NIOSH Current Intelligence Bulletin: Health Effects of Occupational Exposure to Silver Nanomaterials

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The Policy

What it does
Provides updated information and recommendations about the potentially toxic effects of exposure to silver nanomaterials.

Synopsis
The National Agency for Occupational Safety and Health (NIOSH) has reassessed the risks of exposure to silver nanoparticles based on over 50 new research studies. These new studies demonstrate that exposure to silver nanomaterials can damage lung, liver, and kidney function in animal experiments. Based on these findings, NIOSH has drafted a *Current Intelligence Bulletin* [8] (CDC-2016-0001 [9]) on the health effects of exposure to silver nanomaterials and estimates that exposure to silver nanoparticles should be limited to 0.9 micrograms per cubic meter (µg/m³) in occupational settings. NIOSH has also recommended safety protocols to reduce workplace exposure.

Silver nanoparticles have practical uses in the manufacturing of electronics, pigments, antimicrobials, and textiles. Current regulations by the National Institute for Occupational Safety and Health (NIOSH) and the Occupational Safety and Health Administration (OSHA) set recommended exposure limits (REL) for silver at a concentration of 10 µg/m³ over 8 hours. Long term exposure to silver is known to cause argyria, but studies on the adverse health effects of silver nanomaterials in humans are lacking. Cellular studies have revealed that exposure to silver nanoparticles or ionic silver increases DNA damage, cell apoptosis, and necrosis [10]. In vitro studies also suggest that smaller silver particle size may correlate to greater toxicity [11]. Animal studies have been more comprehensive and include inhalation studies in rats. Silver inhalation in rats [12] resulted in silver deposits throughout major organs and tissues [13], lung damage, and changes to kidney and liver function when exposed to airborne concentrations of more than 100 µg/m³. Modeling studies established that silver nanoparticles are distributed systemically by blood circulation and that both dosage and means of inhalation contribute to toxicity. The results of these studies have been used to produce human risk assessment estimates such as those used by NIOSH.

The new guidance drafted by NIOSH recommends that workers not be exposed to silver in excess of 10 µg/m³ in an 8-hour time weighted average (TWA) and should not be exposed to silver nanomaterials exceeding 0.9 µg/m³ in an 8-hour TWA. Nanosilver exposure limits are more stringent than those for common atomic silver because nanosilver is more toxic. NIOSH further recommends that workers exposed to greater than REL levels of airborne silver nanoparticles should also be equipped with respiratory equipment to protect against particle inhalation. Employers are urged to develop risk management programs to identify and reduce worker exposure to silver nanomaterials and to regularly evaluate the safety of existing protocols that prevent worker exposure to airborne silver particles. Specifically, the components of risk management programs should include identification of job tasks where workers could be exposed to silver nanomaterials, installation of dust collection systems and other engineering controls to reduce airborne exposure, routine evaluation of worker exposure, education about safe work practices to reduce exposure to silver, use of personal protective equipment, spill control and routine cleaning procedures, hand washing equipment and protocols, and medical surveillance.

NIOSH acknowledges the need for further research to evaluate the health risks of occupational exposure to silver nanomaterials. NIOSH will continue to review new research as it is available and will make further recommendations if necessary.

**Context**

OSHA, an agency of the United States Department of Labor, sets *Permissible Exposure Limits* [14] (PEL)
for a variety of substances and pollutants. However, OSHA acknowledges that the data used to set PELs are often lacking or outdated and recommends that employers combine PEL guidelines with other federal standards of industry such as Threshold Limit Values (TLV), Biological Exposure Indices (BEI), and NIOSH RELs, such as those described in this report, to protect workers more comprehensively.

OSHA recommends that occupational exposure levels for substances that do not have set PELs should be based on the guidelines set by other agencies. While a REL or TRV is not a regulatory requirement and carries no legal weight, a PEL can be enforced by law. NIOSH has suggested that OSHA should adopt REL thresholds as a new and improved safety standard to update existing PELs.

Policy History

The latest draft of this guidance was released for public comment on 09/18/18 to be discussed in a public meeting that took place on 10/30/2018. The first draft was published on 01/21/18. The public comment period for that draft ended on 02/10/16. A public meeting was held on 03/23/16 and the final window to publish comments on that draft ended on 04/22/16. NIOSH released the August 2018 version of this guidance in response to public and peer review comments requesting updated recommendations.

OSHA does not classify silver as a toxic metal. Despite publishing PEL guidelines for silver metal, dust, and fumes, OSHA also did not mention silver in their National Emphasis Program for the Primary Metals Industries [15] of 2011. Nanosilver is not specifically regulated by OSHA in the United States. However, the European Agency for Safety and Health at Work published a document on “Safe Production of Nano Materials [16]”, in 2012 which voiced concerns about worker exposure to silver nanomaterials and acknowledged risks of silver toxicity. The publication does not establish a recommended exposure limit for nanosilver.

The Science

Science Synopsis

Prolonged or excessive exposure to silver or silver dust can cause a condition known as argyria [17] or argyrosis. Argyria can be localized, meaning limited to a single area of the body, or generalized, affecting large areas of the body. Argyria is immediately recognizable by the dramatic purplish gray color it causes in the skin and eyes. The pigment is caused by the accumulation of silver deposits in the skin. In chronic cases, silver deposits also develop in the eyes and organs. In the body, silver causes changes to the permeability of cell membrane, causing oxidative damage and apoptosis. Argyria is irreversible.

A nanoparticle [18] is any particle that is less than 100 nm in size. They exhibit unique properties that set them apart in behavior and use from larger particles. Silver nanoparticles are manufactured by biological, physical, or chemical processes [19]. Biological synthesis of silver nanoparticles utilizes either bacteria, plant, algae, or fungi cells to concentrate silver ions. Popular physical methods include evaporation-condensation and laser ablation. The evaporation-condensation technique uses a tube furnace or ceramic
heater to evaporate a solvent material, leaving silver nanoparticles behind. The laser ablation process directs laser pulses at silver metal in solution. Laser ablation yields a more chemically pure silver nanoparticle process. Chemical synthesis is usually achieved by reduction using both organic and inorganic reducing agents. Uses of nanoparticulate silver include laboratory or biological catalysis, chemotherapy, or as an antimicrobial agent.

Scientific Assumptions

- Inhalation studies showing adverse effects of silver nanoparticle exposure in rats can be extrapolated to humans: Silver nanoparticle inhalation toxicity studies have not been conducted in humans.
- Silver exposure is dangerous to humans: It has been confirmed that prolonged exposure to silver is toxic to humans.
- Limiting silver exposure to REL levels eliminates the risk of adverse health effects for workers: Limited research has been conducted to confirm that the exposure limits outlines by OSHA or NIOSH have adequately protected workers from silver toxicity.

The Debate

Potential Impacts

Industrial hygienists widely agree that PELs set by OSHA are not longer up to date with the information available about the harmful effects of certain industrial processes and materials and are insufficient to protect workers. PELs for most substances have not been updated since 1968, and do not include may substances that are now regarded by industrial hygienists as potentially dangerous and harmful.

These revised guidelines demonstrate the need to constantly reevaluate and update occupational and industrial safety standards. It may be appropriate to review current RELs and PELs for other substances or to create new exposure limits for substances that have been found to be toxic since 1968. Emerging fields such as nanotechnology create the need for review of existing policy and creation of relevant new guidelines.

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