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Health risk assessment for nanoparticles: A case for using expert judgment

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Abstract

Uncertainties in conventional quantitative risk assessment typically relate to values of parameters in risk models. For many environmental contaminants, there is a lack of sufficient information about multiple components of the risk assessment framework. In such cases, the use of default assumptions and extrapolations to fill in the data gaps is a common practice. Nanoparticle risks, however, pose a new form of risk assessment challenge. Besides a lack of data, there is deep scientific uncertainty regarding every aspect of the risk assessment framework: (a) particle characteristics that may affect toxicity; (b) their fate and transport through the environment; (c) the routes of exposure and the metrics by which exposure ought to be measured; (d) the mechanisms of translocation to different parts of the body; and (e) the mechanisms of toxicity and disease. In each of these areas, there are multiple and competing models and hypotheses. These are not merely parametric uncertainties but uncertainties about the choice of the causal mechanisms themselves and the proper model variables to be used, i.e., structural uncertainties. While these uncertainties exist for PM2.5 as well, risk assessment for PM2.5 has avoided dealing with these issues because of a plethora of epidemiological studies. However, such studies don't exist for the case of nanoparticles. Even if such studies are done in the future, they will be very specific to a particular type of engineered nanoparticle and not generalizable to other nanoparticles. Therefore, risk assessment for nanoparticles will have to deal with the various uncertainties that were avoided in the case of PM2.5. Consequently, uncertainties in estimating risks due to nanoparticle exposures may be characterized as 'extreme'. This paper proposes a methodology by which risk analysts can cope with such extreme uncertainty. One way to make these problems analytically tractable is to use expert judgment approaches to study the degree of consensus and/or disagreement between experts on different parts of the exposure–response paradigm. This can be done by eliciting judgments from a wide range of experts on different parts of the risk causal chain. We also use examples to illustrate how studying expert consensus/disagreement helps in research prioritization and budget allocation exercises. The expert elicitation can be repeated over the course of several years, over which time, the state of scientific knowledge will also improve and uncertainties may possibly reduce. Results from expert the elicitation exercise can be used by risk managers or managers of funding agencies as a tool for research prioritization.

Introduction

The appeal of nanotech results from its protean nature – applications of this technology have the potential to affect all aspects of human life. Worldwide government investment in nanotechnology has increased by a factor of five from $825 million in 2000 to $4.1 billion in 2005 (Roco, 2005). However, like biotechnology before it, concerns about environmental and human health risks have already begun to have an effect on the societal debate around nanotechnology. Fears about risks of nanotechnology result from a basic conundrum: the properties that make nanoparticles so promising – that they can behave very differently from bulk forms of the same material – also make their health and environmental effects extremely difficult to predict (Service, 2004). Uncertainties about health effects feed directly into the risk-benefit debates that increasingly shape societal responses to, and regulation of, new technologies.

The human health impact of toxic substances and pollutants can be studied using frameworks of risk assessment developed over the past 30 years. Risk assessment in this context is a set of tools used to integrate exposure and health effect information for characterizing the potential for health hazards to humans (NRC/NAS, 1983; US EPA, 2004). Such methods typically use quantitative predictions of health impacts (e.g., probability of mortality). However, qualitative risk assessments are also valuable when quantitative assessments are not possible. Even under the best of circumstances, risk assessment cannot estimate risk with absolute certainty. Modern quantitative risk assessment aims not to arrive at a single precise number, but to allow decision makers to face the possible consequences of a range of "not clearly incorrect" answers and decide on the protective policies that are warranted in light of the range of possible future outcomes of alternative policies (Anderson & Hattis, 1999). Thus, for example, if there is uncertainty regarding exposures or dose in a population, one can either collect more data or use numerical models to estimate missing values or extrapolate values from other similar populations.

Numerical models incorporate amounts of pollutants prevalent in the ambient environment, the actual amounts absorbed or inhaled by an exposed individual, the toxicological effects on the human body as inferred from *in vivo*, *in vitro*, *in silico*, and epidemiological studies, and biologic variability. Uncertainties in values of model parameters play a central role in conventional risk calculations. The parameters in such models may be known with some uncertainty, and a degree of subjective professional judgment about the values of such parameters may enter into the analysis. Uncertainties in numerical models such as those used to calculate risks can be divided into two broad classes: (a) "parametric" uncertainty associated with parameter or observational values that are not known precisely and (b) "structural" or "model" uncertainty where important relationships between variables or their functional form may not have been identified correctly. Not surprisingly, assessing model uncertainty is generally more difficult since the uncertainties are likely to be more fundamental. Since key mechanisms for exposure processes and toxicity effects of manufactured nanoparticles remain poorly understood, model uncertainties might dominate in related risk calculations. Uncertainties about mechanism include those related to: (a) how long manufactured nanoparticles may persist in the atmosphere depending on their rates of agglomeration (and some nanoparticles are designed specifically not to agglomerate), thus influencing the probability of exposure; (b) the routes of exposure and the metrics by which exposure ought to be measured; (c) mechanisms of translocation to different parts of the body after nanoparticles enter the body; (d) mechanisms of toxicity. These are not simply uncertainties in the value of some model parameter but rather uncertainties about the causal mechanisms themselves.

This paper examines how risk analysts can cope with extreme uncertainty in nanoparticle risk calculations. In Section "Traditional risk assessment" we begin with a discussion of uncertainties in health risks from particles that are less than 2.5 μm in diameter ($PM_{2.5}$). Risks from $PM_{2.5}$ have been studied for over a decade and provide a starting point for understanding the health effects of particulate matter. In Section "Uncertainty in characterizing health risks from nanoparticles", we extend the analysis to manufactured nanoparticles and show how model uncertainties dominate