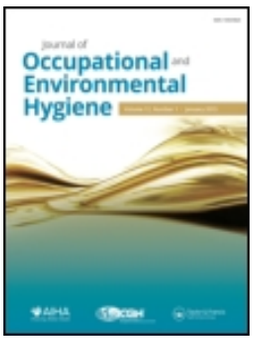

Journal of Occupational and Environmental Hygiene

ISSN: 1545-9624 (Print) 1545-9632 (Online) Journal homepage: https://www.tandfonline.com/loi/uoeh20

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To cite this article: Vladimir Murashov & John Howard (2015) Risks to Health Care Workers from Nano-Enabled Medical Products, Journal of Occupational and Environmental Hygiene, 12:6, D75-D85, DOI: 10.1080/15459624.2015.1006641

To link to this article: https://doi.org/10.1080/15459624.2015.1006641

Published online: 07 May 2015.

Journal of Occupational and Environmental Hygiene, 12: D75–D85
ISSN: 1545-9624 print / 1545-9632 online
DOI: 10.1080/15459624.2015.1006641

Commentary

Risks to Health Care Workers from Nano-Enabled Medical Products

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Nanotechnology is rapidly expanding into the health care industry. However, occupational safety and health risks of nano-enabled medical products have not been thoroughly assessed. This manuscript highlights occupational risk mitigation practices for nano-enabled medical products throughout their life cycle for all major workplace settings including (1) medical research laboratories, (2) pharmaceutical manufacturing facilities, (3) clinical dispensing pharmacies, (4) health care delivery facilities, (5) home health care, (6) health care support, and (7) medical waste management. It further identifies critical research needs for ensuring worker protection in the health care industry.

Keywords health care, life cycle, medical products, nanomaterials, nanotechnology, risk assessment, risk mitigation, workplace

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The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the National Institute for Occupational Safety and Health, the Centers for Disease Control and Prevention, or the US Department of Health and Human Services.

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INTRODUCTION

Nanotechnology refers to a new set of technologies used to develop nanoscale structures—typically between 1 and 100 nanometers in at least one dimension—which are utilized in commercial applications.[1] At the nanoscale, certain materials exhibit new properties not exhibited at the macro or the atomic scale. For instance, materials that were not reactive at the macro scale can become highly reactive at the nanoscale largely because of the greatly increased fraction of atoms exposed on particle surface and because of changes in the electronic structure. At the other end of the dimensional scale, materials in a molecular form composed of only a few atoms have a very limited capacity to accommodate functional groups, while those materials at the nanoscale can have a wide range of surface functional groups. These new size-dependent properties of nanoscale structures represent both the promise of nanotechnology as well as the concern about potential adverse health effects to workers, consumers, and the environment.

Nanotechnology-enabled medical products (NEMPs) in imaging, diagnosis, and therapy offer exciting new possibilities for significantly advancing medical science in the 21st century.[2] Many of these applications are already on the market. The 2010 World Technology Evaluation Center (WTEC) Report states that nano-enabled medical products totaled $60 billion in 2010.[3] Another report identified 22 nano-enabled medical products approved by the US Food and Drug Administration (FDA) and 87 Phase I and Phase II clinical trials of NEMPs initiated in 2011.[4]

Unique properties of NEMPs can also present unique risks. Risks of hazardous materials are often manifested and recognized initially in occupational settings since workers are often the first to be exposed to new materials and those exposures can be at high concentrations and for extended periods of time.[5,6] The health care industry contains at least seven unique settings where workers can be at risk. These are: (1) medical research laboratories, (2) pharmaceutical manufacturing facilities, (3) clinical dispensing pharmacies, (4) health care delivery facilities, (5) home health care, (6) health care support, and (7) medical waste management. Elucidating the occupational health risks of NEMPs is a crucial first step in developing a comprehensive risk assessment and risk management framework for NEMPs in health care industry. This article sets out a research roadmap for assessing and managing the occupational health risks of NEMPs through all stages of their life cycle, including research and development, manufacture, use in patient care and support activities, and in waste disposal (see Figure 1).

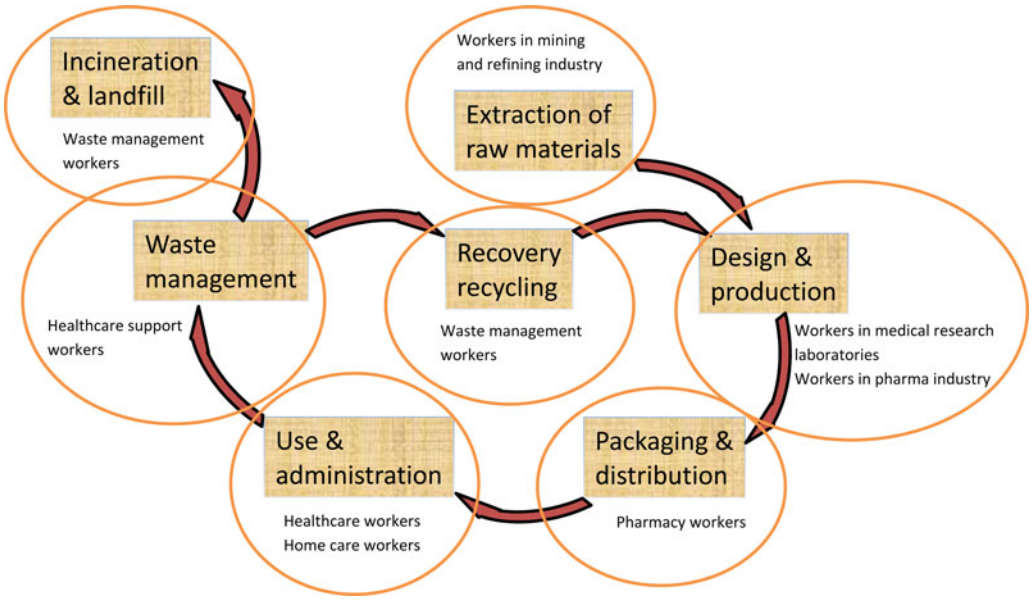

FIGURE 1. A life cycle of nanotechnology-enabled medical products

DISCUSSION

Nanotechnology and Medicine

The field of medicine has been dealing with medical formulations containing nanoscale objects since the creation of the field. Traditional medicine has been relying on natural remedies containing biological nanoscale macromolecules (e.g., proteins) for millennia, while modern medicine has been utilizing such macromolecules (e.g., immunoglobulins, hormones) for medical products for decades. Nanotechnology is poised to revolutionize the health care delivery industry throughout the clinical value chain including prediction, diagnosis, treatment, and monitoring and to contribute to the solution of the most important health challenges of the last century.[7]

NEMPs, including complex nano-enabled therapeutic agents and nano-enabled medical devices, have been growing more and more complex in the last 15 years. Initially, liposomes, micelles, or inorganic nanoparticles were developed merely as transport vehicles for nanoscale formulations of existing pharmaceuticals. Nanoparticles were also incorporated into the first nano-enabled medical devices to improve their mechanical strength or ductility, to ensure chemical inertness and corrosion resistance, or to enhance biocompatibility and microbiocidal properties. The next generation NEMPs became more functionally active, converting from a static structure (through activation by means of an external stimulus such as light) into a dynamic structure capable of detecting and signaling the presence of pathogens or engaging in therapeutic actions.[8]

Medical therapies can be designed for different routes of administration. Inhalational, dermal, oral, and parenteral administration are all considered as potential routes of drug delivery using manufactured nanomaterials. Coupling of pharmacologically active molecules with carrier-nanomaterials has been shown to: (1) facilitate penetration of biological barriers such as the blood-brain barrier and translocation to the blood stream; (2) enhance dispersability, especially for hydrophobic entities; (3) increase stability through coatings capable of avoiding immune system; and (4) improve specificity through active and passive targeting.[2,9–11] Unintentional exposures to NEMPs, however, can also present a number of challenges in assessing and mitigating their risks.

Like other medicines and medical devices, the risk potential of NEMPs is evaluated for intended uses as part of the regulatory approval process by the US Food and Drug Administration (FDA).[12] In this process, NEMP risks are characterized for intentional administration as part of the therapeutic regiment. However, risks of NEMP resulting from unintentional exposures might not be fully delineated through this process. Bioavailability and biopersistence requirements for these products can make unintentional exposures to them especially problematic. High biological activity combined with increased stability and enhanced penetrating and translocating abilities of nano-enabled medicines could lead to their higher risk potential upon unintentional exposure.

Advances towards adaptive/interactive, multi-functional, and personalized medical products based on nanotechnology and nanobiotechnology are blurring boundaries between traditional categories of medical products utilized in risk management decisions (such as medicines, devices, and biologics) and "theranostic" agents (agents capable of simultaneously providing diagnosis and treatment).[7] For example, multifunctional nanoscale platforms based on viral capsid (biologics) and capable of interrogating the tumor microenvironment (device function), subsequently administering therapy (drug function), and providing a readout of therapeutic efficacy (device function) are under development for cancer treatments.[13] Such changes in functionalities leading to changes in categorization

of medical products may represent new challenges in assessing potential risks of transformative (defined as exceptionally innovative and/or unconventional) medical products within traditional approaches to risk management.[14]

Major therapeutic and analytic advantages of these transformative technologies have also brought greater uncertainties related to potential unanticipated adverse health effects[14] and have resulted in calls for their responsible development.[5] The issue of inadequate assessment of risks of transformative medical products has been raised in the recent years, especially in conjunction with the discussion of risks of nanotechnology. For example, some transformative medical products, such as those based on nanotechnology, can represent greater challenges in terms of predicting effects, assessing when "First-in-Human trials" should occur and addressing uncertainty surrounding risks and their relation to potential benefits.[15] The need for extra oversight has been recommended due to a confluence of factors including heightened uncertainty regarding risks, fast-evolving science yielding complex and increasingly active materials, likelihood of research on vulnerable participants including cancer patients, and potential risks to others beyond the research participants.[16]

Life Cycle Approach in Occupational Risk Assessment and Risk Management

Occupational risk assessment and risk management of nanotechnology-enabled products including those in health care industry has been a subject of recent commentaries.[5,8,17–19] In conducting occupational risk assessment and management analysis of nanomaterials and nanotechnology-enabled products, the importance of the life cycle approach has been recognized.[20] Nanomaterials have the potential to change their structure and activity through their interaction with the environment. This can affect their hazard status as they move through their life cycle from raw materials to processes that develop the nanomaterial and incorporate it into a commercial product, to its use by workers, and finally to the end-of-life phase, when it is disposed of or recycled (see Figure 1). At each stage of the life cycle, nanomaterials can also present different exposure potentials to workers, changing their occupational risk profile.

Therefore, it is important to identify for each stage of the life cycle (1) sources of nanomaterials where exposure to workers may occur (e.g., emission from reactors, contact with body fluids), (2) the pathways and routes of potential exposure (e.g., direct and indirect exposures via inhalation, ingestion, and dermal exposure), (3) the form during which exposure occurs (e.g., unbound particles, nanomaterials encapsulated in a solid polymer matrix, liquid dispersions), and (4) hazards of materials to which workers are potentially exposed. A number of documents describe exposure monitoring techniques for nanomaterials, however none of them are specific to NEMPs.[21–23]

One of the promising approaches for exposure monitoring of NEMPs is through assessment of internal exposure, or dose, which is more directly linked to adverse health effects. However, dose assessment involves analysis of biological specimens, which could require use of invasive methods (e.g., for collection of blood and tissues). In the occupational setting, less invasive methods such as collection of urine, hair, and exhaled air are used more commonly. Dose can be determined by measuring the amount of nanomaterials of interest, and/or their metabolites in living organisms. Dose can also be assessed in studies using biological markers of exposure, known as biomarkers. Biomarkers can provide direct evidence for the exposure to a particular toxicant. If there is a unique correlation between a biomarker and a toxicant, the biomarker can be used for screening and monitoring of workers.[24,25]

Biomonitoring studies using various biomarkers of exposure, effect, and susceptibility are increasingly used to assess uptake and/or biological effects of exposure to hazardous medicines.[26] However, biomarkers of exposure to nanomaterials are in the early development stage. Furthermore, development of biomarkers for nanomaterials is complicated by the great variety of nanomaterial chemical and physical properties resulting in a wide range of biological responses. To date, there have not been any biomarkers developed specific to exposure to NEMPs.

US Government Standards Applicable to Nanotechnology

The Occupational Safety and Health Act requires covered employers in the United States to "furnish to each of his employees employment and a place of employment which are free from recognized hazards that are causing or likely to cause death or serious physical harm to his employees."[27] In addition, employers are required to comply with safety and health standards promulgated by the Occupational Safety and Health Administration (OSHA). As yet, OSHA has not developed or adopted a nanotechnology-specific standard. However a number of existing OSHA standards may be applicable to health care industry workplaces. These OSHA standards include, but are not limited to (1) recording and reporting of occupational injuries and illness;[28] (2) personal protective equipment (PPE);[29] (3) eye and face protection;[30] (4) respiratory protection;[31] (5) hand protection;[32] (6) sanitation;[33] and (7) certain substance-specific standards (e.g., cadmium[34]).

In addition, the Hazard Communication Standard (HCS)[35] has particular importance in ensuring worker safety in health care industry workplaces. The HCS requires pharmaceutical manufacturers to evaluate the hazard potential of medications[36] and, for hazardous medications, to report relevant information on Safety Data Sheets. Safety Data Sheets should be available to workers who may be exposed under normal conditions of use or in a foreseeable emergency to the medication. For example, Safety Data Sheets are required for tablets, capsules, or pills which contain hazardous medicines and which are designed to be dissolved or crushed by employees prior to administration to a patient. When there is incomplete hazard information, the HCS is limited in its effectiveness.

Individual drug risk assessments or other information needed to propose occupational exposure limits for newly developed medicines based on nanotechnology is a challenging issue. For example, NIOSH considers medicines hazardous if they exhibit one or more of the following six characteristics in humans or animals: (1) carcinogenicity, (2) teratogenicity or other developmental toxicity, (3) reproductive toxicity, (4) organ toxicity at low doses, (5) genotoxicity, and (6) structure and toxicity profiles that mimic existing medicines determined hazardous by the above criteria.[37] However, data related to each of these criteria may not be available for newly developed medicines. In general, the toxic effects of medicines have been recognized as being highly dose-dependent. The pharmaceutical industry has determined that medicines associated with an occupational exposure limit of less than 10 $\mu g/m^3$ may be recognized as toxic.[38–40] The industry further considers an OEL of less than 10 $\mu g/m^3$ as corresponding to observations of serious organ toxicity, developmental toxicity, or reproductive toxicity after a daily therapeutic dose of 10 mg/day in people or a dose of 1 mg/kg per day in laboratory animals.[38–40]

If the mechanism of action of the drug suggests that there may be a health risk, NIOSH believes that it is prudent to handle them as hazardous medicines until adequate information becomes available to exclude any health risk.[37] This definition of hazardous medicines is based solely on hazardous properties and therefore includes NEMPs that possess those properties. For example, commercially available nanoscale formulations of cancer treatment medicines, such as paclitaxel coated with human serum albumin, have been evaluated using the NIOSH approach.[37]

Due to poor reproducibility and high degree of uncertainty associated with biomarkers, OSHA does not recommend biological monitoring tests for workers exposed to hazardous medicines including hazardous NEMPs during routine use.[41] However, OSHA does recommend that workers handling hazardous medicines should be monitored in a medical surveillance program that includes the taking of a medical and exposure history, physical examination (with emphasis placed on skin, mucous membranes, cardiopulmonary and lymphatic systems, and liver), and laboratory tests (such as blood count, liver function tests, blood urea nitrogen, creatinine, and a urine dipstick).[41] NIOSH also has recommendations for medical surveillance and screening for health care workers exposed to hazardous medicines.[42]

Best Practice Guidance

In the absence of mandatory standards for nanotechnology, a conceptual framework for assessing and reducing worker risk in the presence of uncertainty, which incorporates a life cycle approach, has been applied to nanomaterials and can be adapted to develop occupational risk management for NEMPs use in health care industry.[18] A similar framework for safe handling of nanomaterials in the workplace is at the core of guidance from NIOSH.[43,44]

NIOSH's conceptual framework takes into consideration the potential routes of exposure, the factors that may influence biological activity, and the potential toxicity of nanomaterials. Based on these three considerations, NIOSH's framework then incorporates approaches based on the traditional industrial hygiene hierarchy of controls.

The hierarchy of controls starts with elimination and substitution of hazards. Nanotechnology offers appropriate opportunities for this stage in the hierarchy of controls. Better understanding of the structure, composition, and property relationships for advanced nanomaterials, including those used in NEMPs, offers an opportunity to reduce their risk potential by: (1) avoiding hazardous elements, such as regulated heavy metals, to minimize risks of degradation products, (2) designing safer nanomaterials, which would target only pathogens and would disintegrate into low-toxicity and rapidly cleared moieties, (3) inhibiting ability of nano-enabled medicines to penetrate and translocate through routes other than intended routes of delivery for therapeutic products, and (4) designing safer manufacturing and use processes.[8]

If elimination and substitution cannot reduce risk to acceptable levels, engineering controls can be used. Engineering controls include a variety of measures such as automating and enclosing processes, using extraction ventilation to reduce inhalation exposures, and retractable needles to prevent parenteral exposures. Finally, if engineering controls are not sufficient, PPE such as respirators have been shown to be effective in reducing exposures to nanomaterials.[44,45]

A medical monitoring program serves as a form of secondary prevention by identifying indicators of exposure or early disease.[42] Medical surveillance involves collecting and interpreting data over time to detect changes in the health status of working populations potentially exposed to hazardous substances. Such working populations may include health care workers who directly handle hazardous medicines (including those based on nanotechnology) such as nurses, pharmacists, and pharmacy technicians. In addition, other health care workers who may come directly into contact with contaminated bodily fluids after a patient has received a hazardous drug should be considered for inclusion in a medical surveillance program.[42] The general elements of a medical surveillance program for workers exposed to hazardous medicines have been outlined,[42] but medical screening and surveillance programs should be designed to address the needs of each specific workplace.

Protective workplace practices, along with clean room technologies, as used in the micro-electronics industry, good manufacturing practices in the pharmaceutical industry, and guidelines for health care workers handling hazardous medicines have been recommended for adoption in manufacturing and handling of advanced nanomaterials, including those used in NEMPs.[8]

All these approaches could be expanded to NEMPs, but not before a number of research questions are addressed to ensure that workers are adequately protected.

Critical Questions About the Safety of NEMPs for Workers

Published scientific information about NEMPs to date chiefly concerns their safety and efficacy for the patient, not the worker.[46] Several questions about the safety of NEMPs for workers need to be answered. The answers are critical to effectively assessing and managing any risks that NEMPs, and their byproducts (intermediates and metabolites) pose to workers:

(1) What are the adverse health effects resulting from unintentional exposures to NEMPs?
(2) How can worker exposures to NEMPs be measured?
(3) What are the biomarkers of exposure to NEMPs?
(4) Do accepted exposure mitigation measures perform as anticipated for NEMPs?

These questions represent the major milestones of a research roadmap to ensure working safety with NEMPs. Each of these questions require research specific to stages in the NEMP life cycle. Addressing each of these research questions will lay the foundation for ensuring that health care industry workers—across the spectrum of industry work settings—are protected from harm.

Health Risks by Category of Health Care Industry Worker

Research and Clinical Laboratory Workers

In the United States, the safety and health of workers in medical research laboratories is regulated by OSHA. In addition to the general requirements described in the previous chapter on "U.S. Governmental Standards Applicable to Nanotechnology," research and academic laboratories handling hazardous chemicals are required to establish a Chemical Hygiene Plan that is capable of protecting workers from exposure to hazardous chemicals, including hazardous nanomaterials, in research and clinical laboratories.[47] The Chemical Hygiene Plan also should contain Standards Operating Procedures for safety and health, criteria for implementation of control measures, and employee information and training. In Appendix A of the Occupational Exposure to Hazardous Chemical in Laboratories standard,[47] OSHA provides non-mandatory guidance on developing an appropriate laboratory Chemical Hygiene Plan. Medical research laboratories working with biological agents have to also follow practices and procedures appropriate for biological safety level of the agents, which are specified by the US Centers for Disease Control and Prevention (CDC) and the US National Institutes of Health (NIH).[48]

A number of voluntary guidelines on safe handling of nanomaterials in research laboratories have been recently developed. A compilation of such guidelines can be found in a report published by the Organization for Economic Cooperation and Development (OECD).[49]

More recently, NIOSH published guidance for working with nanomaterials in research laboratories.[50] The NIOSH guidance provides that potential exposures to nanomaterials can be controlled in research laboratories through a flexible and adaptive risk management program. An effective program provides the framework to: (1) anticipate the emergence of nanotechnology into laboratory settings, (2) recognize the potential hazards, (3) evaluate the exposure to the nanomaterial, (4) develop controls to prevent or minimize exposure, and (5) confirm the effectiveness of those controls. Exposure assessment is a key element of an effective risk management program. The assessment should identify work tasks that contribute to nanomaterial exposure and the type of worker performing those tasks. An inventory of tasks should be developed that includes information on the duration and frequency of work tasks that may result in exposure, along with the quantity of the material being handled, dustiness of the nanomaterial, and its physical form. A thorough understanding of the exposure potential will guide exposure assessment measurements which will help determine the type of controls required for exposure mitigation.

The United Nations' pilot program, "Guidance for Developing a National Nanotechnology Policy and Programme," highlights the importance of training for research personnel to be able to undertake a risk assessment using the best available data and information before experimentation with nanomaterials is undertaken.[51]

General risk assessment and management measures in medical research laboratories developing NEMPs should be consistent with guidelines recommended for safe handling of other novel pharmaceuticals and advanced nanomaterials. Even so, a number of questions remain regarding specific elements of the risk management approach involving NEMPs. These include:

(1) How effective are engineering controls used in medical laboratories at reducing exposures to NEMPs and their intermediates and metabolites? Have exposure measurements been done to support a decision one way or another?; and
(2) Would performance-based approaches to minimizing risk for pharmaceuticals in medical research laboratories be as adequate for NEMPs as more specification-based approaches?[52]

Pharmaceutical Manufacturing Workers

In 2012, there were almost 268,000 US workers (in all occupations) employed in the pharmaceutical and medicine manufacturing industry.[53]

In general, risk assessment and management measures in manufacturing facilities producing and packaging NEMPs should be consistent with guidelines recommended for safe handling of other novel pharmaceuticals. Tools developed to minimize risk from manufactured nanomaterials in the workplace could be also helpful in reducing occupational risks in facilities manufacturing NEMPs. The International Organization for Standardization (ISO) published a technical specification "Occupational Risk Management Applied to Engineered Nanomaterials—Part 2: Use of the Control

Banding Approach."[54] This technical specification describes pro-active and retroactive use of a control banding approach for controlling the risks associated with occupational exposures to nano-objects and their aggregates and agglomerates (a subset of nanomaterials with higher exposure potential), when knowledge regarding their toxicity and quantitative exposure estimations is limited or lacking. In this approach nanomaterials are assigned to a hazard band and an exposure band based on available information about hazard and exposure potential. These two bands are then matched to one of five control approaches for minimizing risk to workers.

Despite availability of these tools, additional research questions relating to the safety and health of workers in pharmaceutical manufacturing facilities include:

(1) Are hazardous NEMPs properly identified and reported on Safety Data Sheets?
(2) Would performance-based approaches to minimizing risk for pharmaceuticals in manufacturing be adequate for controlling risks to manufactured nanomaterials or is a specification approach indicated?[52]

Clinical Pharmacy Workers

In 2012, there were 678,000 pharmacy workers in the United States, including: pharmacists (281,560), technicians (353,340), and aides (42,600) in the United States[53] Pharmacists dispense medicines prescribed by physicians and other health practitioners and provide information to patients about medications and their use, while pharmacy technicians prepare medications including measuring, mixing, counting out. and labeling. Pharmacy aides help with tracking and storing medicines. Pharmacy workers can be found in retail pharmacies, hospital pharmacies, and compounding pharmacies (which produce or modify drug products for specific individual patients). In recent years, a drive to reduce health care costs has resulted in a shift away from hospital pharmacies to compounding pharmacies, especially for sterile-injectable medications.

Pharmacy workers may be exposed to nano-enabled hazardous medicines when aerosols are created during mixing or counting out, when spills are cleaned up, or when touching contaminated surfaces during the preparation, administration, or disposal of hazardous medicines.[55] A pharmacist's exposures to hazardous medicines occur most commonly through inhalation and skin contact, but unintentional ingestion from hand to mouth contact is also possible.

The specific research questions to ensure the safety of pharmacy workers working with NEMPs are:

(1) Are hazardous NEMPs properly identified and reported on Safety Data Sheets?
(2) Can hazardous nanotechnology-enabled medicines be safely handled as other hazardous medicines or are special measures necessary?

Health Care Delivery Workers

A hospital is one of the most hazardous places to work in the United States. For 2012, there were 248,100 work-related the non-fatal injuries and illnesses in US hospitals, a rate of 6.6 work-related injuries and illnesses for every 100 full-time employees, which is almost twice the rate for private industry as a whole of 3.4.[56]

In the United States, there are an estimated 10 million health care workers (including health care practitioners and technical and health care support occupations) who are potentially exposed to pharmaceuticals or pharmaceutical waste at their work-sites.[53] Direct health care delivery workers include nurses, physicians, respiratory therapists, infusion therapists, physical therapists, veterinarians, and veterinary technicians.

Health care workers face a number of serious safety and health hazards. These include exposure to bloodborne pathogens and biological hazards, hazardous chemicals and medicines (including NEMPs), waste anesthetic gas exposures, respiratory hazards, ergonomic hazards, laser hazards, workplace violence, and hazards associated with therapeutic radioactive materials and x-rays.[57] Health care workers may be exposed to hazardous NEMPs when they create aerosols, generate dust, clean up spills, or touch contaminated surfaces during the preparation, administration, or disposal of hazardous medicines. Exposure may occur during drug preparation, transport, or administration (including needle stick injuries); during the disposal process; when handling patient excreta; and in the event of spills. Exposure can also occur during handling of contaminated items; consuming food and beverages, which came in contact with medicines; and during cleaning and maintenance.[55] Inhalation and skin contact/absorption are the most likely routes of exposure, but unintentional ingestion from hand-to-mouth contact and unintentional injection through a needle stick or sharps injury are also possible.

NIOSH recommends that an overall safety and health program for health care workers should include medical surveillance to ensure worker protection. NIOSH also recommends that a specific list of hazardous medicines used in the facility, including hazardous NEMPs, be developed and a universal precautions approach to handling those medicines is implemented.[58] Using this approach, exposures to hazardous medicines can be minimized through primary prevention measures such as engineering controls, administrative controls, and PPE.[58]

In health care settings engineering controls include Class II or III biological safety cabinets (BSC), compounding aseptic containment isolators, closed system transfer devices, and needleless systems. Administrative controls include implementing work practices, management policies, and training programs to reduce worker risk. PPE should be used only when engineering controls and/or administrative controls are not feasible in reducing exposures to hazardous medicines or when other control measures are not available or practical.[59]

Despite availability of existing safety guidance, further research is needed to ensure safety and health of health care delivery workers handling NEMPs. Additional research questions for health care facilities include:

(1) Are hazardous NEMPs properly identified and reported on Safety Data Sheets?
(2) Can hazardous nanotechnology-enabled medicines be safely handled as other hazardous medicines or special measures are necessary?

Home Health Care Workers

Home health care is a rapidly growing sector of the health care industry.[4] It is projected that home health care employment will grow 55% between 2006 and 2016, making it the fastest growing occupation of this decade.[60] In 2012, there were 840,000 home health aides.[53] Home health "aides" provide routine individualized health care such as changing bandages and dressing wounds and applying drug infusions and topical medications; they may also provide bathing, dressing, and grooming care.

In addition to home health aides, the workers in the home health care industry include registered nurses, attendants, and personal care workers. They perform a broad range of tasks from assisting with daily activities to more complex care required by chronically ill or post-surgical patients such as dialysis, chemotherapy, and respiratory and infusions procedures. Since a patient's home is not designed as a health care workplace, home health care workers face many of the same occupational hazards as those in health care facilities plus hazards associated with the home environment. Common home-associated occupational hazards include unsanitary conditions and inadequate disinfection, mismanagement of medical wastes including biomedical wastes, exposure to sharps and needle sticks, and exposure to infectious agents.[61]

Home care workers employed by private agencies, hospital-based agencies, and public health agencies are covered by OSHA standards, but some are independent contractors or temporary workers not covered by OSHA standards.[61] OSHA standards that are applicable to home health care industry include the bloodborne pathogens standard[62] and the respiratory protection standard.[63]

NIOSH has conducted a review of occupational hazards faced by home health care workers and recommends several management and prevention strategies to reduce risk from such hazards.[60] Building from that publication, in 2012 NIOSH published six fact sheets for home health care workers to provide practical advice on reducing risk from six specific hazards: (1) exposure in unsafe conditions [64]; (2) driving-related injuries[65]; (3) needlestick and sharps injuries[66]; (4) latex allergies[67]; (5) musculoskeletal disorders[68]; and (6) violence on the job.[69]

Despite availability of such guidance, further research is needed to ensure safety and health of workers in health care facilities and home health care settings handling NEMPs. In addition to research gaps for health care workers, the following question should be answered: What are exposures to NEMPs among workers providing outpatient care?

Health Care Delivery Support Workers

Support workers in health care industry include shipping and receiving personnel, laundry workers, and custodial and maintenance workers. In the US hospital sector, there are estimated to be 240,000 health care delivery support workers.[53] These workers may be exposed to hazardous medicines or drug waste when they dispose of hazardous medicines, clean spills, or handle contaminated objects or touch contaminated surfaces.

Exposure can also occur while consuming food and beverages through the transfer of contaminated residues on hands and through ingestions of contaminated food or drink that was inappropriately located in medicine-handling areas.[55] Questions remain whether nano-enabled medical products represent risk to support workers in health care industry. Additional research is needed to answer the following questions:

(1) Are support workers exposed to hazardous NEMPs?
(2) Do these exposures lead to adverse health effects?

Medical Waste Management Workers

NEMPs are disposed of through recycling, energy recovery, incineration, and landfilling at the end of their lifecycle. In 2012 there were 372,000 US workers employed in waste management and remediation services including medical waste management.[53] The safety of workers managing medical waste is regulated by several government agencies. However, none of them specifically addresses waste containing NEMPs.

OSHA's Bloodborne Pathogen standard[70] provides health and safety protection for workers exposed to blood or other potentially infectious materials and items while performing their duties including workers in waste management. In addition, worker safety and health at hazardous waste treatment on-site and off-site facilities is regulated by OSHA's Hazardous Waste Operations and Emergency Response standard[71] at the federal level. This standard provides worker protection at treatment, storage, and disposal facilities for hazardous substances. Hazardous substance definition includes hazardous waste and any disease-causing agents, thus covering biomedical wastes. OSHA's Hazardous Waste Operations and Emergency Response standard requires employers to establish written safety and health programs including medical surveillance, safety and health training for workers, and standard operating procedures for safety and health.

There are also a number of regulations indirectly related to occupational safety of medical wastes. Emissions from medical waste incinerators are regulated by the Environmental Protection Agency (EPA) under the Clean Air Act.[72] The transportation and packaging of medical waste is regulated by the U. S. Department of Transportation. Some states such as Maine define pathogenic and infectious wastes as hazardous

waste.[73] These states have adopted specific biomedical waste management laws and regulations aimed at reducing public health environmental hazards. Under these laws, most biomedical waste is incinerated or autoclaved, although some liquid wastes such as discarded human waste and blood and body fluids are treated as regular sewage. Once biomedical waste is sterilized it is often treated as regular waste. In Maine, however, the residual incinerator ash is treated as a special waste and must be analyzed for hazardous components prior to landfilling.[73]

These waste management methods for manufactured nanomaterials and products containing them have been reviewed in a series of Organization for Economic Cooperation (OECD) reports published in 2013.[74–76] In recycling operations exposure potential depends on the specific recycling processes. The main concern about possible occupational risks specific to NEMPs is whether nanomaterials might be released into the workplace atmosphere.[74] Worker exposure can occur in several ways: (1) dust containing free nanomaterials emitted during transport, sorting, shredding, milling, grinding, or pouring of manufactured nanomaterials; (2) nanomaterials in liquid media (water, solvents) due to cleaning or rinsing the products before mechanical recycling; (3) nanomaterials on cleaning clothes from maintenance and cleaning of recycling equipment; and (4) nanomaterials that may be set free in the flue gas or in the ambient air with thermal processes (heating, welding, pyrolysis) when there is insufficient occupational control.[77,78]

The risk potential of a nanomaterial during recycling is associated with several factors. First, the quantity or concentration of the manufactured nanomaterials in the product or in the waste stream can determine risk. Second, the mode of incorporation of the manufactured nanomaterials in the product can influence risk. For instance, risk may vary with the product form, increasing for free form and declining when associated with other materials or fixed by chemical binding. Third, the possibility exists that manufactured nanomaterials may be released during specific recycling operations. Fourth, single nanoparticles can agglomerate into larger entities, which would affect their risk potential. Fifth, cross-contamination between secondary materials (e.g., plastics or construction materials) and manufactured nanomaterials may occur during the recycling process.

The available literature and the findings on the risks associated with the incineration of waste containing nanomaterials are inconsistent and further research is needed. On the one hand, there are studies reporting that measurements in a waste incinerator show that majority of metal oxide nanomaterials end up in bottom ash with no emission of manufactured nanomaterials to the air; on the other hand, a preliminary evaluation declares that nanomaterials can pass through scrubbing devices.[75] The OECD report further recommends to use best available techniques in flue gas treatment systems to capture the majority of nanomaterials and to use temperatures above 850°C (1560°F) for effective incineration of carbon nanotubes.

Guidance for the safe recovery and disposal of waste containing nanomaterials has been provided by the German Chemical Industry Association or VCI.[79] The VCI guidance recommends implementation of:

1. Technical measures at the source, e.g., use of hermetically sealed apparatus; minimization of dusts and aerosols; extraction of dusts and aerosols directly at the source; filtering of extracted air, if necessary isolation of the workroom and appropriate modification of room ventilation; and cleaning of recycling equipment by vacuum cleaning with suitable appliances or wiping with a damp cloth, but not by blowing off;
2. Organizational measures, e.g., minimization of the exposure time; minimization of the number of persons exposed; restriction of access; and instructions of personnel concerning hazards and protection measures;
3. Personal protective measures: respiratory protection with particle filters P3/P100; protection gloves; closed goggles; and protection suit (non-woven).

However, questions remain how effective these measures are for protecting workers handling wastes containing NEMPs.

Given the need for greater understanding of the risks associated with recycling, four research questions are important:

1. Are NEMPs destroyed or rendered non-toxic through incineration?
2. To what extent are NEMPs released to the environment during waste management operations and to what extent do they pose exposure risks for workers?
3. How effective are the measures to minimize exposures to nanomaterials during management of NEMP-containing waste streams?
4. How can NEMPs be measured and identified in biomedical products and waste streams?

CONCLUSION

The use of NEMPs is increasing across the entire health care industry due to their value in curing disease and alleviating human suffering. The more NEMPs are used in patient care, the greater the potential exposure to NEMPs among all types of health care industry workers. These exposures can potentially be harmful. To ensure that health care industry workers do not suffer material impairment of health, it is critical that any risk arising from NEMP exposure to workers be assessed scientifically. Depending on what is found from risk assessment, responsible strategies to eliminate or minimize risk will be necessary. Risk mitigation efforts will not only protect workers, but will also ensure a promising future for NEMPs in patient care. Yet, to achieve this goal, additional research needs to be done.

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