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# Medical surveillance, exposure registries, and epidemiologic research for workers exposed to nanomaterials

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ABSTRACT

While there is a growing body of information about hazards of nanomaterials, little is known about the risks to workers exposed to them. However, workers are the first people in society that are being exposed to the growing inventory of "nano-enabled" products in commerce. The number of workers involved in the investigation, manufacture, production, and disposal of these types of products is growing. Although toxicologic research is still the highest priority, it is time to actively anticipate the health needs of workers. To date, precautionary risk management approaches have been widely advocated. Now there is a need to initiate an evolving process to identify the issues in medical surveillance, utilization of exposure registries, and the conduct of epidemiologic research. Each of these are related complex endeavors that build on the toxicologic evidence and extent of exposure. There is a need to assess the scientific basis and research needs for determining early functional changes, organ system and disease responses for use in targeted medical surveillance. There is also need for development of criteria for extrapolating toxicological data in biological systems to predict the risk of adverse outcomes in humans. In the meantime, exposure registries may be pivotal in helping societies act in the face of uncertainty in a precautionary manner, but legal, ethical, and logistical issues need resolution. Epidemiologic research will build on these efforts and may ultimately contribute critical definitive rationale for medical screening, risk assessment and management.

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There is a growing and coalescing level of evidence that exposure to some nanomaterials can cause adverse effects on health. The increasing evidence comes from various sources, for example, animal and human studies of ultrafine aerosols, air pollution, and manmade mineral fibers, as well as from an increasing number of animal studies with engineered nanoparticles providing mechanistic information and demonstrating end effects. This evidence has been reviewed by numerous organizations that have concluded that there is enough preliminary information to treat engineered nanoparticles "as if" they are hazardous (ASCC, 2006; IRSST, 2006; DOE, 2007; BSI, 2007; NIOSH, 2009a,b). Clearly, prudent controls should be implemented and more research is needed but at present, there also is sufficient evidence and concern to consider whether there is need for occupational health surveillance of nanomaterials workers and whether formation of exposure registries and conduct of epidemiologic research is appropriate (Schulte et al., 2008b). These efforts are critical in protecting a workforce with potential exposure to nanomaterials (Fig. 1).

There are many inherent parameters that influence the potential toxicity of engineered nanoparticles. In addition to substance-specific toxicity, toxicity is also likely to vary based on parameters that include size, shape, surface area, solubility, surface reactivity, charge, attached functional groups, crystalline structure, the agglomeration status of the particles, and their contaminants. Depending on the combination of these factors, toxicity can be more or less marked, especially in relation to often chemically identical but coarser particles such as, for example, titanium dioxide, or as found with carbon nanotubes (Bermudez et al., 2004; Pylkkänen et al., 2007; Poland et al., 2008). Potentially confounding differences in how nanoparticles are dispersed and administered for toxicological study may also be reflected in the variability of results concerning nanoparticles toxicity in investigations of "the same" nanoparticles in laboratory animal and *in vitro* models (Mercer et al., 2007). Moreover, there is a multiplicity of organs that can be targets of nanoparticles exposure (Oberdörster et al., 2005a,b). This information, and the fact that increasing numbers of workers may be potentially exposed to these materials (ASCC, 2006; DEFRA, 2006; IRSST, 2006; Schulte et al., 2008c) raises the question of the need for occupational health surveillance for such workers.

## 1. Occupational health surveillance

Occupational health surveillance is the ongoing systematic collection, analysis, and dissemination of exposure and health data on

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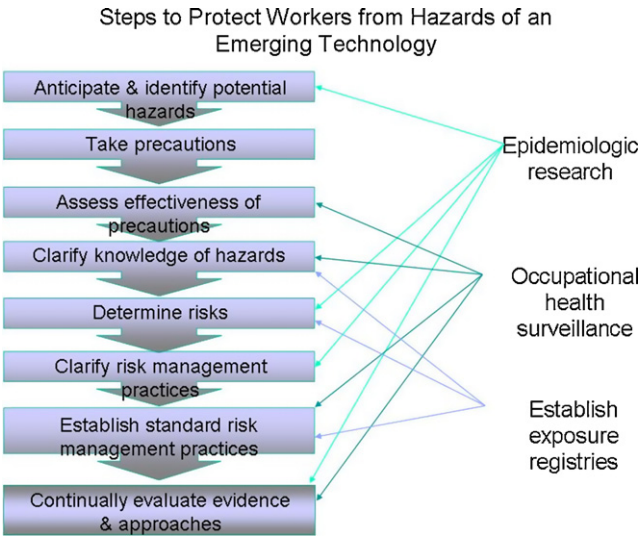


**Fig. 1.** Steps to protect workers from hazards of nanomaterials.

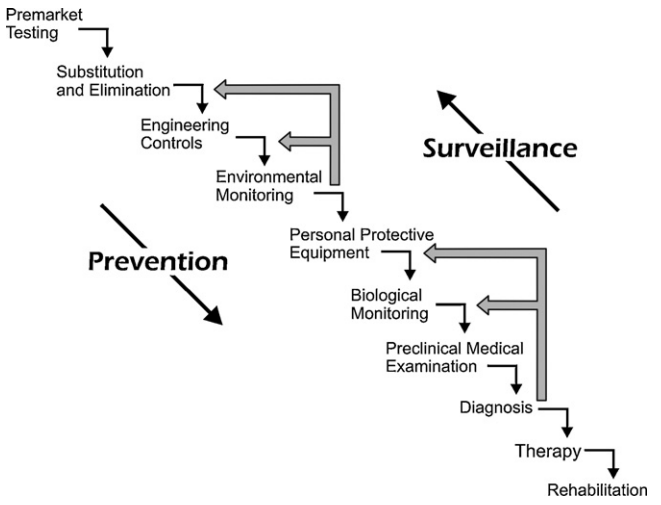


**Fig. 2.** The cascade of occupational health prevention with examples of surveillance feedback (adapted from Halperin, 1996; Schulte et al., 2008b).

groups of workers for the purpose of early detection of disease and injury. It also involves identification of trends or patterns of occurrence presumably leading to prevention of subsequent disease. Occupational health surveillance can help define the magnitude and scope of occupational health issues among groups of workers and guide efforts to improve worker safety and health. These efforts toward prevention of occupational illness can be ordered into primary, secondary and tertiary prevention (Halperin, 1996; Borm et al., 2006). Within this hierarchy are a range of activities from premarket testing for potential toxicity to pre-clinical evaluation of exposed workers; all of which are intended to prevent long-term impairment and disability (see Fig. 2). Occupational health surveillance is the process by which information resulting from any one of these activities is collected and used to support or alter what is done at a step higher in the hierarchy.

The general term *occupational health surveillance* includes hazard and medical surveillance; integration of hazard and medical surveillance is key to an effective occupational health surveillance program (Wegman, 1992; Harber et al., 2003; Baker and Matte, 2005; Wagner and Fine, 2008).

### 1.1. Hazard surveillance

Hazard surveillance involves the periodic identification of 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 (Sundin and Frazier, 1989; Froines et al., 1989).

Hazard surveillance is a critical component of a risk management program. The term *hazard* can be used to describe a substance or process with the potential to cause harm, while risk is a concept used to define the likelihood of harm. Risk may be thought of as a combination of hazard and exposure.

Assessment of hazard involves reviewing the best available information concerning toxicity of materials; such an assessment may come from original research (e.g., epidemiologic investigations, case series or reports, animal studies, or toxicological studies), databases, texts, and published literature or available regulations or guidelines. In most instances involving engineered nanomaterials, there is limited relevant, toxicological, or epidemiologic data with which to make an informed hazard assessment. However, existing toxicity information about a given material of a larger particle size or materials with similar physical characteristics can provide a baseline for anticipating the possible adverse health effects that may occur from nanomaterials.

Another important component of a risk management program involves assessment of exposure including actions intended to minimize exposure to potential hazards (e.g., implementing engineering controls, employing good work practices, and using personal protective equipment) (NIOSH, 2009a,b). In the case of engineered nanoparticles, even in the absence of adequate health information, an understanding of potential worker exposures can form the basis for ongoing risk management. Exposure assessment is an important component of the continuum of occupational health surveillance (Fig. 3). Elements of hazard surveillance, as a basis for establishing prudent measures for controlling exposure to engineered nanoparticles, should be in place in all workplaces where workers are potentially exposed (Schulte et al., 2008b; Wagner and Fine, 2008).

### 1.2. Medical surveillance

Medical surveillance examines health status through tracking of illnesses or a change in a biologic function in an exposed person or persons. It essentially involves a process of looking for health trends in a worker population. This is distinct from “medical screening” (also termed “medical monitoring”) which is one form of medical surveillance that is designed to detect early signs of work-related illness by administering tests to apparently healthy persons to detect those with early stages of disease or those at risk of disease (OSHA, 2008; Kelly, 2009).

The elements of a medical surveillance program generally include the following:

1. An initial medical examination and collection of medical and occupational histories.
2. Periodic medical examinations at regularly scheduled intervals, including specific medical screening tests when warranted.
3. More frequent and detailed medical examinations as indicated on the basis of findings from these examinations.
4. Post-incident examinations and medical screening following uncontrolled or non-routine increases in exposures such as spills.
5. Worker training to recognize symptoms of exposure to a given hazard.
6. A written report of medical findings.

7. Employer actions in response to identification of potential hazards and risks to health.

Medical surveillance and screening programs are established components of sound occupational health practice and should be based on established criteria (Halperin et al., 1986; Harber et al., 2003; Baker and Matte, 2005; Borak et al., 2006). Over 30 Occupational Safety and Health Administration (OSHA) standards and hundreds of National Institute for Occupational Safety and Health (NIOSH) guidance documents recommend medical surveillance for various occupational hazards, although none are specific for occupational exposure to nanomaterials (NIOSH CIB 60 2009).

### 1.2.1. Initiation of medical surveillance

Critical in the discussion of medical surveillance for workers potentially exposed to nanomaterials is assessment of criteria for initiation of medical surveillance. A standard approach with known hazards, that is, substances with a documented evidence base and occupational exposure limit (OEL), is to utilize the concept of an "action level." OELs are generally set or recommended by government or professional associations such as The American Conference of Governmental Industrial Hygienist (ACGIH). The action level represents some fraction of the OEL, usually 50%, which if exceeded will trigger various preventive actions including, in some cases, a medical screening program. This situation generally does not occur with nanomaterials since there are no OELs specifically for nanomaterials.

In the absence of OELs and attendant action levels for nanomaterials, medical surveillance should be considered based on qualitative job hazard exposure analyses. In workplaces where risk (based on an assessment of hazard and occupational exposure information) is felt to be present, or at least cannot be ruled out, initiation of medical surveillance may be prudent to protect workers' health. Such medical surveillance may consist, at a minimum, of collecting medical history information on a targeted population. A determination of whether medical surveillance is instituted, the components of the medical surveillance, and how frequently data are collected should be made on a workplace by workplace basis. This type of health surveillance approach has been pioneered in the pharmaceutical industry and in the UK (Naumann and Sargent, 1997; HSE, 2006). Generally, these approaches are based on some knowledge of the degree of hazard. When this is not known as with some nanomaterials various other approaches may need to be utilized; for example, by determining whether toxicity information exists for a similar type of nanoparticle that can be used as a surrogate for triggering action (Kuempel et al., 2007).

### 1.2.2. Current knowledge concerning risk of occupational exposure to engineered nanoparticles

If specific hazards of nanomaterials are identified, appropriate steps could include modification of exposure potential through risk management interventions, supplemented by medical surveillance intended to assess pre-clinical changes through medical testing or to detect the occurrence of overt adverse outcomes. Such medical screening is not meant as the primary means for protecting workers but rather as a secondary prevention effort, after risk management efforts (e.g., engineering controls and use of personal protection equipment) have been implemented (Schulte et al., 2008a,b; NIOSH, 2009a,b). If known or anticipated biological changes or clinical outcomes linked to exposure to engineered nanoparticles can be identified, then medical testing can serve to identify sentinel events (Rutstein et al., 1983; Mullan and Murthy, 1999).

Toxicological studies, review of information concerning exposure to nanomaterials, previous research of ultrafine particles, and the nature of nanoparticles currently used in commerce and research all support the idea that the predominant target organ systems of concern for health effects will be the respiratory and circulatory systems (Donaldson et al., 2005; Gwinn and Vallyathan, 2006; DEFRA, 2006; Oberdörster et al., 2007). However, some nanoparticles, e.g., manganese might pose other appreciable risks, such as neurotoxicity (Elder et al., 2006). The greatest amount of available information related to hazards of nanomaterials includes research on titanium dioxide particles and carbon-based nanomaterials, including various forms of carbon nanotubes. Recommendations for specific medical surveillance are most likely to first be proposed for these specific groups/classes of nanomaterials. Such medical testing may include tests that evaluate the respiratory system which could help to indicate changes in pulmonary function or provide early indicators of inflammation or fibrosis. An example of such a program is in the National Institute for Occupational Safety and Health (NIOSH) Criteria for a Recommended Standard for Occupational Exposure to Refracture Ceramic Fibers (NIOSH, 2006). One of the challenges faced in recommending medical surveillance for nanomaterial workers (or RCF workers) is that a key endpoint of concern (e.g., slowly developing interstitial lung disease) maybe not readily detected at early stages by the two mainstays of current pulmonary biomonitoring, chest X-rays and spirometry. Although not widely validated, tests of exhaled nitric oxide or isoprostanes have been used as non-invasive markers of pulmonary inflammation (Beilman, 2004; Birrell et al., 2006; Makris et al., 2008) and possibly could be tests used in the future for workers exposed to nanomaterials.

Potential health effects related to occupational exposure to nanomaterials beyond the respiratory and circulatory systems is also an evolving area of investigation. Nanoparticles in the circulatory system could reach many other organs and specific tests related to early changes in organ function may be warranted (Oberdörster et al., 2005a,b). Translocation of nanoparticles to the brain has been demonstrated, but the clinical relevance is not known, nor is there enough information to suggest what type of testing could be useful to assess such effects (Elder et al., 2006). Application of standard criteria for medical testing for workers would be particularly important to keep in mind before implementation of specific medical screening of workers is conducted related to these less well understood health outcomes (Nasterlack et al., 2007).

Another factor to keep in mind when considering medical surveillance for workers potentially exposed to engineered nanoparticles is whether or not there are other medical surveillance programs in place for these workers (Schulte et al., 2008b). These programs, in place because of existing hazardous substances in the workplace other than engineered nanoparticles, may also be relevant for workers exposed to engineered nanoparticles. For example, three such types of medical surveillance that might be occurring in a workplace include assessment of the worker's ability to wear or use required respiratory or other personal protective equipment, medical examination pertaining to job placement, and medical examination as part of emergency medical care after a work-related exposure or incident. Employers should continue using these established applications of medical surveillance; data collected in these types of programs may be informative in the future about whether there is an increase in the frequency of adverse health effects related to exposure to engineered nanoparticles.

### 1.2.3. Illustration of a medical screening and surveillance program for workers potentially exposed to carbon nanotubes

The toxicologic evidence to date while not conclusive suggests that workers exposed to carbon nanotubes may be at some risk from a respiratory hazards (Drew et al., 2009). Therefore, initiation of basic medical surveillance is prudent to protect these workers'

health through the establishment of a program consisting of the following components:

- An initial evaluation, consisting of occupational and medical history, conducted by a qualified health professional with an emphasis on the respiratory system.
- Other examinations or medical tests, performed at the time of the initial evaluation, deemed appropriate by the responsible health care professional. The need for specific medical tests may be based on factors such as:
  - Work-related symptoms noted on evaluation.
  - Results of hazard (e.g., toxicity information) and exposure (i.e., worker exposure to CNT) assessments.
- Periodic evaluations, potentially including symptom surveys, physical examinations, or specific medical tests, deemed appropriate by the responsible health care professional based on data gathered in the initial evaluation.
- Post-incident evaluations as indicated by nature of incident, and as deemed appropriate by the responsible health care professional.
- Worker training, to include information sufficient to allow workers to understand the nature of potential workplace exposures, routes of exposure, and instructions for reporting health symptoms.
- Periodic analysis of the medical screening data collected at a workplace by an epidemiologist or other knowledgeable person to identify patterns of worker health that may be linked to work activities or exposures.

#### 1.2.4. Data collection and use responsibilities

Regardless of the level of medical surveillance action that may be selected; the gathering, storage, and use of individual-level or individually identifiable data carry certain legal and ethical obligations. Issues that will be important to consider, but that are outside the scope of this discussion include issues related to confidentiality and privacy, understanding of original and intended use of surveillance data, informed consent, and reporting test results, among others (Ashford et al., 1990; ILO, 1998). Less well appreciated are possible ethical responsibilities to properly analyze and report findings from constructed databases. For example, if an occupational health professional at a company conducts an exploratory analysis to see if spirometry data collected as part of a respirator fitness evaluation has any relation to work with nanomaterials, the question may be raised whether this constitutes "research" requiring approval by an Internal Review Board (IRB). Additional questions may include the point at which, upon detection of a preliminary/unvalidated association, an occupational health professional would have an obligation to inform the workforce (Kosnett, personal communication 2009).

### 1.3. Exposure registries

There is a 50-year history of the use of exposure registries in public health; they are especially useful when the risks to workers are not well defined (Schulte and Kaye, 1988). Since the formation of cohorts for an epidemiological study may involve combining workers from different companies and possibly different countries, there may be a need for a preparatory step such as the establishment of exposure registries (Nasterlack et al., 2007). Exposure registries are useful tools for surveillance of new or perceived hazards since they provide documentation of who is working with which materials, when, and where in the facility (Kelly, 2009). A registry provides a structured and orderly approach to identifying and maintaining communicating with workers exposed to hazardous materials, utilizing a common set of variables (Schulte et al., 2008b). An exposure registry is the enrollment of persons exposed, or likely to have been exposed, to occupational or environmental hazards that can serve as a means of identifying persons for primary or secondary preventive efforts. In occupational situations, company employee rosters are de facto registries; however, they may not address employees who leave a company. Many employers may not have the capability or will to establish a meaningful sentinel event medical surveillance program at this time (Kelly, 2009). However, for new technologies, such as nanotechnology, registries could be developed and maintained by government entities, but there also are examples of private sector registries related to exposure to commercial products (Schulte and Kaye, 1988). Whether such registries would foster potential discriminatory actions or legal liabilities would need to be addressed. Exposure registries may serve as sampling frames for epidemiological studies and provide for standardized approaches for exposure assessment (Marsh and Cassidy, 2003; Bunch et al., 2009). Many of the issues in conducting epidemiologic studies are foreshadowed in the establishment of exposure registries. This includes identification of target companies, obtaining participation of management and workers, collection of exposure data, and addressing issues of business and personal confidentiality.

When considering exposure registries the following questions arise:

- Who would manage them?
- What data would be collected?
- Who would have access to the data?
- Could any investigator with an epidemiologic research proposal have access to registry data?
- Are there non-research implications and responsibilities for those who manage a registry and expectations by those who participate in them (Schulte et al., 2009)?

### 1.4. Considerations for epidemiologic research

#### 1.4.1. Heterogeneity of nanoparticles

The most critical factor that may influence the conduct of epidemiological studies of workers exposed to nanomaterials is the heterogeneity of nanoparticles. Various physicochemical parameters (size, shape, composition, charge, crystallinity, solubility, added functional groups, and impurities) can be combined in any particular nanoparticle leading to different toxic potential (Maynard and Aitken, 2007; Schulte et al., 2009). The variability in toxic potential can make it difficult to identify similarly exposed occupational groups for study. Failure to account for particle heterogeneity can lead to misclassification on exposure and bias measures of association toward the null hypothesis. This is an issue that generally exists in every occupational epidemiological study but which might possibly be more prevalent in studies of workers exposed to nanomaterials. Because of the tremendous variability of particle types it may be difficult to identify adequately large cohorts with exposure to the same materials (Schulte et al., 2009).

#### 1.4.2. Selecting disease endpoints to study

In hypothesis testing studies it is important to know what diseases are included in the hypotheses. The current body of information on the human health effects potentially related to nanomaterials comes from the studies of incidental nanoparticles, air pollution epidemiology (Dockery et al., 1993; Gwinn and Vallyathan, 2006), and studies of workers with various occupational exposures such as welding fumes, ultrafine carbon (e.g., carbon black), or diesel fumes (Aitken et al., 2004; Lam et al., 2004; Donaldson et al., 2005; Oberdörster et al., 2005a,b; Shvedova et al., 2005; Mercer et al., 2007). From these studies and experimental

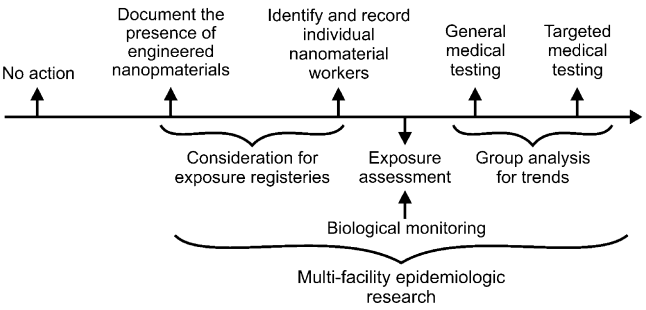


**Fig. 3.** Continuum of hazard and medical surveillance and related research approaches for nanomaterial workers.

animal studies, malignant and non-malignant respiratory disease and cardiovascular disease are thought to be primary health effects of concern for exposed workers, although it is clear that not all incidental nanoparticles give the same biological responses (Dockery et al., 1993; Ibald-Mulli et al., 2002; Oberdörster et al., 2005a,b; Borm et al., 2006; Berglind et al., 2009).

One problem is that many air pollution studies do not indicate specific size particles, only categorical ranges, and many studies are ecological with no individual measure of exposure. Nonetheless, there have been numerous studies that investigated health effects of ambient and occupational air pollution particles of various size ranges using personal monitoring (Dockery et al., 1993; Ibald-Mulli et al., 2002; Gwinn and Vallyathan, 2006; Mark, 2007; Berglind et al., 2009). Exposure to incidental nanoparticles (e.g., generated from combustion or hot processes) has been associated with various adverse health effects in workers. For example, diesel exhaust has been associated with eye and respiratory irritation, endothelial dysfunction (impaired vasodilation) with mild systemic inflammation, and lung cancer, whereas welding fume exposure has been associated with lung cancer, metal fume fever, susceptibility to pulmonary infection, obstructive lung disease, and possible neurologic changes (Oberdörster and Yu, 1990; Castranova, 2000; Chalupa et al., 2004; Garshick et al., 2004).

### 1.4.3. Temporal factors

Despite scientific awareness and utilization of some types of nanoparticles (e.g., as catalysts and colloids) for decades, the major commercial emergence of nanotechnology is generally about 10 years old. The initial phases in the emergence have involved research and pilot facilities, rapidly changing nanomaterial products, and a relatively small number of workers. Consequently, currently it is unlikely that a population of workers with long-term exposure to nanomaterials large enough for epidemiological study exists at this time (Schulte et al., 2009) (Fig. 4). Moreover, given the absence of extensive toxicological data, including data on acute effects from exposures, a discussion of temporal issues is problematic. Even though nanotechnology is permeating most economic sectors and is used to develop numerous products that result in various exposures, the number of people actually exposed for some period that could significantly put them at risk of chronic effects may not be large enough to form an adequate recruitment pool or sampling frame for conducting epidemiologic studies for many years (Schulte et al., 2009). This means that obtaining results from statistically powerful studies of chronic effects with adequate latency may not be feasible in the near future. Determination of when there would be adequate exposures and latency to begin to conduct epidemiological studies is compounded by issues related to the exposure, such as heterogeneity of exposure, lack of contemporaneous exposure information that is consistently collected within and across industries, and extent/magnitude of exposure (Schulte et al., 2009). Nonetheless, it is worth noting that some of the cardiovascular effects associated with ultrafine particulate exposure (e.g., increased daily cardiovascular disease mortality within 1 or 2 days of high particulate air pollution exposure) suggests that cardiovascular effects of nanoparticle exposure might not require long periods of follow-up (Berglind et al., 2009). This might particularly be true in middle-aged or older workers with pre-existing cardiovascular disease or risk factors.

### 1.4.4. Exposure identification and characterization

A feature that is most important in conducting occupational epidemiological studies is assurance of the sufficiency of exposure of study participants to the exposure of concern (relative to this discussion, engineered nanomaterials). If workers are minimally exposed, due to enclosed processes or handling of materials in which nanoparticles are embedded, such studies may be uninformative. Nevertheless, if there is sufficient exposure to cause acute and chronic health effects, epidemiological studies may be able to be conducted. In order to select subjects for study, there will be a need to know the level of exposures by jobs and processes, which are necessary for proper study design and data analysis. The choice of exposure metrics is important since it is likely that various metrics such as weight/unit volume, particle number, particle size distribution, surface area, and surface chemistry will be useful for characterizing risks. Moreover, nanoparticle aerosols are highly dynamic; nanoparticles in sufficient concentrations will agglomerate rapidly (Tran et al., 2005; Mark, 2007; Oberdörster et al., 2007). This can affect particle number concentrations, as well as physical and chemical characterizations.

Currently, there are no national or international consensus standards on measurement techniques or metrics for nanomaterials in the workplace, and there have been few published studies of exposure concentrations of workers to nanomaterials. The NIOSH has proposed a strategy for conducting exposure assessments that discusses the strengths and limitations of numerous nanoparticle measurement techniques (NIOSH, 2009a,b).

Critical in the assessment of exposure-response relationships is the distribution of exposures and exposure variability. Epidemiologic studies require sufficient variability in exposures and sufficient distribution of exposures to provide contrasts necessary to estimate relationships reliably (Tran et al., 2005; Schulte et al., 2009). It may be in nanotechnology-related industries that such variability will be difficult to identify in terms of duration or intensity of exposure, reaffirming the need to document exposures by job and job tasks so that appropriate exposures can be assigned to individuals.

### 1.4.5. Identification of the study population

Central in developing epidemiological studies of workers exposed to nanomaterials is identifying the workers in the source population and in the study population. Nanotechnology is not a specific industry, but a value chain (the chain of activities and companies that give products additional value) with various functional sectors and occupational groups (Holman et al., 2007). Therefore, understanding the current and future nanotechnology market trends, along with business- and research-targeted surveys, will be essential to identifying workers with potential exposure to nanomaterials in the source population. Nanomaterials are likely to be used in every economic sector. It is projected that by 2014 about 16% of manufactured goods in health care and life sciences, and 50% of manufactured goods in electronics and information technology will involve nano-enabled materials and products (Holman et al., 2007). Potential study and registry populations might be located not only from workers involved in the

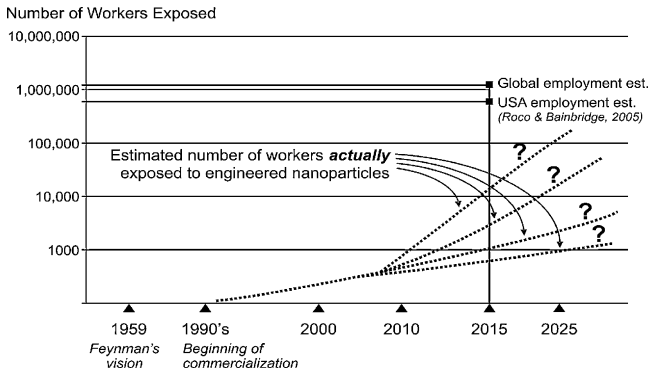


**Fig. 4.** Dilemmas in identifying workers exposed to engineered nanoparticles.

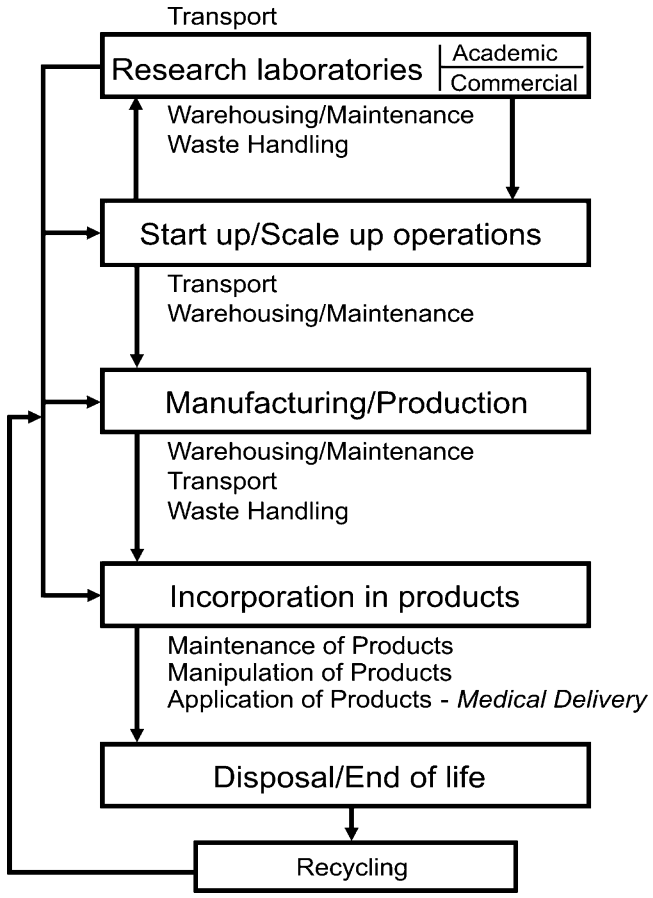


**Fig. 5.** Range of workplaces that could involve exposure to engineered nanoparticles (adapted from the paper by Schulte et al., 2008a,b).

manufacture of nanomaterials but also among downstream users of them (Fig. 5). Currently, there is not a widely used, standardized nomenclature for nanomaterials; however, one is being developed (http://www.ansi.org/isotc229tag). Generally, the most common nanomaterials types are fullerenes, carbon nanotubes, quantum dots, metal nanoparticles, nanowires, nanoporous materials, metal oxide/ceramic nanoparticles, and nanofibers (Holman et al., 2007).

## 2. Conclusion

Increasing numbers of workers are involved with the production, use, distribution, and disposal of nanomaterials. It is not known whether occupational exposures to nanomaterials pose an unintended risk of adverse health effects. There are, however, a growing number of reports of adverse biological effects of certain nanomaterials. Air pollution and various occupational studies of ultrafine particles also indicate various adverse effects.

The growing body of evidence that occupational exposure to various engineered nanomaterials may cause health effects requires that prudent approaches be implemented to control exposures and protect workers (Schulte et al., 2008a). Practitioners, employers, governmental agencies, and workers do not have the luxury of debating health effects for years before action is taken. Prudent precautionary control measures have been widely recommended for workplaces where nanomaterials are manufactured, used, distributed, and disposed. In addition to controls, there will be need for various types of occupational health surveillance, most notably, hazard surveillance, but also including medical surveillance and in some circumstances, medical screening (Mercer et al., 2007; Poland et al., 2008; Shvedova et al., 2005). Specifically, evidence is increasing that various high aspect ratio nanomaterials such as carbon nanotubes are associated with effects that may ultimately lead to chronic obstructive pulmonary disease or cancer (such as mesothelioma); increased consideration of specific medical surveillance and screening is warranted for workers potentially exposed to those substances.

Exposure registries and epidemiologic studies will also be needed to help assess risks among worker populations and in individual workers. A critical factor upon which occupational health surveillance, exposure registries, and epidemiologic studies are based is high quality exposure assessment. Given the heterogeneity of nanoparticles and the various candidate metrics that could be considered, advancement in exposure assessment will be a challenge, and require extensive collaboration among interested parties.

In the face of uncertainty about potential occupational health effects among workers exposed to nanomaterials, medical surveillance and screening guidelines, along with development of exposure registries and conduct of epidemiologic research, will be important in guiding future research and the prevention of health effects among these workers.

## Conflict of interest statement

None.

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