Nanomaterials and Worker Health

Medical Surveillance, Exposure Registries, and Epidemiologic Research

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Objective: This article provides an overview of the issues that arise with medical surveillance, exposure registration, and epidemiologic research involving nanomaterial workers. **Methods:** An occupational health perspective is applied to detecting risks in nanomaterial workers individually and as a group. **Results:** General principles for medical surveillance, exposure registration, and epidemiologic research are identified. A model Nanomaterial Worker Health Study is for consideration. **Conclusions:** The Nanomaterial Worker Health Study can be developed as a tangible action in assuring the public that steps are being taken to learn of any adverse effects from exposure to nanomaterials.

Increasing numbers of workers are involved in research, manufacture, use, and disposal of nanomaterials, but it is not known whether these workers are at risk for adverse health effects, despite a coalescing body of evidence that exposure to some nanomaterials can cause adverse health effects in animals.[1] To protect these workers, precautionary risk management guidance has been issued worldwide.[2–7] To further support the precautionary approach, it is necessary to consider what medical surveillance is warranted for nanomaterial workers and the issues that arise in establishing epidemiologic studies and exposure registries. Critical in protecting the health of workers involved with a new technology, such as nanotechnology, is the need to assess their risks and determine whether risk management programs are functioning effectively. Medical surveillance, exposure registries, and epidemiologic research are three related ways to provide such risk-related ascertainments.[8] The evidence for a precautionary approach to preventing adverse effects from engineered nanomaterials includes research concerning health effects from exposure to small-particle air pollution, incidental nanoparticles in welding and diesel engines, as well as studies in the last 10 years, specifically addressing engineered nanoparticles.[4,9–17] Underlying knowledge of the health effects of particles and fibers also supports concern over worker exposure to nanomaterials.[17] A precautionary approach includes following the hierarchy of prevention (substitution, engineering controls, administrative controls, personal protective equipment, and training) and supporting that hierarchy requires industrial hygiene evaluation to determine whether controls are working and whether there is any residual risk.[18] Also, incumbent in the precautionary approach is the need to anticipate hazards of nanomaterials and develop material screening and testing strategies and guidance for controlling categories of nanomaterials.[19–21]

EXTENT OF EXPOSURE TO NANOMATERIALS

There is an extremely small (but growing) published literature base on the extent of exposure to nanomaterials.[22–29] In part, this is due to a variety of issues, including the relative newness of exposure scenarios, the inconsistencies over how to identify and classify nanomaterials, questions about metrics and practical instrumentation, and difficulty finding and gaining access to workplaces. For the most part, the published literature shows relatively low mass (weight) exposure to nanomaterials compared with bulk counterparts.[27,28] Nevertheless, this finding must be qualified since low mass concentrations can represent high numbers of airborne nanoparticles, and the methods for sampling and analyzing these materials are still evolving.[29] Many companies where nanomaterials have been investigated, manufactured, or utilized have operations that are controlled (isolated, contained, or exhausted).[30,31] Nevertheless, some do not and relatively high, process specific, short-term exposures have been reported.[28,31] Thus far, there has not been a wide range of operations assessed, and in many cases, personal breathing zone measurements are lacking. There is virtually no published information to date on exposures of workers using engineered nanomaterials downstream from their manufacturing (eg, repackaging of dry nanoparticles spray application involving nanomaterials). Nevertheless, simulations indicate that exposures can occur.[32] A more complete understanding of toxic potential and the extent of exposure within and across companies is required and will be the foundation on which occupational health surveillance programs will be based.

OCCUPATIONAL HEALTH SURVEILLANCE

Occupational health surveillance includes hazard surveillance, which involves identifying potentially hazardous practices or exposures in the workplace and assessing the extent to which they can be linked to workers, the effectiveness of controls, and the reliability of exposure measures.[8,18,33,34] Occupational health surveillance is also an umbrella term that includes monitoring of health outcomes or biological changes,[35,36] including medical surveillance of effects at the group and individual level. At the individual level, medical screening involves examination of the health status of an exposed person or persons by tracking of illness or change of biologic functions to detect early signs of work-related disease by administering tests to asymptomatic workers.[37] Numerous Occupational Safety and Health Administration standards and National Institute for Occupational Safety and Health (NIOSH) recommendations specify this type of medical surveillance of workers when there is exposure to a specific workplace hazard.

Occupational health surveillance is part of the standard practice of occupational safety and health.[38,39] National Institute for Occupational Safety and Health guidance issued in 2009 concerning surveillance for workers exposed to engineered nanomaterials included the general recommendation that occupational health surveillance is an important part of a risk management program.[39] In that guidance, a strong recommendation for the conduct of hazard surveillance was made, however, no specific medical screening recommendation was given. The evolving evidence base about potential hazards of occupational exposure to engineered nanomaterials most likely will increase the need to include specific medical surveillance and screening programs as part of the complete occupational health surveillance program. For example, animal studies on carbon nanotubes have shown that pulmonary fibrosis can be a significant health effect of exposure.[13,15,16] In January 2011, NIOSH posted

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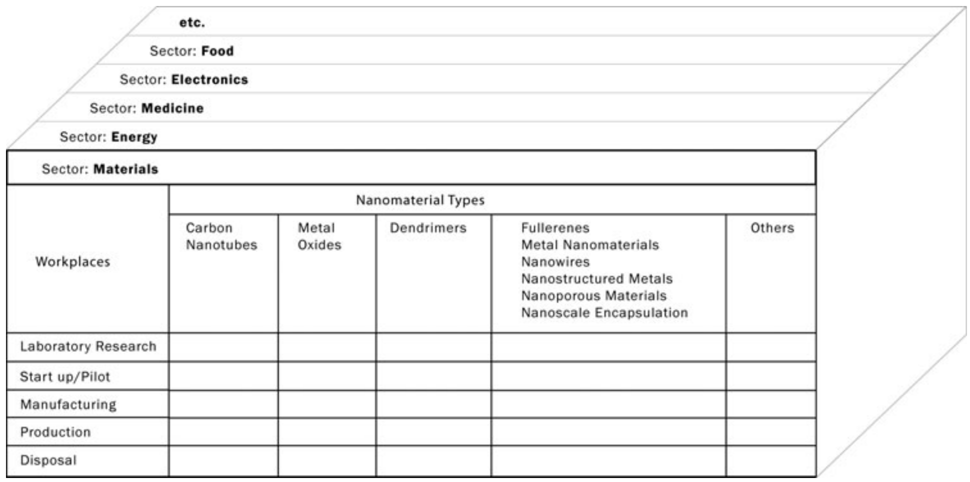

FIGURE 1. Framework for identifying worksites with occupational exposure to engineered nanoparticles (Adapted from reference 42).

on its Web site for public comment a draft Current Intelligence Bulletin on carbon nanotubes/carbon nanofibers.[40] In it, in addition, to risk assessment, recommended exposure limits, and control recommendations, NIOSH recommended baseline and periodic medical surveillance. They included x-ray and spirometry among other assessment techniques.

As nanotechnology permeates the various economic sectors, more products will be manufactured and more occupational exposure will be likely. The workplaces where worker exposure can occur can be depicted by a three-axis matrix of workplace types (functions) × nanomaterial types × business sectors as shown in Fig. 1. The number of cells in this matrix is vast due to the many different types of potential nanoparticles and nanomaterials and the broad array of products and uses.[41,42] While the recommendation for hazard surveillance and precautionary risk management applies across the matrix, specific medical surveillance guidance will need to be tailored categorically. Implementing occupational health surveillance at work sites will allow for the development of baseline and then, if the surveillance is ongoing, periodic assessments and analysis of data, which can serve to alert workers, employers, governmental authorities of any failures of prevention.

EPIDEMIOLOGIC RESEARCH AND EXPOSURE REGISTRIES

Two tools will be useful to augment the implementation and impact of occupational health surveillance. These are the conduct of epidemiologic research and the formation of exposure registries. Epidemiologic research can involve the analysis of occupational health surveillance data to identify potential health effects of exposures, and it can include etiologic investigations of the relationship between exposure to specific nanomaterials and resultant health effects. While epidemiologic investigation of the health effects of nanomaterials is not inherently different from assessing the effects of other potential occupational hazards, there are some factors that are more pronounced.[41] These include heterogeneity of nanoparticles, temporal factors, difficulty identifying a study population, and difficulty obtaining exposure information. The heterogeneity of nanoparticles is the result of a large number of physicochemical parameters and production conditions that can lead to a vast number of different types of nanoparticles. These parameters and conditions include combinations of such factors as size, shape, solubility, surface change, surface coating, crystal structure, and contaminants. The potential toxicity of a nanoparticle can vary, depending on the combination of these factors. Thus, it may be difficult to find study population with similar enough exposures to form cohorts of adequate size for epidemiologic study.

Another issue is that engineered nanomaterials have only been in commerce for limited time. The current size and location of the nanomaterial workforce is difficult to ascertain; although growing, the nanomaterial workforce still could be relatively small currently; however, there are few useful published estimates. Nanotechnology and nanoscience, while having historical precursors, did not readily begin to emerge until the 1980s with the development of techniques to "visualize" nanoparticles and the understanding of scientific and commercial properties of matter at the nanoscale. Commercial production of "nano-enabled" products generally began in the late 1990s. Clearly the first workers to be exposed are those in scientific laboratories in academia and commercial enterprises. The next workers exposed included those involved in pilot and start-up operations.[42] As these efforts become viable on larger scales, manufacturing will increase in volume. Nanomaterials will likely be provided to an increasingly wide array of users who will incorporate them in an increasing variety of products. An increase in occupational exposure of workers involved in the handling, machining, or otherwise processing products containing nanomaterials should be expected. Finally, workers involved with all aspects of end of life of products containing nanomaterials may have increasing exposures to nanomaterials in the future.

As discussed previously, large industrial cohorts (which were the source populations for occupational epidemiology in the past) do not exist for nanomaterials currently. The difficulty in obtaining exposure information and characterizing study populations is exacerbated by the fact that the necessary information for epidemiologic research is often viewed as proprietary. Employers may not be willing to make such information available, because it may affect their competitive edge. New approaches for identifying and characterizing study populations will be needed. One approach that may be useful in setting the stage for epidemiologic research is the use of exposure registries. An exposure registry is the enumeration and identification of exposed individuals for the purpose of providing them information and guidance about potential risk from exposures.[43] Exposure registries also may be sampling frames for epidemiologic research. While exposure registries have been used in public health for more than 50 years, they are costly and have various positive and negative aspects. On the positive side, they may provide for timely information to workers and fostering development of epidemiologic studies. On the negative side, they may raise undue expectations among workers about medical monitoring and treatment and may be a vehicle for premature legal action. Another article in this issue provides a comprehensive overview of the history of exposure registries and their positive and negative aspects.[44]

PROSPECTUS FOR A NANOMATERIALS WORKER HEALTH STUDY

Rationale

The growing body of evidence about the potential health risks of nanomaterials demands that industry, labor, and government take concerted action to protect the health of workers. Workers are the first people in society with significant exposure to a new technology such as nanotechnology. It is critical that the potentially highly beneficial impact of harnessing phenomena at the nanoscale is not delayed or impaired because society did not take the appropriate anticipatory steps. First and foremost is the need, already begun, to take precautionary steps to control engineered nanomaterial exposures in all workplaces throughout the life cycle of the material. While further investigation is still required, effective control knowledge is available and has been recommended by many governments and organizations.[2–8] Nevertheless, to ensure that all efforts are being taken to learn of any deleterious effects that can occur from exposure to nanomaterials, there is need for a program of workforce medical surveillance and epidemiologic investigation that will indicate any failures of the preventive efforts that are in place. This program can serve as a model effort that combines exposure registration, medical surveillance, and epidemiologic research in a coordinated effort. Already such a program is being proposed in France (Boutou-Kempf et al).[45]

Scope of the Study

A health surveillance and epidemiologic investigation program can be envisioned to include a registry of a large number (perhaps at least 5000) of workers from companies handling different nanomaterials. This registry would serve as a source group in which various analytical studies will be conducted. The exposure and health of the entire group would be monitored initially and periodically over a 5- to10-year period (Fig. 2). In addition, parallel registries and studies in other countries would be promoted by using common metrics and health endpoints. The addition of these workers may allow for the development of cross-national cohorts with common exposures that can be studied prospectively. There are many questions that would need to be resolved in the planning of such a study. These include such issues as participation, coordination, access to data, confidentiality, funding, representativeness, and many more.

Partnership—Funding, Planning, and Initiation

The critical issues in the success of this endeavor are the participation of all three of the major stakeholders: industry, labor, and government. It is envisioned that there would be a transparent tripartite partnership that will be the governing body for this study. The National Institute for Occupational Safety and Health could serve as a coordinator of the study in collaboration with investigators from other agencies and organizations. The governing body of this partnership should consist of business trade associations, government agencies, labor unions, and academia.

Industry, government, and labor, all have responsibility in ensuring that workers are protected from a new technology such as nanotechnology, and all would have an interest that responsible efforts are made to consider and prevent potential health effects in workers. It is envisioned that industry and government would provide funds for this partnership and for studies that are developed.

To initiate this process, a working group (with representatives of industry, labor, government, and academia) would be established to formulate the basis of the partnership (including such aspects as a governing council and plans for initial funding) and plan for future studies. It is beyond the scope of this article to identify the details and estimate the costs of initiating and maintaining such a study; that will be a function of the working group.

STRENGTHS AND WEAKNESSES

The idea of a Nanomaterial Workers Health Study is outlined in brief terms. The strength of this approach is that it would serve as a useful resource to assess questions about worker exposure to

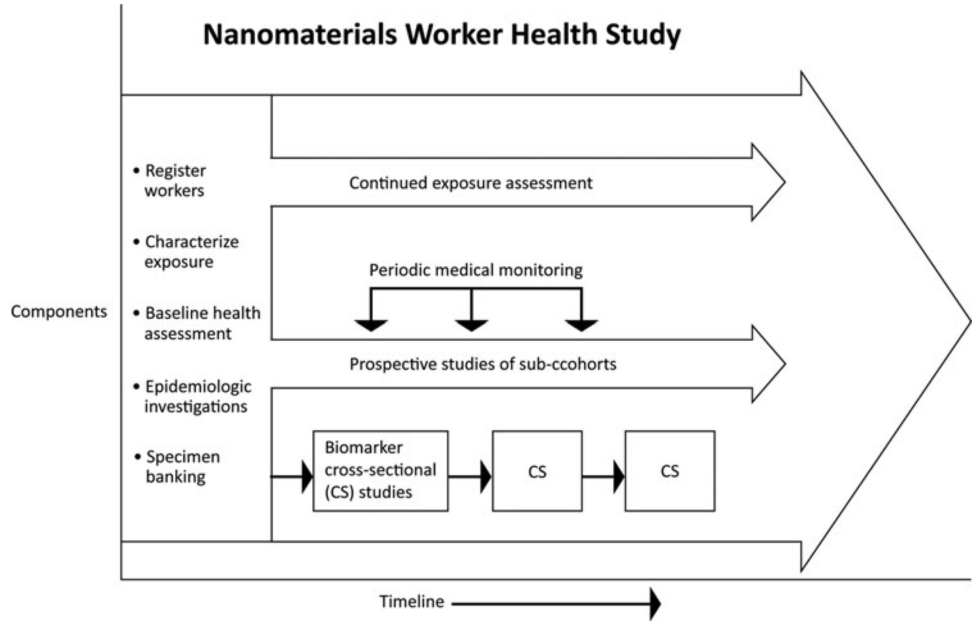

FIGURE 2. Schematic of a nanomaterials worker health study.

nanomaterials, risks from exposure, and utility of controls. It can inform investigators of issues in conducting further studies, and it can provide leads for assessing early indicators of effects. In terms of weaknesses, it may not be representative of the range of exposures and controls since the companies willing to participate in such a multiorganization study may well be those with the best occupational hygiene performance. This can influence the prospect of detecting any health risks, if a causal relationship between nanomaterials and adverse health effects exists. Consequently, it will be important to recruit a range of companies to participate in the study.

CONCLUSION

Implementing occupational health surveillance with focused medical surveillance components is of growing importance as more is learned about the hazards of occupational exposure to various nanomaterials. Since there are current and future workforces that have or will have exposure, precautionary approaches to controlling exposure are warranted. Along with these approaches is the need for developing an investigational strategy for assessing risks to groups of workers through consideration of exposure registries and epidemiological research. Both occupational health surveillance and epidemiologic research will help to identify risks to workers from uncontrolled or poorly controlled exposures. This will allow for further refinement of controlled procedures. If society is to benefit from nanotechnology, it is critical that all steps to protect and assure worker safety are taken, including occupational health surveillance, consideration of exposure registries, and epidemiologic research.

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