BILLING CODE 4163-19-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Centers for Disease Control and Prevention

[Docket Number CDC-2012-0014; NIOSH-260]

Silver Nanoparticles (AgNPs); Information and Comment Request

Agency: National Institute for Occupational Safety and Health (NIOSH) of the Centers for Disease Control and Prevention (CDC), Department of Health and Human Services (HHS).

Action: Request for information and comment.

Summary: The National Institute for Occupational Safety and Health (NIOSH) of the Centers for Disease Control and Prevention (CDC), as part of its mission to investigate new and emerging hazards, has initiated an evaluation of the scientific data on silver nanoparticles (AgNPs) to ascertain the potential health risks to workers and to identify gaps in knowledge so that appropriate laboratory and field research studies can be conducted. NIOSH has identified a number of relevant publications on AgNPs. This listing (*Evaluation of the scientific data on silver nanoparticles (AgNPs)* can be found in Docket CDC-2012-0014 at *http://www.regulations.gov*.

NIOSH is requesting additional information on the following: (1) published and unpublished reports and findings from *in vitro* and *in vivo* toxicity studies with AgNPs, (2) information on possible health effects observed in workers exposed to AgNPs, (3) information on workplaces and products in which AgNPs can be found, (4) description of work tasks and scenarios with a potential for exposure, (5) information on measurement methods and, workplace exposure data, and (6) information on control measures (e.g., engineering controls, work practices, PPE) that are being used in workplaces where potential exposures to AgNPs occur.

DATES: Electronic or written comments must be received on or before *[insert date 60 days from posting]*.

ADDRESSES: You may submit comments, identified by CDC-2012-0014 and docket number NIOSH-260, by any of the following methods:

- *Federal eRulemaking Portal:* *http://www.regulations.gov*. Follow the instructions for submitting comments.
- *Mail:* NIOSH Docket Office, Robert A. Taft Laboratories, MS-C34, 4676 Columbia Parkway, Cincinnati, OH 45226.

All information received in response to this notice must include the agency name and docket number (CDC-2012-0014; NIOSH-

260). All relevant comments received will be posted without change to *www.regulations.gov*, including any personal information provided. For access to the docket to read background documents or comments received, go to *www.regulations.gov*.

FOR FURTHER INFORMATION CONTACT: Ralph Zumwalde, NIOSH, MS-C14, Robert A. Taft Laboratories, 4676 Columbia Parkway, Cincinnati, Ohio 45226, telephone (513) 533-8320 or Eileen Kuempel, telephone (513)533-8363.

Background

Nanotechnology is generally defined as the intentional manipulation of matter to form novel structures with one or more dimension or features less than 100 nanometers (nm). Nanotechnology involves a wide range of chemistries and almost unlimited types of structures that have highly unpredictable interactions with biological systems. Producing materials at the nanoscale often results in specific physicochemical characteristics that may differ from those of the bulk substance. Because of these specific characteristics the use of substances in nano-form may pose certain health risks not observed from the use of the bulk form of the substance. Nano-silver is one type of nanomaterial that may have different physical-chemical

characteristics than the bulk form of silver. The National Institute for Occupational Safety and Health (NIOSH) is interested in gathering data to determine whether a health risk to workers may exist from exposure to AgNPs and if specific risk management guidance is needed to prevent exposure.

Several recently reported short-term experimental animal studies with AgNPs [Kim et al. 2008, 2009; Sung et al. 2008,2009; Song et al. 2012] have shown consistent physiological and toxicological responses including: (1) uptake of AgNPs to the blood and their subsequent distribution to all major organs and tissues, (2) decrements in lung function and induction of inflammatory responses, and (3) histopathology changes in the kidney and especially in the liver, in which bile duct hyperplasia was identified as the principal toxicological effect. Evidence is available from the 90-day inhalation study in Sprague-Dawley rats that AgNPs can deposit in the lung and be transported via the blood to the liver [Sung et al. 2008, 2009]. Studies also indicate that AgNPs can be transported and deposited in major organs and tissues when administered via gavage to Sprague-Dawley and F344 rats for 28 and 90 days [Kim et al. 2008, 2010]. A common feature of the systemic toxicological effects of AgNPs, irrespective of the exposure route, was the onset of histopathological effects to the liver

in exposed Sprague-Dawley and F344 rats [Sung et al. 2009; Kim et al. 2010]. High-dose animals in both studies developed bile duct hyperplasia along with some signs of hepatic necrosis. In the 90-day oral study, these effects were accompanied by changes in some clinical chemistry parameters indicative of perturbations in liver metabolism, for example, increases in serum cholesterol concentration and AP activity [Kim et al. 2010]. In the 90-day inhalation study of Sung et al. [2008, 2009] these systemic effects were accompanied by lung function deficits, the development of inflammation responses, and alveolar accumulation of macrophages [Sung et al. 2008]. In another 90-day inhalation study by the same group of researchers [Song et al. 2012], decreases in lung function and lung inflammation were observed in male rats that persisted in the high dose group at 12 weeks after cessation of exposure. In female rats, no decrease in lung function was observed, and the lung inflammation showed gradual recovery after cessation of exposure [Song et al. 2012].

Published reports on worker exposure to AgNPs are limited but indicate the potential airborne release of AgNPs during their production [Park et al. 2009; Lee et al. 2011a, b] or as an exposure resulting from the electro-refining of silver [Miller et al. 2010].

Information Needs

Additional data and information are needed to assist NIOSH in evaluating the occupational safety and health concerns of working with AgNPs. Information is particularly needed for determining the relevance of bile duct hyperplasia and hepatocellular necrosis observed in AgNP exposed rats, as well as information on: 1) sources of AgNP exposure, 2) factors that influence worker's exposure, 3) in-place exposure control measures (e.g., engineering controls) and work practices that are effective in reducing worker exposures, and 4) appropriate measurement methods and exposure metrics for characterizing workplace exposures.

NIOSH seeks to obtain materials, including published and unpublished reports and research findings, to evaluate the possible health risks of occupational exposure to AgNPs. Examples of requested information include the following:

1) Identification of industries or occupations in which exposures to AgNPs may occur.
2) Trends in the production and use of AgNPs.
3) Description of work tasks and scenarios with a potential for exposure to AgNPs.

4) Workplace exposure measurement data in various types of industries and jobs.
5) Case reports or other health information demonstrating potential health effects in workers exposed to AgNPs.
6) Research findings from *in vitro* and *in vivo* toxicity studies, including physical-chemical characterization of AgNPs.
7) Information on control measures (e.g., engineering controls, work practices, PPE) being taken to minimize worker exposure to AgNPs.
8) Information on measurement methods and exposure metrics that can be used to quantify worker exposure to AgNPs including information on the limitations of those methods in quantifying exposures?

References

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_____December 12, 2012

John Howard, Date

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