (Nano geoscientist)

ML – "If it is the diet, it is not going to be an issue in the real world…. [loading on the gills] If you continue with long term exposure, the effect gets exacerbated with time such that the toxicity occurs at the lower level than the acute." (Molecular eco-toxicologist)

Low – none

Six out of ten experts elaborated on the chronic exposure to nanosilver. Each experts referred to a different case or concern for chronic exposure scenarios. Human exposure cases presented included low level chronic exposure from a medical implant and accumulation in various organs such as the lung, liver and spleen. Another major concern was the creation of resistant bacterial strains through low level chronic use around the house, although this also applies to use in medical facilities.

Two experts concentrated on chronic exposure within the environment. Due to the various applications of nanosilver among a wide variety of products, the potential for low level chronic exposure and even accumulation in the environment becomes an issue. It was mentioned that another factor to consider when looking at chronic exposure, is that toxic effects can occur at much lower levels. In regards to fish and silver, if concentrations are high enough and exposure is long enough, the same result from acute toxicity can be observed. Even if extreme effects of silver poisoning are not reached, he opined that chronic exposure can put undue stress upon the animal.

One expert pointed out the importance of considering the micro environment with which the nanosilver interacts. This can include looking at different surface environments, the interactions, which take place in different biological systems, basically considering the complex environments found within other environments.

Risk Triggers

In this part of the interview process the experts were asked to identify particular Risk Triggers (RT) or critical criteria that should be considered when analyzing silver nanotechnology. The Risk Triggers are divided into two sections, exposure related risk triggers and hazard related risk triggers. It was discovered that experts had very little problems talking about risk exposure scenarios but when it came to ranking exposure RTs and material properties the experts would not commit to any judgment. In lieu of the rankings for exposure-related Risk Triggers, the following section will explore some of the issues raised when discussing the RT with the experts. Hazard-related Risk Triggers are divided into three categories: material properties, material reactivity and material toxicology. Rankings or means, standard deviations and number of experts who responded are displayed for these criteria.

Exposure Related Risk Triggers

While the above exposure scenarios were what the experts focused on, some experts had specific criteria which related to exposure to nanosilver. These criteria often were more focused to their area of expertise. This section illustrates the diversity of thought that is achieved when using this method.

<u>Bioavailability</u>

> *Could the nanosilver display bioavailability characteristics? Bioavailability is the ability of a substance to be absorbed and used by the body. (This has to do with migration of nanosilver into an organism. The more bioavailable it is, the more organisms have the chance to be exposed.)*

Bioavailability describes exposure to an organism and whether or not nanosilver has access to that organism. Its counterpart is bioreactivity, which describes the hazard a substance poses to an organism. For a substance to have an adverse effect on an organism it must both be bioavailable and bioreactive. When talking about bioavailability there were two main concerns raised by the experts, one was the methods by which nanosilver could be transported within the body. This included understanding the cellular interactions between different cells and the nanosilver and the final fate of the particles. Factors such as surface interaction, accumulation and aggregation of the particles come into question.

The second main concern was the size of the particle, not only would this determine the fate of the particles within the human body, but it would also allow the particles to behave uniquely in the environment. Nanoparticles within a watershed have the potential of transporting far greater distances than larger particles due to Brownian motion.

Rate of Ag+ release

Is the rate of silver ion release an important factor in evaluating exposure? (This factor is important because silver ions are considered one of the most toxic forms of silver. If the experts acknowledge this factor as being important, it could be key in determining a products overall risk.)

Rate of silver ion release is a criterion within the exposure related risk triggers because this was determined to be a highly critical factor in investigating nanosilver exposure. One of the major points that came up when discussing bioavailability was the question of whether exposure would be to the nanoparticle itself or to silver ions being released from the particle. A silver ion is highly reactive and will quickly react when released in an environment. It is unclear what the fate of the particle will be. If the particle is in an environment where ion release can occur, there is cause for concern, as the silver ion is considered the most toxic form of silver. Different environments might cause a particle to release more or less silver ions, resulting in more or less exposure to silver ions.

One dangerous exposure scenario, which demonstrates the problem with rate of silver ion release is accumulation of nanosilver within an organism. If conditions are such that the organism has nanosilver accumulate within its internal tissues and this nanosilver releases silver ions over time. There is the potential for chronic exposure to a known toxic form of silver.

Rate of agglomeration

> *Is the rate of particle agglomeration (from nano to not nano) an important factor in evaluating exposure? (There is a dispute as to whether particle agglomeration renders a particle non toxic, but if this is the case, then the rate of agglomeration will be an important factor in determining exposure scenarios.*

A controversial topic is the rate of agglomeration of silver nanoparticles. Most expert's opinions were that when the particles agglomerate, they are rendered nontoxic and are no longer bioavailable. Others state that we simply do not know the behavior of these new agglomerated particles and should proceed with caution. Whether or not agglomeration changes the toxicity of the particles, it is still an important factor when examining exposure to nanosilver. Most of the discussion about agglomeration focused on water based exposure scenarios.

Silver as discussed before has a high affinity for sulfur groups. This fact along with the opinion that in many of these exposure scenarios there would be lots of particulate matter within the water convinced most of the experts that exposure to unbound nanosilver would be unlikely. The geochemist experts pointed out that most natural environments are sulfur-deficient. So in exposure conditions like rivers and lakes where there might not be a lot of sulfur groups, silver has the potential to be bound with various other reactive species such as nitrates, phosphates, oxides, carbonates. To determine what reactions would take place, the surface chemistry of the nanoparticles must be better understood. The expert on biogeochemical cycling mentioned that in his work with dissolved silver (<1nm) in salt water, he did not observe metal associating with colloidal particles or with particulate matter. This demonstrates that under some circumstances silver may not quickly agglomerate, as many experts suggest.

If the particles do agglomerate there are other issues of exposure to consider. If the nanoparticles are attached to larger particles they could eventually end up in the sediment, thereby creating an exposure scenario for organisms, which live within that sediment. Agglomerated nanosilver also may not possess the same transport properties as nanosilver alone and will interact differently with cells.

Coating/Matrix stability

Are there scenarios where the particle is freed from the coating / matrix? (The issue as to whether coating / matrix stability is an important factor in evaluating a product was addressed here. While many experts could not directly comment on individual products they were asked to comment on possible coating / matrix scenarios.)

Similar concerns exist for the coating/matrix stability criteria as for rate of agglomeration. How does a coating change the reactivity of the silver nanoparticle? Coatings, while meant to provide a way to affix nanosilver to certain products, are also meant to allow for the antibacterial action of the silver to work without interference. One of the main concerns raised by the experts was the question as to how the nanosilver was adhered to the product: whether it was free or fixed. In some cases there was concern for the migration of nanoparticles from the coating into the surrounding environment. The major concern was for those applications where free nanosilver was coated on products and not secured by a matrix such as a polymer.

The bioengineer pointed out no coating containing silver nanoparticles will ever be perfect and at some point flaking of that coating will occur. Therefore it is important to understand the properties of those flakes that come off. In particular, food storage containers were a concern for experts when talking about exposure to nanosilver. Another question about silver nanoparticles contained within coatings was raised, is it possible for migration of nanosilver to occur from the packaging to the food?

Multiple disposal pathways

Does the product disposed in different ways contribute to different patterns of exposure, each with a different effect on the environment? (This factor focuses on the issue of disposal / end of life treatment of a product. This addresses the multiple disposal pathways, asking the expert to list them and identify the areas of concern such as sewage treatment.)

The disposal of nanosilver seems to fall into two categories, water and land. Many experts were concerned with the burden of responsibility, which would fall on sewage treatment plants in which discharge is regulated. If the majority of silver waste passes through sewage treatment centers, another question which is raised is aquatic exposure a significant concern? One expert opinion was that the majority of silver waste would agglomerate with the biosolids and be removed from the liquid phase during treatment, thereby moving the burden of silver exposure to those who use those biosolids as fertilizer. This could result in creating problems for beneficial soil bacteria. There is also exposure by means of storm discharge systems which often bypass sewage treatment under storm conditions.

What about beneficial bacteria in soil? In wastewater treatment plants?

Besides the use of biosolids containing nanosilver on crops, exposure of land was not a significant concern. This, in part, was due to the nature of the products which might end up in a landfill such as coated refrigerators. As mentioned before, soils are perhaps one of the most complex environments to analyze and understanding exposure to this environment is extremely difficult.

<u>Exposure route dependent</u>

Does the route of a product help determine its exposure? (Can environmental factors such as water quality or soil content effect the overall exposure to nanosilver? Silver ions are highly reactive and will bind quickly with sulfur groups, especially in organic matter, minimizing their ability to cause harm, however it is unclear as to whether the same applies with these new applications of silver nanotechnology.)

This criterion for exposure related Risk Triggers was created because of concerns raised during the interviews that were not covered in the other criteria. These concerns dealt with how the exposure to nanosilver could change due to its surrounding micro-environment such as water characteristics or cell surface and charge interaction. Some of these factors were hinted at in Ag+ release where the environment might alter the exposure to silver ions and in rate of agglomeration where sediments and other chemicals might cause the nanosilver to combine into larger particles. The focus here is to understand what role the environment which the nanoparticle is in plays in exposure.

The exposure to nanosilver can be greatly modified by the water characteristics. Two separate experts mentioned the EPA's regulation of copper in freshwater through the Biotic Ligand Model (BLM) where the amount of copper is determined through a calculation that considers 10 different water criteria: temperature, pH, dissolved organic carbon (DOC), calcium, magnesium, sodium, potassium, sulfate, chloride, and alkalinity.[52] They suggested that such a method could be used to determine acceptable levels of silver in different aquatic environments.

Hazard Related Risk Triggers: Material Properties

<u>Particle size & Particle shape</u>

> *Does the particle size factor into the hazard of the nanosilver application? (Nanotechnology is generally considered arbitrarily from 1-100nm. The experts were asked how size played a part in the hazard of nanosilver.)*
> *Does the particle shape factor into the hazard of the nanosilver application?*

Particle size and shape are the first two properties that the experts wanted to know about. Both size and shape help to determine where the nanosilver can migrate to and with what it can interact. In the SNCI 45% of the 240 products reported the nanoparticle size used. They ranged from 0.3nm to 250nm with an average size of 24nm.[53] The expert in biomaterials noted that the most effective bactericides were those silver particles less than 10nm while the biogeochemical cycling expert expressed concerns for particles ranging from 1-40nm. One question is, at what size so the properties change or become enhanced?

The bioengineer mentioned that size is more of an important factor than shape when looking at cellular uptake. And a biologist cited an example of how dermal absorption of titanium dioxide in sunscreen is prevented because of its shape. Therefore suggesting that bioavailability and hazard associated with nanosilver can be both a function of size and shape.

<u>Aggregated nanoparticles</u>

> *Are the properties of the free silver nanoparticles different from the aggregated forms of the nanoparticle? (This asks the experts to consider the hazard of free nanosilver vs. the aggregated form of the nanoparticles.)*

Does the agglomeration or aggregation of silver nanoparticles render them nontoxic?

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[52] U.S. Environmental Protection Agency. (2007, February). *2007 Update of Ambient Water Quality Criteria for Copper (EPA-822-F-07-001).* Retrieved July 1, 2008, from http://www.epa.gov/waterscience/criteria/copper/2007/fs-2007.htm
[53] Fauss, E. (in press).

While rate of agglomeration addresses the exposure side of the complex of nanosilver, this criterion addresses the hazard associated with those aggregated particles. The main question is how does the aggregation of nanoparticles change their characteristics? Does it make them more or less hazardous? As briefly discussed in the rate of agglomeration, there is a controversy on whether silver is rendered nontoxic when it is agglomerated or aggregated. It was suggested that one possible outcome of aggregated nanoparticles is that they start to display the same characteristic as those found in bulk silver. Overall the experts would not comment on what the hazard would be of these new larger particles but they did acknowledge that it would be an important factor in evaluating silver nanotechnology.

Hazard-Related Risk Triggers: Material Reactivity

Before the experts were asked to evaluate the level of risk of exposure to nanosilver through different scenarios, the experts were also asked to assess the hazard of different forms of exposure. In this section the level of material reactivity and toxicity of nanosilver is evaluated in respect to different hazard-related Risk Triggers. Below is a chart that displays the mean ranking of each Risk Trigger denoted by the black square, the standard deviation of those responses represented by the black line and the number of experts who responded to that scenario shown with the blue bar. (See Appendix: Data Tables and Calculations for calculation of mean and standard deviation)

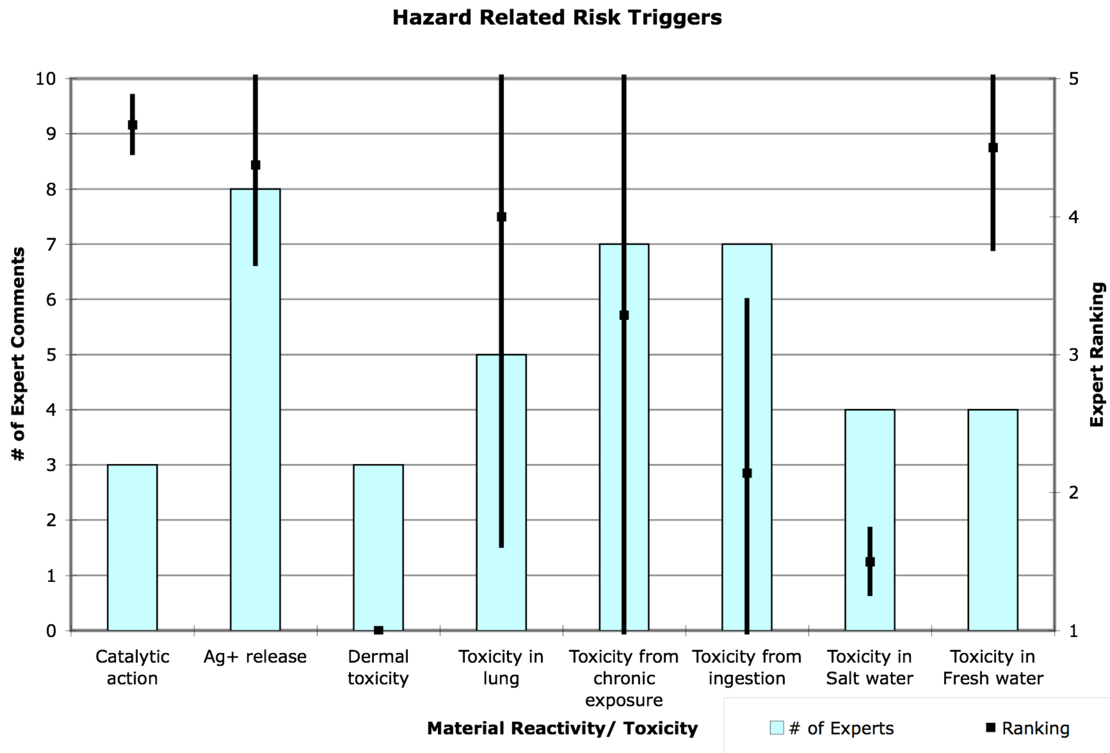

Figure 8. Hazard Related Risk Trigger Rankings

This table shows the combined scores of each of the individual expert ranked Risk Triggers. If an expert did not talk about that particular RT, they were not included in the calculation of the mean or standard deviation. (See Appendix: Data Tables and Calculations for Individual Scores)

In regards to material reactivity both antibacterial action and catalytic action ranked high on the scale of 1 to 5. While both criteria were deemed critical in the evaluation of silver nanotechnology, catalytic action was the highest with the lowest standard deviation. Demonstrating that there was more concern for the unknown effects of nanosilver as a catalyst compared to the known dangers of silver ion release.

The highest hazard level due to material toxicity is that in fresh water followed by toxicity in the lung, due to chronic exposure, ingestion, in salt water and dermal absorption. The standard deviation for toxicity in the lung and from chronic exposure were unusually large. One of these discrepancies had do to with the difference between toxic effects on different organisms such as fish versus human. The other had to do with a disagreement about effects. The reasons behind the divides will be discussed in the following subsections.

Antibacterial action

Silver nanotechnology is primarily used in products for its antibacterial action. It can provide an antimicrobial coating/surface, it can prevent the growth of odor causing bacteria within treated fabrics and be used as a disinfectant that can be applied in liquid form. As mentioned before, the regulation of the majority of these products (except those having to do with supplements, cosmetics, food and food containers) fall under FIFRA, that is the regulation of a product is based on whether or not the manufactures makes an antimicrobial or antibacterial claim. So even if a product is in fact "antibacterial," unless that claim is made, the product is not regulated.

The experts actively discussed the antibacterial properties silver nanotechnology. Many of them referred to the concentration of silver being available, whether it be silver nanoparticles, silver ions or in general, free silver. Some experts pointed out that there were still many data gaps which existed around understanding the antibacterial action of silver. The mechanism of antibacterial action of nanosilver is unknown, its effect on gills and tissue residue, and even straight toxicity levels. These may be understood in terms of silver ions and various silver compounds but not for nanosilver. One expert also noted that it is important to understand the antibacterial lifespan when looking at any silver nanotechnology application.

One of the benefits of nanosilver is that even at low concentrations it has been shown to be effective against harmful resistant strains. All cells are not affected equally; the toxicity of nanosilver depends very much on the cell type. Another interesting trait is that nanosilver has been shown to promote the healing of wounds.[54]

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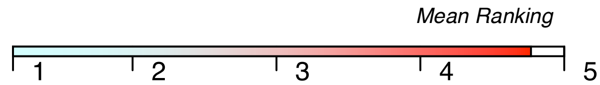
[54] Tian, J., Wong, K. K. Y., Ho, C., Lok, C., Yu, W., Che, C., et. al. (2007). Topical Delivery of Silver Nanoparticles Promotes Wound Healing. *ChemMedChem,* 2, 129-136.

The creation of reactive oxygen species such as ozone and the release of silver ions are two of the know antibacterial effects of nanosilver. These two aspects were explored within the context of the interviews.



Catalytic action

Is catalytic action a factor in nanosilver antibacterial action? (In some cases it is thought that silver reacts with oxygen to produce antimicrobial activated oxygen.)

High –	"Silver surface acts as a catalyst to O2 in water, hydroxyl radicals or oxygen radicals forming… that is what attacks the cells and kills them" (Environmental Engineer); "in this case, the silver nanoparicle would be a catalyst and reactants would land on the surface, and because of the presents of silver surface a product would form, that product could be something that is highly toxic or beneficial." (Geochemist)
HM –	"Silver nanoparticles are highly reactive due to their size, compared to bulk silver" (Expert experienced with surface modifications of polymers and metals at the nano level)
Med. –	none
ML –	none
Low –	none

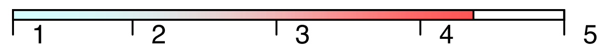
A catalyst as defined in Merriam-Webster Dictionary is "a substance that enables a chemical reaction to proceed at an unusual rate faster or under different conditions (as at lower temperature) than otherwise possible."[55] Catalysts effectively lower the energy it takes for the said reactants to react, allowing a reaction to occur that would normally not take place on its own. In terms of nano-sized silver, the reaction occurs on the surface of the particle with the reactants while the surface itself remains unchanged. These reactions will continue to take place until there are no more reactants available.

Four out of ten experts commented on catalytic action. Two experts mentioned the possible role of activated oxygen or ozone plays in making nanosilver antimicrobial. The geochemist suggested that silver makes a good catalysis and has the potential of enabling the creation of either highly toxic or beneficial products. The third expert pointed out that the antibacterial action of the silver nanoparticles are due to their size, and as the size decreases they become highly reactive.

[55] catalyst. (2008). *Merriam-Webster Online Dictionary*. Retrieved June 17, 2008, from http://www.merriam-webster.com/dictionary/catalyst

Therefore as the size of the particle decreases the antimicrobial action has the potential to increase. But as one expert mentioned, the products of the catalytic reactions depend on the reactants available to the surface of the particle. With one highly reactive surface there exist the potential to create thousands of products.

Mean Ranking



Ag+ release

What is the hazard of nanosilver releasing silver ions? (Before we looked at the exposure side of these particles releasing silver ions, here we are looking at that associated hazard due to release.)

High – "Antibacterial properties could be due to silver ion…. As it gets smaller, release might go up…. Even from a piece of silver, ions can be released, except now these smaller particles can move around and become like motors, releasing more and more ions. It has access to any place in the body." (Chemistry, polymer chemistry and biomaterials expert); "the silver ion is the most toxic" (Expert experienced with aquatic toxicology of silver and various silver compounds)

HM – "Rate of uptake would depend on how the surface or charge interaction on the cell works…. Reactivity of the ions would be different when ingested…. Ion salts circulating around, hoping that I will be cleared through the kidney. But is transported to interstitial tissue, that is where you are worried about accumulation" (Bioengineer)

Med. – "Maximum containment limit in water, [the toxic effect of silver (silver ions, by way of silver nitrate) has been assessed) not found toxic to humans" (Biologist)

ML – none

Low – none

It is accepted that silver ions are the most toxic forms of silver. Even the federal EPA regulations are based off of tests performed with silver nitrate which in water creates silver ions. Here eight out of ten experts responded to the topic of silver ion release. Ion release along with catalytic action might be both a function of size and of the surrounding environment. As size decreases the surface area increases, allowing a larger surface from which ions can be released. The dissolution of the silver particle, however, will largely depend on the surrounding environment. For instance, if the surrounding environment is acidic, the particle might dissolve faster than in a basic environment. In this case a greater exposure due to an increased release corresponds to an increase in hazard. The majority of responses, six out of eight, focused around concern for aquatic exposure of silver ions from silver nanoparticles.

Three out of the eight referred to the hazard associated with human exposure. One was not concerned saying that silver is non-toxic to humans, while the other two expressed concern. One talked about the interaction of silver ions from nanoparticles on a cellular level and how those mechanisms are poorly understood. The other suggested that due to the size of the nanoparticles, they would have broad access across the entire body allowing silver ions to reach places they never before were able to infiltrate thereby creating new hazardous conditions.

Hazard Related Risk Triggers: Material Toxicity

Mean Ranking

Dermal toxicity 1 2 3 4 5

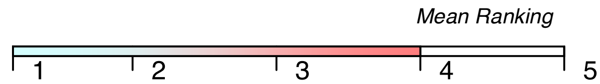
Hazard level due to dermal toxicity. (How dangerous is nanosilver in dermal contact?)

High – none
HM – none
Med. – none
ML –none
Low – "Normal wound dressing and coat in silver nanoparticles, with silver particles it is completely healed after 10 days. In the group treated with nanoparticles they noticed an expression of certain proteins that promote wound healing." (Chemistry, polymer chemistry and biomaterials expert); "The dermal toxicity of silver is low [in humans]" (Expert experienced with aquatic toxicology of silver and various silver compounds)

Three out of ten experts talked about the dermal toxicity of silver nanotechnology. In all three cases it was assumed that dermal exposure would cause no hazard to humans. One of the experts even mentioned a wound care scenario where silver nanoparticles were used and the expression of certain proteins that are responsible for wound healing were regulated.[56]

The large standard deviation in the category comes from two experts taking a cautious stance and the other three not believing there to be much of a problem. This discrepancy could arise from the comparison of nanosilver to bulk silver characteristics. In bulk form, silver is not considered to be very toxic and only chronic exposure seems to pose a real risk of cosmetic effects.

[56] Tian, J., Wong, K. K. Y., Ho, C., Lok, C., Yu, W., Che, C., et. al. (2007).



Toxicity in lung

Hazard level of nanosilver through entry into the lung. (How dangerous is nanosilver if absorbed in the lung or gill?)

High – "Everyone knows that nanoparticles can be dangerous if inhaled" (Biologist); "if you get very high levels of silver (very unlikely to exist in nature) can get a respiratory blockage, produce too much mucus and suffocate, but they dismiss that as being improbable in a real environmental scenario." (Fish physiologist and toxicologist)

HM – "The fish have a directly exposed surface, it is basically irritated by any irritant added to the water. You get mucus production… leads to poorer oxygen update… this does happen with nanoparticles" (Expert experienced with acute and chronic mechanisms of toxicology of silver in fish)

Med. – none

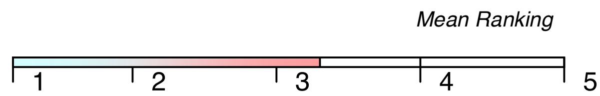
ML – none

Low – [Dissolved silver] "No clear evidence that toxicity to the adult in the environment, no effect on swimming behavior, but if it came in the food [not dissolved silver] it resulted in effecting the egg production [of copepods and fresh water daphnia]" (Biologist)

Five out of ten experts expressed concern about toxicity in the lung. Two were referring to human exposure, however, and three were referring to aquatic exposure such as in fish and crustaceans. In the case of human exposure the powder/ dust-containing products were a concern for many experts even if they did not have an opinion as to whether a hazard existed or not. One expert went so far as to say that all nanoparticles are hazardous if inhaled.

When talking about the hazard to aquatic life, there were two experts who said that the silver nanoparticles might act like an irritant that would lead to respiratory blockage and eventually death if the exposure was high enough. The third expert to respond about hazard to aquatic life had an opinion at the other end of the spectrum, stating that there is little chance of toxic effect on adults if exposed through the water and therefore the hazard is low.

The large standard deviation for this criterion is explained by the response of one expert. It was only this one expert who gave a low toxic ranking to this criterion and he was making a reference to aquatic life.



<u>Toxicity from chronic exposure</u>

Hazard level for chronic exposure to nanosilver. (How dangerous is it to be chronically exposed to nanosilver, even at a low dose?)

High – It is the same problem as acute, effecting the sodium uptake in the gill, develops slowly and generally runs down the health of the animal (Fish physiologist and toxicologist)

HM – "If it is chronic silver you still may develop silver poisoning over time. May interact with proteins over time. So even if it is low concentration, if it is chronic it could still be a problem." (Chemistry, polymer chemistry and biomaterials expert)

Med. – "If you continue with long term exposure, the effect gets exacerbated over long time such that the toxicity occurs at the lover level than the acute, much lower levels than you would expect." (Expert experienced with acute and chronic mechanism of toxicology in fish)

ML – none

Low – [In reference to colloidal silver] "We used [silver sulfide placed with polymers around the molecules] in a chronic study with fish… and it was not killing them" (Industry expert)

As seen from the chronic exposure scenario, there are many circumstances under which chronic exposure could occur, but the question still exists, if there is chronic exposure what are the associated hazards? There were seven out of ten experts who mentioned problems that could arise from chronic exposure to nanosilver. Three of the seven were concerned about hazards for humans, and another three about hazards to fish. The seventh expert expressed concern for the development of resistant strains through the inappropriate and prevalent use of antibacterial products.

In terms of human hazard, one expert did not expect there to be any problems so long as the EPA's silver regulatory limit was upheld. Two others expressed more of a concern, with the opinion that even with low concentrations silver poisoning could develop over time as well as cause problems in the liver, spleen and interstitial tissue.

When discussing the chronic effects on fish, one expert opined that there would be no significant effect on fish while two others opined that the same acute effect of silver would occur over time. This toxic effect could occur at a much lower level than the acute and even if acute levels are never reached, the nanosilver will erode the health of the animal. It has been shown in long term studies that most of the silver deposits in the liver and induces the production of a certain protein.[57] It has been suggested that the production of this protein might be detrimental to the animal.

There seemed to be an overall disagreement with the toxic effects of chronic exposure to nanosilver both in regards to humans and aquatic life. The large standard deviation in this case cannot be explained by different classifications of organisms. This criterion should be highlighted in further studies conducted with silver nanotechnology, as the effects are not clearly understood.

Mean Ranking

Toxicity from ingestion 1 2 3 4 5

Hazard level for ingestion of nanosilver. (How dangerous is nanosilver is ingested, either through diet or another means?)

High – none

HM – "Metals including silver that are associated with food, portion that is absorbed is from the cytoplasm were assimilated…. Sub-lethal or lethal toxicity to the adults not so much, but the females stopped producing as many eggs when it was in their diet" (Biogeochemical cycling expert)

Med. – [Assuming the release of silver ions] "reactivity of the ions would be different if ingested… the silver ion in solution is not necessarily crossing into the cells very easily, but does not mean that this is not toxic to the cells" (Bioengineer); [comparison to silver] "[in the gut] Macrophages will gobble up these nanoparticles and produce an inflammatory effect, eventhough titanium is considered inert" (Molecular eco-toxicologist)

ML – "If you look at all the work that has been done on dietary exposure of silver, they never cause more than 50% reproductive impairment. Which does not have a dose response." (Industry expert)

Low – "Intestinal toxicity is low in humans" (Expert experienced with aquatic toxicology of silver and various silver compounds)

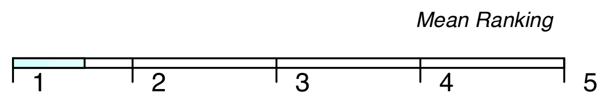
Seven out of ten experts commented on toxicity from ingestion of nanosilver. Five out of this seven referred to toxicity to humans and the other two responded in relation to the toxicity to fish. Overall the experts did not express a critical problem with ingestion. The worst effects were thought to be irritation and a reproductive effect on aquatic life such as fish. One expert was concerned about the silver ions, which could be released from the nanoparticles in the digestive tract. Another was concerned about the ability for ingested particles to deposit in any number of

[57] Hogstrand, C., Galvez, F., & Wood, C. M. (1996). Toxicity, Silver Accumulation and Metallothionein Induction in Freshwater Rainbow Trout During Exposure to Different Silver Salts. *Environmental Toxicology and Chemistry, 15*(7), 1102-1108.

places in the body such as the brain and reproductive organs. Another expert suggested that the nanoparticles might produce an inflammatory effect. This has been demonstrated in experiments with titanium which is considered inert.

The two experts who talked about toxic response for fish both agreed that dietary exposure to silver can cause reproductive impairment. One had the opinion that this was more of a hazard while the other expert did not seem concerned, as there was no dose response.

Toxicity in salt water



Hazard level of nanosilver in a marine environment. (How dangerous is nanosilver in salt water? Why is it less or more toxic than in fresh water?)

High – none

HM – none

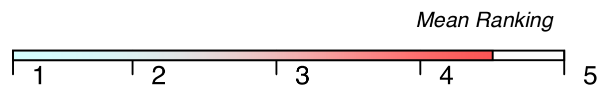
Med. – none

ML – "In salt water more of a problem of water balance, it cannot excrete the sodium. Cannot take water up in the gut, similar mechanism as the sodium in the gut." [leads to death if exposure is too high] (Expert experienced with acute and chronic mechanisms of toxicity of silver in fish)

Low – "Silver is less toxic in sea water than in fresh… most of the silver ends up in chloride complexes that have low toxicity." (Expert experienced with aquatic toxicology of silver and various silver compounds)

Due to the large number of products which have the potential for entering both wastewater systems and waterways, the experts were asked to evaluate the exposure scenario of release of nanosilver into the aquatic environment, as mentioned before, and its dangers to aquatic life within those systems. There was a divide between two types of water systems, that of fresh water and of salt water. Experts had the opinion that nanosilver would behave very differently in each environment. This is primarily due to the differences in water chemistry. In salt water free silver ions will associate with chloride ions forming the precipitate $AgCl$, which is relatively non-toxic. It is not entirely clear what will happen to the silver nanoparticles. In fresh water silver ions and silver particles have the opportunity to bind with many other chemicals, primarily sulfur groups, nitrates, phosphates, oxides, and carbonates, if available.

Four out of ten experts talked about silver in salt water. Experts either had the opinion that there would be no significant hazard in salt water or mentioned that a toxic response could be observed in fish is exposures levels were unrealistically high (acute toxicity of fish for silver will occur at 300-3000 mcg/L). Most of these comments were made in light of silver ions being released from nanoparticles and not for silver nanoparticles themselves.



Toxicity in fresh water

Hazard level of nanosilver in a freshwater environment. (How dangerous is nanosilver in fresh water? Why is it less or more toxic than in salt water?))

> High – "Mechanism of toxic action, which is a big problem in fresh water is to block the active uptake of sodium in the gills." (Expert experienced with aquatic toxicology of silver and various silver compounds)
>
> HM – none
>
> Med. – "Toxicity is greatly modified by the water characteristics. As you got closer to what natural water would be, the toxicity was reduced in the presence of organic matter. Other components in the water effected the toxicity of silver. In most cases, it clumped or removed (by being bound and no longer available)" (Industry expert)
>
> ML – none
>
> Low – none

Four out of ten experts discussed the toxicity of silver nanotechnology in fresh water, three of these experts were the same as the experts mentioned with toxicity in salt water. Two of the four focused on the acute toxicity silver can have on fish (acute toxicity at 5-70 mcg/L). Silver in fresh water has been shown to block the active uptake of sodium in the gills and thereby cause ion regulatory failure resulting in cardiac arrest. Another expert mentioned that the toxicity of silver will be greatly modified by the water characteristics such as the presence of organic mater. It is assumed that as organic matter increases the toxicity of the nanosilver will decrease due to agglomeration of the particles. Another expert considered the presence of nanosilver in water filtration methods to kill bacteria. If nanosilver is used to kill harmful bacteria in drinking water, there is no reason that nano silver in fresh water scenarios would not also affect beneficial bacteria populations such as those used in wastewater treatment and those in the natural environment.

Exposure Scenarios: Investigation into Product Types

This next stage of analysis assigned rankings for each product type. For each expert, product types were evaluated in relation to each exposure and hazard was related to Risk Trigger criterion. This coding was determined by looking first at their general ranking for each criterion and then by looking at specific phrases from the interviews regarding product types. Rankings were assigned by the interactional expert.

In the following figure, high (5), medium (3) or low (1) scores were assigned for each exposure scenario. Three product types (coatings, colloids, and powder) were chosen to be represented because out of the given examples in the handout, these three were the categories focused on by the experts. These scores were averaged together for all the experts who that responded to that particular criterion. The corresponding exposure scenarios are labeled in the table under the figure. The Data Tables and Calculations for this figure can be found in the Appendix.

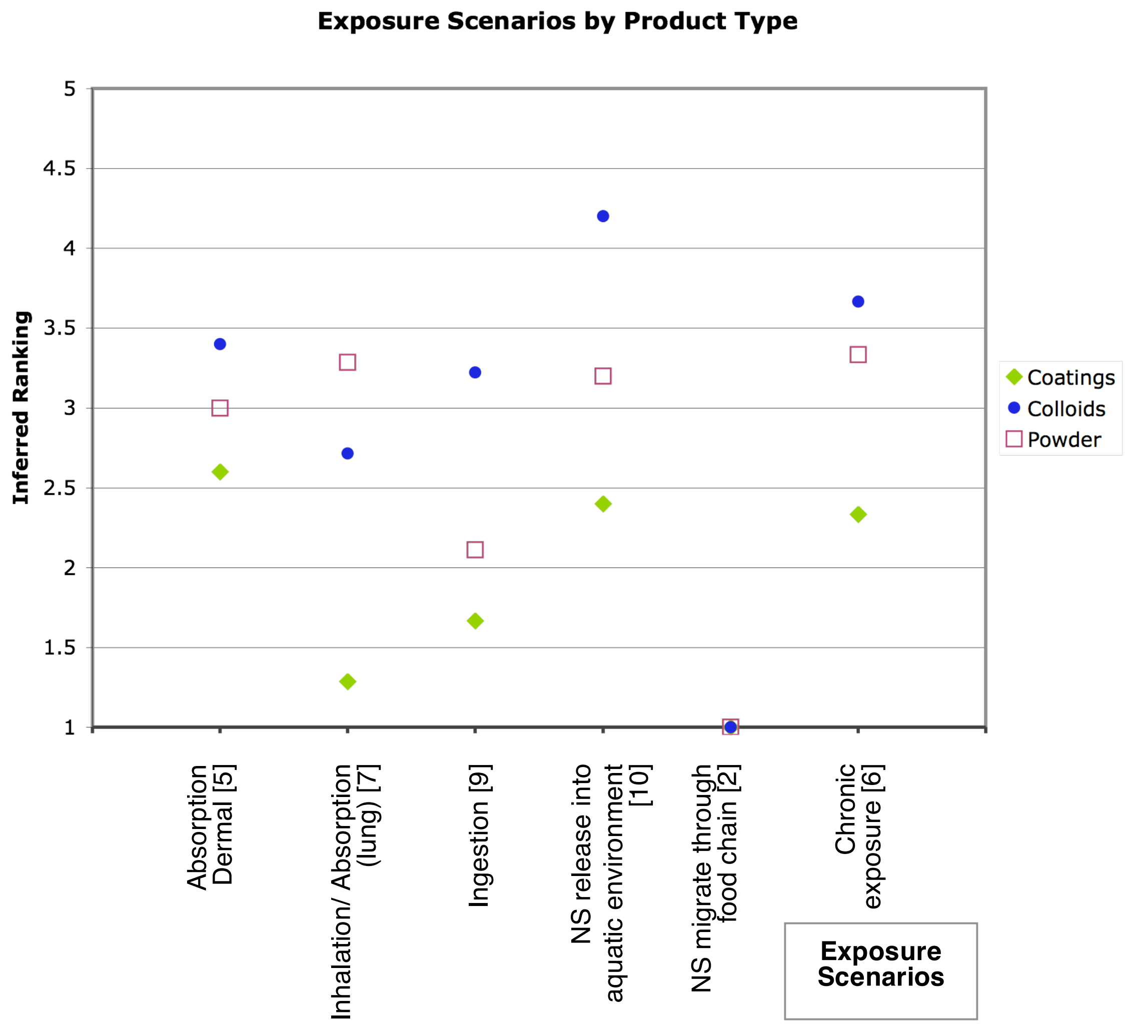


Figure 9. Exposure Scenarios by Product Type

In each exposure scenario, except for inhalation and nanosilver migrating through the food chain, colloids pose the greatest concern. Out of all the colloids, the highest concern was for aquatic exposure.

In the next figure, hazard-related Risk Triggers rankings by product type are presented. Scores of high (5), medium (3) or low (1) scores were assigned for each Risk Trigger. These scores were averaged together for all the experts who responded to that particular criterion. The corresponding Risk Triggers are labeled in the table under the figure. The Data Tables and Calculations for this figure can be found in the Appendix.

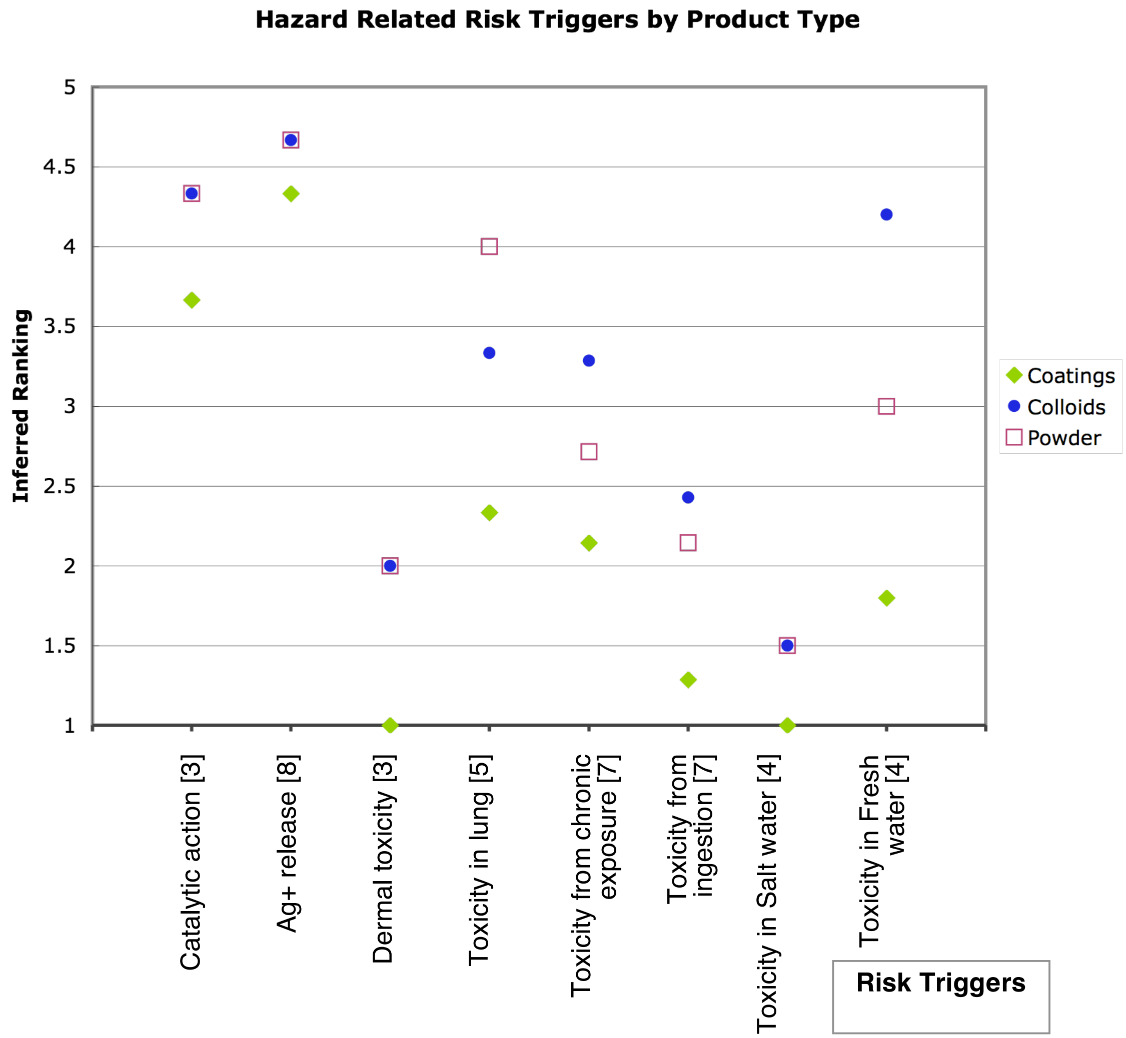


Figure 10. Hazard-related Risk Triggers by Product Type

As with exposure scenarios, colloids overall ranked high on the list for hazard-related Risk Triggers. In half of the cases, powder matched colloids with the hazard level. In terms of toxicity to the lung, powder was ranked higher than colloids. Here Ag+ release is ranked higher than catalytic action, which is different than the general rankings earlier in Figure 8. Hazard Related Risk Trigger Rankings. This discrepancy arises from the difference in the number of experts that responded to these criteria. Three experts commented on catalytic action and while two ranked high for each product type, one expert was more optimistic. In the case of Ag+ release, eight experts responded to this criterion. The majority of experts here expressed on average overall more of a concern.

In the following graph two sources of information were combined: inferred exposure scenario rankings and inferred toxicology rankings. While this only captures one dimension of a product type's exposure and hazard criteria, it is an example of what types of inferences can be derived with information from the expert elicitation process. An example, dermal absorption for coatings, was given an average score of 2.6 for risk of exposure and 1 for toxicology risk. This is found to have the lowest hazard ranking but a medium-low risk of exposure.

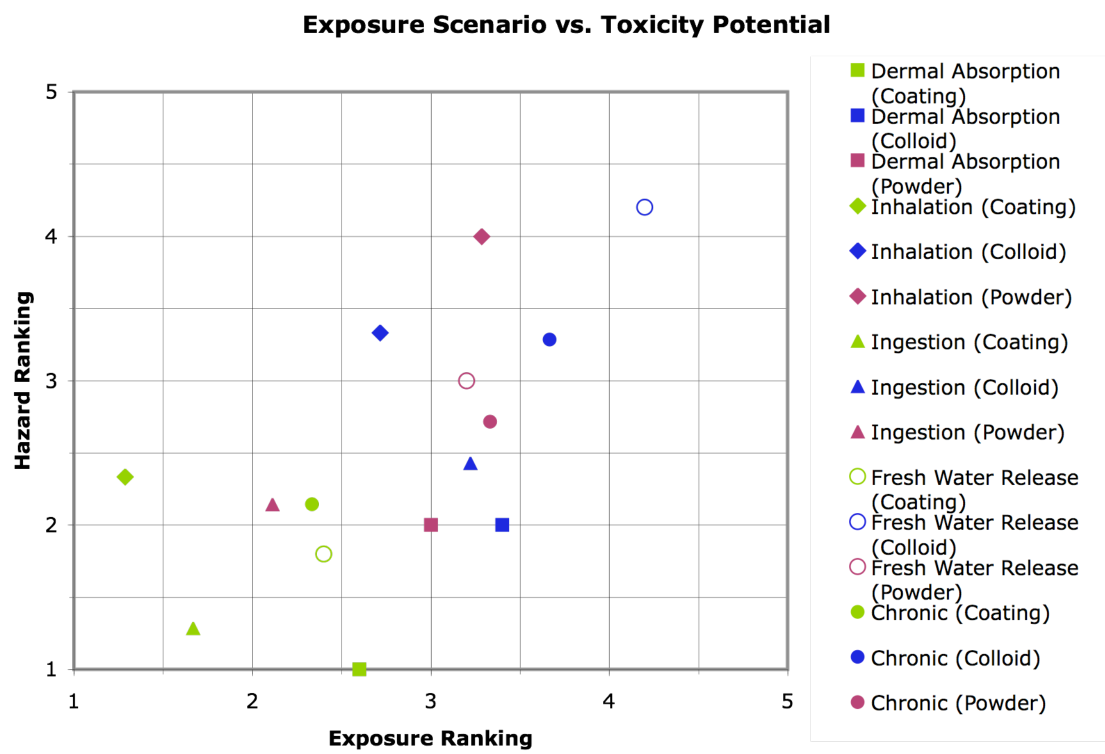


Figure 11. Comparison of Exposure Scenarios and Toxicity Potential by Product Type

While this figure does not include important criteria, such as exposure-related Risk Triggers and non-toxicity hazard related Risk Triggers, it shows the relative risk levels of different product types. Taking exposure scenarios and material toxicity into consideration, fresh water exposure of colloids poses the highest risk and ingestion of coatings poses the least risk.

Susceptible Populations

Experts were asked at the end of each interview, what if any were specific populations were at risk due to the use of nanosilver products. Generalizing their responses, four categories emerge: fish, organisms found at the bottom of the food chain, early life stages, and beneficial bacteria.

Table 17. Susceptible Populations to Silver Nanoparticles

Fish
Organism at the bottom of the food chain
Early life stages
Beneficial bacteria

Most of the experts who commented on fish, in their opinion, did not think there would be enough exposure to nanosilver to cause acute toxicity. Concern for fish primary rested with chronic exposure and the nanosilver indirectly affecting the fish's food sources such as zooplankton. Silver has been shown to hinder the reproduction of aquatic organism in field studies conducted by the USGS.[58] Organism at the bottom of the food chain such as those that reside in sediments in some cases may have a greater exposure to nanosilver. If nanosilver agglomerates and becomes trapped in the sediments, invertebrates and other organisms which eat the sediment might be directly affected.

Early life stages refer to critical early development of organisms such as in the egg or womb. Developing organisms tend to be more susceptible to environmental contaminants than their adult counterparts. Interrupting hormonal development, embryonic or child development can cause serious deformities if not death.

Nanosilver applications are specifically designed to target bacteria, however not all bacteria is bad. Various beneficial bacteria populations have the potential to be affected; as one expert put it "there is no reason that it would not affect beneficial bacteria." There are bacteria populations, which exist on and within organisms helping with digestion and normal functioning of that organism. Bacteria is also used to treat wastewater. Sludge from the wastewater treatment plants is used as fertilizers. This use of sludge that contains nanosilver may have effects on the

[58] U.S. Geological Survey. (n.d.). *Headlines: Silver Can Affect Fish Reproduction in San Francisco Bay*. Retrieved July 7, 2008, from http://toxics.usgs.gov/highlights/silver.html

soil bacteria. Recently an assistant professor in civil and environmental engineering at MU's College of Engineering, Zhiquiang Hu, said that silver nanoparticles generate a greater number of highly reactive oxygen species than bulk silver and basically halt the reproduction activity of the "good bacteria."[59] He will be investigating how silver nanoparitlces impair wastewater treatment.

Benefits of Silver Nanotechnology

Many of the questions in the interview focused on areas associated with the risk of silver nanotechnology. As mentioned earlier, social acceptance of risk is a function of the public's awareness of its benefits. In this section, the experts were asked what are some benefits of using nanosilver; are there justifiable uses? The responses centered on medical uses, water filtration and general household conveniences. Silver can be used to filter water and has been used for many years to treat swimming pools.[60] Uses in water filtration were discounted by some experts because they thought there was already technology which provided the same benefit without the risk. Convenience uses of silver nanotechnology involve household disinfectants and treated clothing which prevents the growth of bad smelling bacteria. These uses were viewed as trivial by a handful of experts. They did not believe the benefit of these products outweighed the risk of creating resistant strains through the chronic use of antibacterials.

Almost all the experts agreed that medical uses of nanosilver, such as in wound care treatment and the use of coated implants in immune compromised patients, were acceptable uses of this technology. It could also be beneficial in biomedical imaging applications and use against harmful resistant strains found in hospitals. Most of the experts believed these types of applications, if limited to a specific population and area, were highly beneficial uses. It was pointed out that there is no way easy way to allow the use of nanosilver only for medical purposes

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[59] University of Missouri-Columbia (2008, April 30). Silver Nanoparticles May Be Killing Beneficial Bacteria In Wastewater Treatment. *ScienceDaily.* Retrieved July 7, 2008, from http://www.sciencedaily.com/releases/2008/04/080429135502.htm
[60] Verlinden, Y. L. (2002). The Use of Algicides in Swimming Pools. In Karsa, D. R. & Ashworth, D. (Eds.), *Industrial Biocides Selection and Application*. (pp. 127-144). Cambridge: The Royal Society of Chemistry 2002.

and silver resistance found in bacteria is not unusual. In the 1970's resistant strains emerged in patients where silver was used to treat burn wounds.[61]

Knowledge Gaps & Future Research

There are still unknowns about silver nanotechnology. The experts were asked to identify knowledge gaps and area for future research, which would be needed in order to make a more comprehensive analysis. The following list displays the types of toxicity testing, transport research and particle properties and mechanisms identified for further investigation.

Table 18. Knowledge Gaps and Future Research for Silver Nanotechnology

Toxicity • Basic toxicity testing on silver nanoparticles • Investigate human health risk specifically to nanosilver and its long term effects • Long and short term studies on the effects of nanosilver on organisms from different taxa • Silver nanoparticle effects on cells
Transport • Life cycle analysis • Research on transport mechanisms • Geochemical cycling analysis of silver nanoparticles
Particle Properties/ Mechanisms • Research on stability of silver nanoparticles • Mechanisms of antibacterial actions (ion release and reactive oxygen species) • Investigate risk posed by agglomerated particles

Regulation Issues

Experts were also asked if there were any foreseen regulatory issues which involved silver nanotechnology. The discussion of this topic focused on the Environmental Protection Agency possibly because the majority of products will at one point have an impact on environmental systems. It was noted that the FDA would have jurisdiction over products which come in contact with food, cosmetics and medical applications but these regulations were not discussed. They responded with issues involving the EPA regulation process itself, problems the

[61] Lansdown, A. B. G. (2006). Silver in Health Care: Antimicrobial Effects and Safety in Use. *Biofunctional Textiles and the Skin, 33,* 17-34.

EPA has currently dealing with nanotechnology, and problems which involve specifically silver and nanosilver.

Table 19. Regulation Issues of Silver Nanotechnology

EPA Specific • Avoidance of registration, violators must be reported (EPA does not search for them)
Nano Specific • Nano is not unique, materials regulated under bulk standards • Testing requirements for registration, do they take into consideration nanotechnology special characteristics • No labeling requirements for nanotechnology products
Silver & Nanosilver Specific • EPA regulation loop hole, “claim” based registration • Silver is not listed as a “Hazardous Waste” under the EPA • Regulations based on total amount of silver discharge, not the formation of silver ions

Discussion

Highlights

Through the expert elicitation method key issues surrounding silver nanotechnology have been presented. Specifically, factors such as critical criteria or Risk Triggers, knowledge gaps and regulatory issues have been identified. A preliminary ranking of these criteria has been performed using the experts recorded interviews. Justifications for these rankings, along with specific examples, have been provided.

After reviewing the rankings and justifications there are a handful of issues that stand out among the rest. In terms of exposure scenarios, the two which were ranked the highest were chronic exposure and release into the aquatic environment. As demonstrated from the SNCI, liquid-type products (liquid & coating/spray) consist of about 30% of the 240 listed products. That does not include solid soaps, which would be listed under the solid category. Also taking into account that these products are meant for frequent, if not daily use, from the perspective of the inventory, this creates an opportunity for both types of exposure that the experts are concerned about.

When discussing different Risk Triggers it is clear that while each one explores one area of exposure or hazard, they are very much interconnected. Rate of silver ion release could be a factor of size but it could also be a factor of the environment (exposure-route dependent). Two overarching themes seemed to have emerged, those of transport and the micro-environment surrounding the particle. As mentioned in the section on knowledge gaps, there is a whole list of things we do not understand in terms of how silver nanoparticles transport through both the environment and the body. It is a topic that mainly presents concerns about exposure involving all of the exposure-related Risk Triggers.

Once silver has been transported to a specific location, the focus changes to what happens to the silver next. This is where the theme of micro-environments emerged. As discussed before, the silver can be greatly influenced by its surrounding environment. It can be as simple as fresh water in a lab or as complex the cytoplasm of a cell. This area of inquiry mainly focuses on hazard-related Risk Triggers which deal with reactivity and toxicity. In this case such as with transport, exposure-related Risk Triggers can also play a role in determining how the silver nanoparticle will act in its new environment.

While many benefits come from the use of silver nanotechnology, it is important to evaluate the areas of greatest risk and the possible trade-offs of using such a technology. In looking at susceptible populations, beneficial bacterial populations stood out from the rest for being at risk. In other cases, there were disagreements between experts of how or if populations of larger animals like fish would be affected. It was clear that silver nanotechnology was designed to kill bacteria and had the very real potential to effect other bacterial populations. Due to the nature of the exposure, this could occur in an aquatic environment, specifically in wastewater treatment, in soils treated with sludge, or within organism themselves. The risk of developing resistant strains also seemed to be an important consideration. With the pervasive, non-discretionary use of an antibacterial comes the real possibility of bacteria developing resistance as has already been demonstrated within the medical field in the 1970's .

Along with the knowledge gaps and the identified Risk Triggers, there are regulatory issues which must be addressed to manage silver nanotechmonlogy successfully. A list of these brought up by the experts is presented in the results section. There are two that need immediate attention. First and foremost there must be a way to measure the amount of silver nanoparticles within a sample. Without a device to detect and categorize the particles, no regulations on silver nanoparticles can be enforced. Second, the loophole regarding an "antibacterial claim" must be dealt with. The primary use of silver nanotechnology and nanoparticles is to produce an antibacterial effect. In the database 88% of the 240 products made an antibacterial or antimicrobial claim. While some of them are made outside the country, they should be regulated under FIFRA if they are sold in the U.S.

Room for Improvement

To improve this methodology, there are several techniques which could be introduced into the method. One variable is the period of time required to develop the knowledge base of the interactional expert; it is often difficult for that individual to objectively review each interview in the early stages of the elicitation. Due to the nature of how humans acquire and assimilate data, the interactional expert is flooded with information that is then internally ranked based on personal experience and bias. The interactional expert's strength is understanding the big picture and the connections between different areas of expertise. They can provide insight into how conclusions about a particular criterion were made. While this allows the interactional expert to create better trading zones for experts to share their knowledge, this can hinder the coding process. In reviewing the interviews and applying the ranking scheme, consistency in the interactional expert enhances objectivity. To avoid these personal biases, it might be beneficial to have more people from within the research group review and code the interviews. Due to resource and time constraints of this project, only one person was able to review and code besides the interactional expert. It is still advised that the interactional expert determine the final ranking assigned to each criterion. As mentioned before, the interactional expert has the advantage of seeing the criterion from many different perspectives.

Another improvement to this method would be the incorporation of a set of feedback mechanisms. First, allowing the experts to review the proposed list of exposure scenarios and Risk Triggers and critique them after the data collection is completed would make the process more thorough. This would help because the experts would have an incubation time between the interview and the critique where their opinions might change or new ideas could have emerged and they might be able to point out key areas that perhaps were overlooked. Second, a long term feedback mechanism could be put in place to review the technology at issue after a set amount of time such as two years. By performing new elicitations at regular intervals, even if they are on a small scale, the list of exposure scenarios, Risk Triggers, knowledge gaps, and regulation issues would be kept up to date and relevant.

As the interactional expert develops greater experience through the interview process, he becomes more adept in integrating and differentiating the various disciplines involved. The interactional expert can then gradually build a more comprehensive trading zone which can be utilized to define the exposure scenarios and Risk Triggers. This is key to the interative process of feedback and to build a global view of the case study.

Conclusion

This paper presents a risk analysis method to help identify Risk Triggers needed to assess a specific nanotechnology with the use of expert elicitation. This model involved five parts: contribution, elicitation, synthesis, ranking and analysis. Silver nanotechnology was used as a case study to demonstrate this method. A database was created as a means to assess the current state of silver nanotechnology in the market place as well as provide information to bring to the experts. An elicitation was carried out that involved experts from many different fields in an attempt to integrate various perspectives and create trading zones, which would help assess silver nanotechnology from different levels. Then a synthesis of information from the interviews helped to create a list of Risk Triggers or critical criteria. The Risk Triggers were then ranked and an analysis on them and the other information provided in the interviews was presented. Through this method many issues surrounding silver nanotechnology were discussed including, a variety of exposure scenarios, Risk Triggers, knowledge gaps and regulatory issues.

Recommended Future Research

The key to this method is utilizing a broad range of expertise from various experts in academia, industry and government. It is proposed that this method be used to evaluate different forms of emerging technology or nanotechnologies that are evolving at a pace which current governmental regulatory structure cannot keep up with. This preliminary evaluation of a technology could be used in the early stages to assess particular criteria which are important in evaluating that technology. As a second step, these exposure scenarios and Risk Triggers, along with example quotes and rankings in the form of a survey, could be presented to a larger sample group of experts. In this second round of elicitation, the focus would not be on determining the criteria but in ranking those criteria assembled and having each expert provide a range of uncertainty around that judgment. By having a data set from a larger sample size that provides rankings and uncertainties, it allows the research group to perform more extensive analysis on each criterion. Factors assessing each expert, such as dependence and weights based on expertise, could also be integrated into the final analysis. The results from such a survey would move this work from the realm of risk analysis to risk assessment.

In continuing to develop the first part of risk analysis, as was performed with the silver nanotechnology case study, a different "contribution" or first step could be used. Here a database of silver nanotechnologies (SNCI) was assembled and used as the contribution and basis for the expert elicitations. Instead of providing information on current market data, experimental data could be provided. If mock up exposure scenarios were tested or Risk Triggers measured in a laboratory setting, this data could be presented to the experts during the elicitation process. It is another form of information that would give the experts a sense of how this technology might behave in real world settings. Due to the specific nature of the experimental data, this might have the effect of narrowing the range of experts who could be used to interpret the data. For instance, if air exposure of nanoparticles was being investigated in the fabrication of nanowires, an aquatic toxicologist would not necessarily be the right expert to interpret the results from that experiment. While this elicitation would provide useful information for real world fabrication scenarios of nanowires and other similar structures, the results of this case study might not translate so easily to other types of exposure scenarios.

Expert elicitation has the advantage over more traditional research initiatives, however, in that a broader spectrum of issues can be addressed and evaluated at relatively low cost and quick speed for initial analysis of risks and other relevant criteria in a variety of emerging technologies. It is a methodology which combines philosophical, psychological and scientific techniques to focus attention for regulatory and research concerns. As this approach evolves to become more standardized in the steps, parameters for controlling variables and language, it holds promise for integration into the broader scientific community.

Glossary

Adaptive management – use of trading zones, where multiple stakeholders "exchang[e] ideas, resources, and solutions across different communities and interests." requires constant communication between the stakeholders and the system they are managing, having the flexibility to adapt new strategies to new situations

Anticipatory governance – use of trading zones, where multiple stakeholders "exchang[e] ideas, resources, and solutions across different communities and interests." policy institutions must be included in the group of stakeholders

Bulk silver – silver that is larger than 300nm

Brownian motion – random movement of microscopic particles suspended in liquids or gases resulting from the impact of molecules of the surrounding medium[62]

Dissolved silver – silver that can pass through a filter <1nm in diameter

Glutathione – a peptide C10H17N3O6S that contains one amino acid residue each of glutamic acid, cysteine, and glycine, that occurs widely in plant and animal tissues, and that plays an important role in biological oxidation-reduction processes and as a coenzyme[63]

Holarchy – a hierarchy of holons, where a holon is both a part and a whole. Every holarchy is part of a larger holarchy.

Homeopathic remedy – a system of medical practice that treats a disease especially by the administration of minute doses of a remedy that would in healthy persons produce symptoms similar to those of the disease[64]

Interactional Expert – An individual who becomes an expert at maintaining and coordinating various trading zones.

Nanosilver – nano-sized silver particles, approximately1-100nm in diameter

Nanotechnology – the manipulation and fabrication of materials and devices in one or more dimensions in the range of 1-100nm. (see section on What is Nanotechnology?)

Precursor Products – products defined in the SNCI as those that are used in the fabrication/production of a separate end product.

Risk Trigger – Specific physical properties or criteria that are critical in evaluating the risk of a silver nanotechnology.

Thiol groups – any of various compounds having the general formula RSH which are analogous to alcohols but in which sulfur replaces the oxygen of the hydroxyl group and which have disagreeable odors[65]

Trading Zone – creating a space for information to be exchanged between two or more groups

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[62] Brownian motion. (2008). In *Merriam-Webster Online Dictionary*. Retrieved July 9, 2008, from http://www.merriam-webster.com/dictionary/Brownian motion

[63] glutathione. (2008). In *Merriam-Webster Online Dictionary*. Retrieved July 8, 2008, from http://www.merriam-webster.com/dictionary/glutathione

[64] homeopathy. (2008). In *Merriam-Webster Online Dictionary*. Retrieved July 21, 2008, from http://www.merriam-webster.com/dictionary/homeopathy

[65] thiol. (2008). In *Merriam-Webster Online Dictionary*. Retrieved July 8, 2008, from http://www.merriam-webster.com/dictionary/thiol

Acronyms

BPT – Best Practicable Technology

CCC – Criterion Continuous Concentration for EPA's Priority Pollutants

CMC – Criteria Maximum Concentration for EPA's Priority Pollutants

CTA – International Center for Technology Assessment

CWA – Clean Water Act

EPA – Environmental Protection Agency

FIFRA – EPA's Federal Insecticide, Fungicide, and Rodenticide Act

IDLH – NIOSH's Immediate Dangerous to Life or Health Concentrations

NIOSH – National Institute for Occupational Safety and Health

NRDC – Natural Resources Defense Council

OSHA – US department of Labor Occupational Safety and Health Administration

PEL – OSHA's Permissible Exposure Limit

RCRA – Resource Conservation and Recovery Act

REL – NIOSH's Recommended Exposure Limit

RT – Risk Trigger

SNCI – Silver Nano Commercial Inventory, can be found at www.nanotechproject.org

TWA – 8hr total weight average

Appendix

SNCI Independent Conclusions

Below is a summary of the Silver Nano Commercial Inventory (SNCI) Analysis Document. These conclusions are not included in the original document provided by the Woodrow Wilson International Center for Scholars. They are personal observations made after compiling the database of silver nanotechnology products.

Conclusions of SNCI

This report helps illustrate trends in the use of an emerging technology: specifically, the incorporation of silver nanotechnology into a wide array of commercial and consumer products. While the regulation of nanosilver reflects indiocencracies, because of its distinct uses,, there are three challenges for nanosilver as well as other nanotechnologies entering today's market, including a compounding effect, dealing with various non-point exposure scenarios; an overall lack of clarity within the industry with naming conventions and terminology; and an overall low level of transparency for the "inquisitive" consumer.

The Compounding Effect

While this analysis only provides a snapshot of commercial products on the market which contain silver nanotechnology, it illustrates how pervasive this technology is becoming. The major issue is not that there will be a few point source areas of both human and environmental exposure, but rather that there will be thousands and potentially hundreds of thousands of non-point sources of exposure. The question which should be raised is: "will the compounding of these products produce a problem?"

It should be noted that we are not just talking about one type of silver. It is exposure to a combination of nanosilver particles with a wide range of cappings, colloid mixtures and the ionic form of silver.

To illustrate this, imagine starting off the day at home, getting out of bed with your silver impregnated sheets, brushing your teeth with your silver coated toothbrush, washing with silver antimicrobial soap and shampoo, styling your hair with your silver coated brush and hair dryer.

You then proceed to get dressed in your silver odor inhibiting socks and your clothes that have been washed with nanosilver detergent. You eat breakfast from leftovers contained in a silver treated food storage container from your nanosilver lined refrigerator. To clean your counters you use your colloidal silver antibacterial spray. On your way to work you cut yourself and place a silver bandage over the wound. And as you ride the bus you touch the silver coated handrails. You then arrive at the office to work at a desk with a silver coated stapler, keyboard and mouse. You also have the option to buy silver sprays that can coat any product that does not already provide that silver antimicrobial protection.

By the end of the day, the exposure to silver in its various forms accumulates not just for the individual but also for the environment. Some of these products, if marketed well, will be present in hundreds of thousands of households across the country.

Currently, there are no regulatory structures to handle this type of widespread non-point source exposure. Silver and its compounds are listed as “toxic pollutants” under section 307(a) of the Clean Water Act.[66] Silver appears again in the list of “priority pollutants.”[67] In the most recent Project on Emerging Nanotechnologies publication, two end-of-life regulations were considered with regard to nanotechnologies, the Resource Conservation and Recovery Act (RCRA) and the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA, or the Superfund law). Neither of these regulations would sufficiently cover the current uses of silver nanotechnology.

The compounding effect depends on the number of products used and the dose of silver released and at this point, the dose is unknown. Many of the companies do not provide information on the size of the nanoparticle used or concentration of their product. This compounding effect of silver raise additional issues concerning chronic low levels exposure, resistant strains of bacteria developing, problems with sewage treatment and exposure to the aquatic environment.

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[66] 40 C.F.R. §401.15 (1974).
[67] Appendix A to 40 C.F.R. §423 (1982).

Overall Lack of Clarity

One of the other observations made during this analysis is that the terminology around these products and silver nanotechnology generally is often unclear, misguided or vague if any information is provided. Silver nanotechnology has been described with such words as: silver nanoparticles, metallic silver, silver nanocolloids, colloidal silver, nano-sized silver ions, and silver nanoparticles (Ag^+). Calling ions, nanotechnology or nanosized is extremely misleading. A silver ion (Ag^+) is a silver atom with a missing valance electron and happens to be considered the most toxic form of silver. In some cases it is unclear if silver ions are being used exclusively or if in fact, when ions are mentioned, if any form of nanotechnology is being used at all in the product.

Colloids are defined as a mixture of a dispersed phase (such as silver nanoparticles) and a dispersion medium. An accepted range of sizes for the dispersed phase in at least 1 dimension is from 1-1000nm. Yet we find a handful of colloids claiming to be <1nm. Particles below 1nm are generally considered to be dissolved. As demonstrated in this database, scientific terminology is being used but it is not always a guarantee that it is being used correctly.

Low Level of Transparency

The third trend is an overall lack of information provided to the consumer. These searches were performed in part to see what an "inquisitive" consumer could learn and find out about commercial products already in the marketplace. While there are limitations to any search, this analysis reflects what data is available for a consumer to find.

In many cases, companies that produced "precursor" products advertised to manufacturers with a more informed and technically detailed product description, such as concentrations, nanoparticle size, polymers in which the particles are contained and even the description of the mechanism of antibacterial action. Larger companies where a "precursor" product might be produced in house, severely limit the available information about their silver nanotechnology. The focus of information released to consumers in these cases is on silver nanotechnology providing antibacterial benefit. This limited information is demonstrated by the following two companies:

LG Electronics, a large, international corporation, produces a front load washer, vacuum cleaner, and refrigerator that contain silver nanotechnology (Bio Silver and Bio Shield).

> *In the frontload washer, they are "coated by silver nano particles (Ag+)."*
> *In the LG Cyking vacuum cleaner, they are "with nano-sized silver particles coated and melted in keeps various bacteria from breeding."*
> *In the Side-by-Side refrigerators, the "silver particles coat the interior of LG side by side refrigerator (Bio silver) and the gasket (Bio shield) of the refrigerator. "*[68]

Samsung, another large corporation, produces a wide range of silver products from coated notebooks to refrigerators. It becomes difficult to find more than antibacterial claims mentioned for their products.

> *"Silver Nano technology takes advantage of the anti-bacteria properties of silver to protect computer users from potentially harmful germs, moulds and bacteria. It is applied as a high-tech coating on the Q40's keyboard and palm rest."*[69]

It should be noted that as a consumer, we rarely know all the ingredients or components to the products we use on a regular basis. The argument could be made that the manufacturers are providing the consumer with the minimum level of information to promote a better and smarter product. This low level of transparency also raises some concerns. How is the public reassured that proper safety and regulatory procedures are being observed? If approximately 90% of the products listed in the database make an antimicrobial claim, does that mean they should be regulated under FIFRA? If so, are any of them regulated? What rights do the consumers have? Do they have the right to know what is in the products they consume so that they can make an informed decision?

While these questions are not new or specific to the use of silver nanotechnology, we are beginning to talk about particles that do not always behave like their bulk counterparts. Each of these silver applications will have varied human and environmental exposure characteristics. Do the companies producing these products have the foresight to address these issues; do they

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[68] *LG Electronics Inc. (June 28, 2004) Nano technology-applied LG home appliances (Press Release) Retrieved June 18, 2007 from http://www.lge.com/about/press_release/detail/PREIMENU_4035_PREIMENU.jhtml*

[69] *Samsung Corporation. (Febuary, 15, 2007). Samsung Unveils SSD-enabled Q40 Notebook (Samsung Press Center). Retrieved July 12, 2007 from http://www.samsung.com/he/presscenter/pressrelease/pressrelease_20070215_0000324173.asp*

have the resources or manpower to investigate these potential problems; do they have the responsibility to look beyond the impact of their products domain?

These are the questions that different stakeholders, the public, industry, academia and government, will have to face. Will it be necessary to adapt the regulatory structure so that it can encompass non-point pollutants? Perhaps as nanotechnology is integrated into the public's consciousness there will be less confusion over scientific terms or companies may be held to higher standards. To answer the questions raised on transparency and required disclosure, a public discourse should take place take place with all of the stakeholders.

Expert Elicitation Handout

Interview Information Packet
University of Virginia
Emma Fauss
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434.774.6437

Memo:

This document provides a brief outline of how the interview is laid out and a few examples that illustrate the cases we will be reviewing during the interview itself. It would be helpful if you reviewed these before our pre-interview talk. I can clarify any questions you might have on these examples during the talk, thereby making the interview run more smoothly.

The primary goal of this interview is to more clearly identify high risk scenarios. This involves investigating any “knowledge gaps”, regulation, exposure and hazard issues surrounding different applications of silver nanotechnology.

Interview Outline:

1) EXPERTIESE:
I will ask you to briefly describe, on tape, what your area of expertise is and what, if any, experiences you have had with nanotechnology, silver or silver nanotechnology.

2) EXPOSURE, HAZARD & RISK TRIGGERS:
We will then review a list of scenarios of silver nanotechnology. (See attached list of scenarios and example products) We will explore different methods of use (“exposure”) and disposal (“hazard”) and review a list of risk triggers. To give you an overview of the information we will be seeking in our conversation, two excel pages are provided at the end of this document which contain a selection of possible topics. Not all of these topics will be covered due to time constraints, but any expert advice or insight that you can provide will be welcome.

3) REGULATIONS, KNOWLEDGE GAPS & RESEARCH:
In the final portion of the interview I would like to hear your opinion on what types of regulations might come in to play or influence the technologies we will have discussed and what information might be pertinent in the regulation of these technologies. I would also like to hear where you think “knowledge gaps” lie and, if you could, where you would recommend research funds be directed.

Nano Silver Cases

The following cases each deal with only one specific type of silver nanotechnology that involves nano sized silver particles being utilized for their antimicrobial properties. This is the predominant use of silver nanotechnology in the consumer market and its application continues to grow. These scenarios each may have their own set of issues concerning risk and regulations.

1. **Coatings Incorporating Nanotechnology**
Description: Products coated with a polymer containing nano silver during production.
Prevalence: This is the most prevalent use of nano silver.*
Intermediary/Product: In this case, it is only an intermediary process.
Uses & Type: There are multiple uses for this application. The is not a great variation between different applications. (i.e. all products are coated)
Example: Nano Care Technology Ltd. [China]

2. **Colloidal Silver**
Description: Colloidal silver used in products ranging from cleaners to makeup to personal care items such as toothpastes, soaps and shampoos.
Prevalence: This is the 2^{nd} most prevalent use of nano silver.*
Intermediary/Product: This is most often involves colloidal silver being added to a product. Therefore the nano silver itself is an intermediary product.
Uses & Type: There are single to many uses for this type of product, depending on the company producing the product. There is a great deal of variation between different applications.
Example: NANOVER™ by Nanogist Co., Ltd. [South Korea]

3. **Homeopathic Nano-Silver Applications**
Description: I found many homeopathic applications of Nano silver in colloidal form for use in supplements and disinfectant sprays.
Prevalence: This category is contained under the 2^{nd} most prevalent use of nano silver.*
Intermediary/Product: This is both an intermediary product and a product that consumers use directly.
Uses & Type: The uses for this application do not vary greatly and there is not a lot of variation between the different applications. (i.e. it generally is pure silver in pure water, with only a variation in the size of the nano silver)
Example: Mesosilver by Purest Colloids, Inc. [USA]

4. Spun **Nano Silver Applications**
Description: Nano silver is integrated or spun into a variety of different fabric applications, from cottons to a wide range of polymers during the production the thread itself.
Prevalence: This is a large group found in clothing, sporting goods and other fabrics.*
Intermediary/Product: This only occurs as an intermediary product which is then used in a variety of fabric applications.
Uses & Type: There are different variations of integrating nano silver into the fabric. Overall, the single major application of spun nano silver is the integration of it into a fabric.
Example: SmartSilver by NanoHorizons Inc. [USA]

5. Solid **Nano Silver Applications**
Description: Nano silver is integrated into a master batch or polymer that is then used to create items such as food storage containers to hair care products.
Prevalence: These are another large group of products, contained within the 4^{th} largest group.*
Intermediary/Product: Intermediary master batches are needed to produce a final consumer product.
Uses & Type: Many different polymers with widely varying properties can have nano silver incorporated into them for a variety of different uses.
Example: Hair Brush by Sang Shin Industrial Co., Ltd.

6. **Nano silver powder**
Description: Nano silver powder is used on products for its antimicrobial properties.
Prevalence: This is the smallest group of products. Only a handful exist.*
Intermediary/Product: This product is generally applied to other products to impart its properties.
Uses & Type: There are few applications.
Example: Nano silver powder on socks.

*according to the entries found in the Nano Silver Commercial Database designed and compiled by Emma Fauss in 08.2007

Examples

Antibacterial Handrail

Company:
Nano Care Technology Ltd.

Country:
China

Type/Form: Coating

Particle: 50 nm

Expected Lifetime: NA

Applied How: It is applied in a coating of thickness 2.88~3.79 micro meters (average 3.32 micro meters)

Recommended Uses: "Typical Applications: Tableware, kitchenware, personal care products, watch accessories, door handles, pet care products, public facilities, etc."

Antibacterial?: "On the completion of four years R&D program, NCT is pleased to introduce a revolutionary nano-silver based patented technology to be applied on the surface of products, providing antibacterial substance and hardness enhancement."70

NANOVER™

Company:
Nanogist Co., Ltd.

Country:
Korea

Type/Form: Liquid

Particle: "Since the size of Entire Nano particle including Nano Silver particle is average 5nm, has high bulk rate and surface area rate with same mass."

Applied How: "applied"

Recommended Uses: "Nano-silver can be applied to a range of other healthcare products such as dressings for burns, scald, skin donor and recipient sites; plasters for surgical and trauma wounds; aqueous gel for spots, acne and cavity wounds; and female hygiene products - panty liners, sanitary towels and pants."

Antibacterial?: "NANOVER™ shows antibiotic and sterilizing effect in lower than 10ppm concentration, when producing application products, possible to produce transparent product." [71]

_______________Uses_________________

Cosmetics	Cleaner
Make Up	Disinfectant Spray
Mask Pack	Detergents
Personal Care	
Cleansing Soap	Hair Spray
Toothpaste	Hair Wax
AG-toothbrush	Hair Gel
AG-Garglin	Hand Sanitizer
AG-Mouth Deodorant	Wet Tissue
Shampoo & Conditioner	Body Cleanser
Hair Mousse	

[70] Nano Care Technology Ltd., "Company Profile," http://www.nanocaretech.com/En_index.asp (accessed August 1, 2007).

[71] Nanogist Co. Ltd., "What is Nanosilver?," http://www.nanogist.com/English/nano/silver.htm (accessed September 10, 2007)

Mesosilver

Company:
Purest Colloids, Inc.

Country:
USA

Type/Form: Liquid

Particle: <0.65 nm and 20 ppm "True colloidal silver. Colloid means silver particles, not silver ions....Highest nanoparticle concentration, 80% particles (typical). "[72]

Expected Lifetime: "infinite shelf life"

Applied How: silver particles suspended in water

Recommended Uses: "Dosage
The dosage for Mesosilver is typically one teaspoon (5mL) daily to help maintain health. Up to one tablespoon taken 4 times per day may be taken to help fortify the immune system when needed. Actual dosage will vary based on individual needs."

Antibacterial?: "Because of the research showing colloidal silver's superior performance in fighting microbes, it has attracted the attention of leading scientists and medical researchers throughout the world....
According to experts, no microorganism ever tested has been able to stay alive for more than six minutes when exposed directly to colloidal silver"[73]

SmartSilver™

Company:
NanoHorizons Inc.

Country:
USA

Type/Form: Spun

Particle: ~10-15nm on average "SmartSilver is available in Masterbatch, CottonPro, Staple Fiber and Polyurethane"

Expected Lifetime: permanent

Applied How: Nanoparticles "are also chemically and permanently bonded to the fibers that are being enhanced."[74] "SmartSilver™ is available in Masterbatch, CottonPro, Staple Fiber and Polyurethane"[75]

Recommended Uses: fabrication of fabrics

Antibacterial?: "SmartSilver™: The Smarter Anti-Odor and Antimicrobial Answer"[76]

[72] Purest Colloids, Inc. "Colloidal Silver - Mesosilver® Brand Colloidal Silver," http://www.purestcolloids.com/mesosilver.htm (accessed September 10, 2007).

[73] Purest Colloids, Inc., "A Brief History of The Health Support Uses of Silver," http://www.purestcolloids.com/history-silver.htm (accessed June 19, 2007).

[74] NanoHorizons Inc., "Understanding SmartSilver™ Antimicrobial Fiber Technology," http://www.nanohorizons.com/documents/Nano.SSFiberbg6.20Rev.pdf (accessed July 3, 2007).

[75] NanoHorizons Inc., "SmartSilver™," http://www.nanohorizons.com/prodSmartSilver.shtml (accessed July 3, 2007).

[76] NanoHorizons Inc., "SmartSilver™," http://www.nanohorizons.com/prodSmartSilver.shtml (accessed July 3, 2007).

Professional Hair Brush

Company: Sang Shin Industrial Co., Ltd.

Country: USA

Type/Form: Solid

Particle: NA

Expected Lifetime: NA

Applied How:
"Using Nano Silver technology, Sang Shin is producing high-quality brush bristles for your healthy hair. To accomplish this, we produce brush bristles by mixing and processing Nylon 66 raw materials and anti-bacterial Nano Silver materials."[77]

Recommended Uses: hair brush

Antibacterial?: "Silver(Ag+) has been recognized since ancient times as a substance with natural benefits to prevent bacteria and fungus, to sterilize and to detoxify. Taking full advantage of those benefits, Sang Shin is applying the new concept technology called 'Nano Silver' to our brush products."[78]

Socks

Company: AgActive

Country: United Kingdom

Type/Form: Powder

Particle: 25 nm

Expected Lifetime: life of product

Applied How:
" AgActive socks ship with at least a hundred times more silver in them than they actually need to work. This silver 'dust' is invisible but extremely effective at disinfecting shoes of bacteria and fungi. When you first wash the socks, the silver levels will drop to normal. Don't miss out on the opportunity to take advantage of the extra dust they are shipped with: wear the socks in every pair of problem shoes you own before you first wash the socks. The extra dust will drop out and clean the inside of your shoes. Remember: you can wear AgActive socks in a new pair of shoes every day and they won't become smelly. You don't need to wash them unless they pick up visible dirt."[79]

Recommended Uses: socks

Antibacterial?: "SilverSure, the technology applied to our socks is based on silver, which is naturally anti microbial so it kills the bacteria that causes foot odour (it doesn't just hide it). Silver is also anti fungal (so it kills the fungus that causes athlete's foot)"[80]

[77] Sang Shin Industrial Co., Ltd., "Products Professional Hair Brush," http://www.i-sangshin.com/ (accessed August 7, 2007).

[78] Sang Shin Industrial Co., Ltd., "Nano Silver(Ag+) Bristles," http://www.i-sangshin.com/ (accessed June 21, 2007).

[79] AgActive, "How to get the most out of your socks," http://www.agactive.co.uk/index.cfm?fuseaction=feature.display&feature_id=7 (accessed September 10, 2007).

[80] AgActive, "About our technology," http://www.agactive.co.uk/index.cfm/fuseaction/page.display/page_id/24/.htm (accessed September 10, 2007).

Evaluation Criteria (version 09/10/2007)	Coating	Colloid (Intermeidary)	Colloid (Homeopathy)	Spun	Solid	Powder
Exposure related						
Coating/Matrix stability - Are there scenarios where the nanoparticle is freed from the polymer matrix/the coating?						
Media dependent property - Does the material behave differently in water, air etc?						
Free nanoparticles - Would there be scenarios where the nanoparticles could be biologically available available within the product lifecycle?						
Used with other products - The effect of the nanomaterial would probably be different if the product is used with other products.						
Multiple Disposal Pathways - Is the product disposed in different ways, each with a different degree of effect on the environment? Recycling would have the least effect.						
Dispersibility - Does the material disintegrate into free nanoparticles in water? A hydrophobic coating would probably make it less dispersible?						
Exposure Score						
Hazard Related						
Toxicology - Is there enough toxicology informations currently available?						
Particle size < 100nm						
High aspect ratio - does the shape enhance transport?						
New product - Is the product itself a new nano-application or is the nano material used only for performance enhancement?						
Catalytic Property - Does silver catalyze anything						
Susceptible population - Are there scenarios during the product use where significant number of people would be more susceptible to have a higher degree of effects?						
Antibacterial - Does the nanomaterial kill/harm useful bacteria in the environment or the human body?						
Hazard Score						

	Exposure scenario	Coatings				Colloid (Intermeidary)				Colloid (Homeopathy)				Spun				Solid				Powder			
		G	L	M	H	G	L	M	H	G	L	M	H	G	L	M	H	G	L	M	H	G	L	M	H
Use	Inhalation																								
	Skin absorption																								
	Ingestion																								
	Fresh Water Entrainment																								
	Salt Water Entrainment																								
	Air Release																								
Disposal	Inhalation																								
	Skin absorption																								
	Ingestion																								
	Fresh Water Entrainment																								
	Salt Water Entrainment																								
	Air Release																								

G = knowledge gap
L = low chance of exposure
M = medium chance of exposure
H = high chance of exposure

Data Tables and Calculations

The data tables contain the individual rankings assigned to each exposure scenario and hazard related Risk Trigger. Under each score is the number of expert that were assigned that particular ranking or a score or NA if they did not respond to that criterion.

Table 20. Data Table of Exposure Scenarios

Score	5	4	3	2	1	0
Exposure Scenario	High	HM	Med.	ML	Low	NA
Absorption (dermal)	1	1	0	2	1	5
Inhalation / Absorption (lung)	1	1	0	2	3	3
Ingestion	1	1	2	2	3	1
NS release into aquatic environment	4	1	3	2	0	0
NS migrate through the food chain	0	0	0	0	2	8
NS chronic exposure	2	1	2	1	0	4

Table 21. Data Table for Hazard Related Risk Triggers

Score	5	4	3	2	1	0
Hazard Related Risk Trigger	High	HM	Med.	ML	Low	NA
Catalytic action	2	1	0	0	0	7
Ag+ release	5	1	2	0	0	2
Dermal toxicity	0	0	0	0	3	6
Toxicity in lung	3	1	0	0	1	5
Toxicity from chronic exposure	2	2	1	0	2	3
Toxicity from ingestion	0	1	2	1	3	3
Toxicity in Salt water	0	0	0	2	2	6
Toxicity in Fresh water	3	0	1	0	0	6

The following tables provide the calculated mean and standard deviation for each exposure scenario and hazard related Risk Trigger. A plus one and minus one standard deviation is also provided. This information is provided graphically in Figure 7. Exposure Scenario Rankings & Figure 8. Hazard Related Risk Trigger Rankings.

Table 22. Calculated Values for Exposure Scenarios

Exposure Scenario	Total # to Respond	Mean	Standard Deviation (SD)	+1SD	-1SD
Absorption (dermal)	5	2.8	2.16	4.96	0.64
Inhalation / Absorption (lung)	7	2.3	2.20	4.49	0.08
Ingestion	9	2.4	1.80	4.25	0.64
NS release into aquatic environment	10	3.7	1.41	5.11	2.29
NS migrate through the food chain	2	1.0	0.00	1.00	1.00
NS chronic exposure	6	3.7	1.22	4.89	2.44

Table 23. Calculated Values for Hazard Related Risk Triggers

Hazard Related Risk Trigger	Total # to Respond	Mean	Standard Deviation (SD)	+1SD	-1SD
Catalytic action	3	4.7	0.22	4.89	4.44
Ag+ release	8	4.4	0.73	5.11	3.64
Dermal toxicity	3	1.0	0.00	1.00	1.00
Toxicity in lung	5	4.0	2.40	6.40	1.60
Toxicity from chronic exposure	7	3.3	2.49	5.78	0.80
Toxicity from ingestion	7	2.1	1.27	3.41	0.88
Toxicity in Salt water	4	1.5	0.25	1.75	1.25
Toxicity in Fresh water	4	4.5	0.75	5.25	3.75

The following tables display the sum of inferred rankings assigned to each exposure scenario and hazard related Risk Trigger by Product type. Each criterion was given a score of 5 for high, 3 for medium,1 for low or marked under NA for not applicable for that expert. For example, in Ingestion nine experts responded to that criterion and one did not, therefore under each product type there are a total of nine responses. In coatings one expert was scored at a high, one at a medium and seven under low ranking.

Table 24. Data Table for Exposure Scenarios by Product Type

Score	5	3	1	5	3	1	5	3	1	0
	Coating			Colloid			Powder			NA
Exposure Scenario	H	M	L	H	M	L	H	M	L	
Absorption (dermal)	2	0	3	2	2	1	2	1	2	5
Inhalation / Absorption (lung)	0	1	6	2	2	3	4	0	3	3
Ingestion	1	1	7	4	2	3	2	1	6	1
NS release into aquatic environment	2	3	5	7	2	1	4	3	3	0
NS migrate through the food chain	0	0	2	0	0	2	0	0	2	8
NS chronic exposure	2	0	4	3	2	1	3	1	2	4

Table 25. Data Table for Hazard Related Risk Triggers by Product Type

Score	5	3	1	5	3	1	5	3	1	0
	Coating			Colloid			Powder			NA
Hazard Related Risk Trigger	H	M	L	H	M	L	H	M	L	0
Catalytic action	2	0	1	2	1	0	2	1	0	7
Ag+ release	5	0	1	5	1	0	5	1	0	4
Dermal toxicity	0	0	4	1	0	3	1	0	3	6
Toxicity in lung	1	2	3	3	1	2	4	1	1	4
Toxicity from chronic exposure	1	2	4	3	2	2	2	2	3	3
Toxicity from ingestion	0	1	6	2	1	4	1	2	4	3
Toxicity in Salt water	0	0	4	0	1	3	0	1	3	6
Toxicity in Fresh water	0	2	3	3	2	0	2	1	2	5

The following tables display the average scores calculated for each product type. These averages are calculated from the data in Table 24 and Table 25.

Table 26. Calculated Average Scores of Exposure Scenarios by Product Type

	Average score		
Exposure Scenario	Coating	Colloid	Powder
Absorption (dermal)	2.6	3.4	3.0
Inhalation / Absorption (lung)	1.3	2.7	3.3
Ingestion	1.7	3.2	2.1
NS release into aquatic environment	2.4	4.2	3.2
NS migrate through the food chain	1.0	1.0	1.0
NS chronic exposure	2.3	3.7	3.3

Table 27. Calculated Average Scores of Hazard Related Risk Triggers by Product Type

	Average score		
Hazard Related Risk Trigger	Coating	Colloid	Powder
Catalytic action	3.7	4.3	4.3
Ag+ release	4.3	4.7	4.7
Dermal toxicity	1.0	2.0	2.0
Toxicity in lung	2.3	3.3	4.0
Toxicity from chronic exposure	2.1	3.3	2.7
Toxicity from ingestion	1.3	2.4	2.1
Toxicity in Salt water	1.0	1.5	1.5
Toxicity in Fresh water	1.8	4.2	3.0