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Risk Assessment at the Crossroads of the 21st Century: Opportunities and Challenges for Research

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INTRODUCTION

Although one could say that assessing risks is as old as man, formalized human health risk assessment is a relatively new discipline that has largely developed as a result of environmental (U.S. Environmental Protection Agency [USEPA]) and occupational regulations (Occupational Safety and Health Administration [OSHA]) that were adopted in the 1970s. Court decisions, such as the U.S. Supreme Court's ruling on the OSHA benzene standard (*Industrial Union Department v. American Petroleum Institute,* 448 U.S. 607, 655 [1980]), have reinforced the requirements that these agencies make their best efforts to quantify risks and benefits when setting standards for protecting the public health. For better or worse, risk assessment has become a *sine qua non* for regulatory decision making in the U.S.

CHALLENGES

One word that would best describe the last 20 years of experience with risk assessment in the U.S. is "controversy." Performing quantitative assessments of risk requires extensive toxicological dose-response information in animals and, to the extent possible, in humans. Controversy arises largely from the gaps in the scientific data available for risk assessments. There is often considerable debate regarding the practice of predicting human risks based on outcomes in experimental toxicological studies with their accompanying assumptions regarding similarities or differences in interspecies metabolism of xenobiotic compounds (*e.g.*, Ames and Gold 1990).

Risk assessments based on epidemiologic data are often no less contentious. For example, risk analyses of the effects of diesel exhaust on human health has been the subject of numerous analyses, reanalyses, and debates in the last decade (Crump

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2001; Dawson and Alexeeff 2001). There are many potential biases and other factors in epidemiologic investigations that are difficult to control for and that can distort the shape of the exposure-response relationship, such as the "healthy worker survivor" effect (Steenland and Stayner 1991; Steenland *et al.* 1996; Kolstad and Olsen 1999).

Methods used for performing risk assessments have also been a major source of uncertainty and controversy. USEPA and other agencies have used the linear multistage model (Crump *et al.* 1976, 1977) for cancer risk assessment. This model has been under considerable attack over recent years for its failure to consider possible effects of carcinogens on cell growth and differentiation, and for ignoring alternatives such as the "two-stage clonal expansion model" (Moolgavkar *et al.* 1980; Moolgavkar and Knudson 1981; Moolgavkar 1994). In response, the USEPA (1996) has developed draft guidelines for cancer risk assessment to address these issues. However, the fact that these guidelines have been under review for the last 5 years reflects the degree of debate over this issue. Similar debates exist over current methods for assessing noncancer risks, particularly over the continued use of the no observed adverse effect level (NOAEL) and uncertainty factors for determining "safe" levels of exposure and alternative methods have been proposed (Bailer *et al.* 1997; Hattis 1998; Hattis *et al.* 1999; Hattis *et al.* 2002).

Controversy also surrounds risk assessment because it provides the scientific basis for regulations that have major social and fiscal implications. Groups most affected by these regulations frequently raise questions about either the data and/or the methods used in risk assessments as a means of either strengthening or weakening the proposed regulation. The net effect of these debates has often been to delay the finalization of a risk assessment and associated regulatory actions. Diesel exhaust particulates (DEP) is a classic example (see Figure 1) of how difficult the risk assessment process has become for many regulatory agencies (Stayner *et al.* 1999). The USEPA initiated its efforts to assess the potential lung cancer risk associated with environmental exposures to DEP before 1980 (Albert *et al.* 1979, Albert, 1983). In 1987 the USEPA formally reinitiated its efforts, and after four drafts the risk assessment was just recently approved for finalization by their scientific advisory committee and it is anticipated that this assessment will be published in the next few months. Thus, it has taken the USEPA more than 20 years to complete its risk assessment for DEP. The USEPA risk assessment for dioxin has taken nearly as long and has also not yet been finalized.

The process of risk assessment and regulatory actions has been equally difficult in the occupational arena. To illustrate this, the number of occupational permissible exposure limits (PELs) set by OSHA since its existence is presented in Figure 2. OSHA set a relatively large number of RELs in the 1970s with a peak of 15 standards in 1974. There appears to have been a clear drop off in standard setting after the benzene Supreme Court case in 1980, which made the quantification of risks and benefits a requirement for setting standards. Only 10 standards have been set since 1980. In the last 4 years, OSHA only finalized one standard, the ergonomics rule (CFR, 29CFR 1910.900). However, this rule was just recently overturned by Congress under the Congressional Review Act of 1996. The development of NIOSH Recommended Exposure Levels (RELs) has been nearly as slow, as illustrated in Figure 3 with only 6 new RELs set in the 1990s.

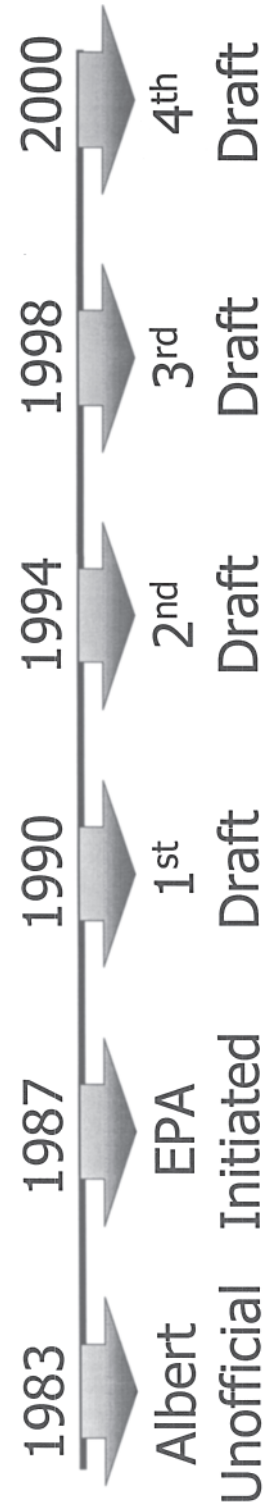


Figure 1: History of EPA Diesel Risk Assessment

Figure 2: Number of OSHA PELS set since passage of the Occupational Safety and Health Act in 1970

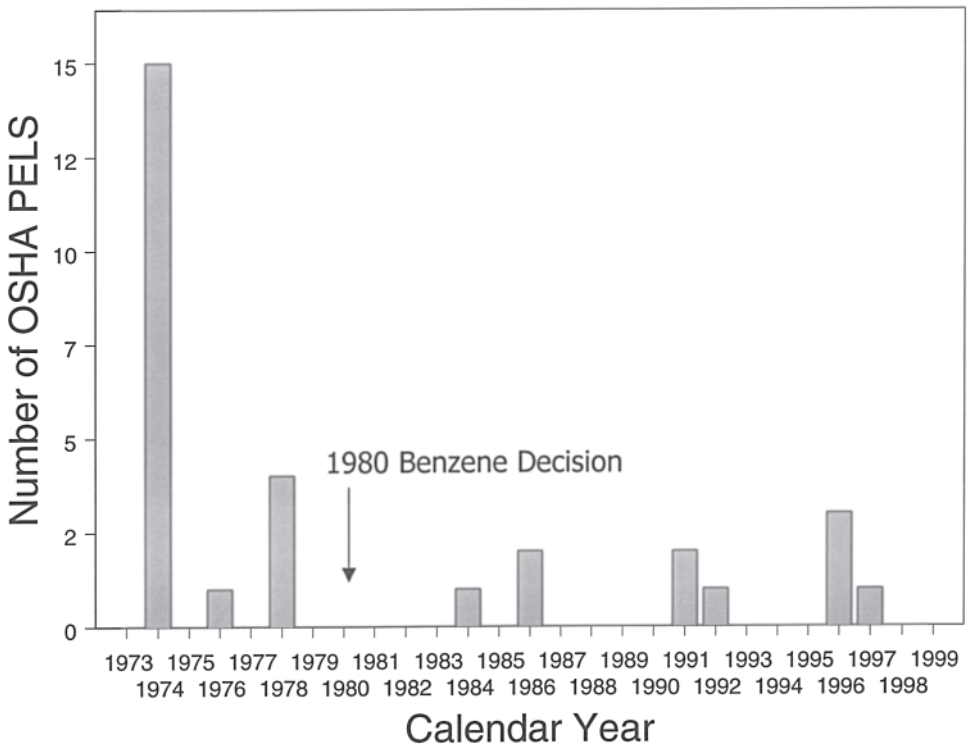
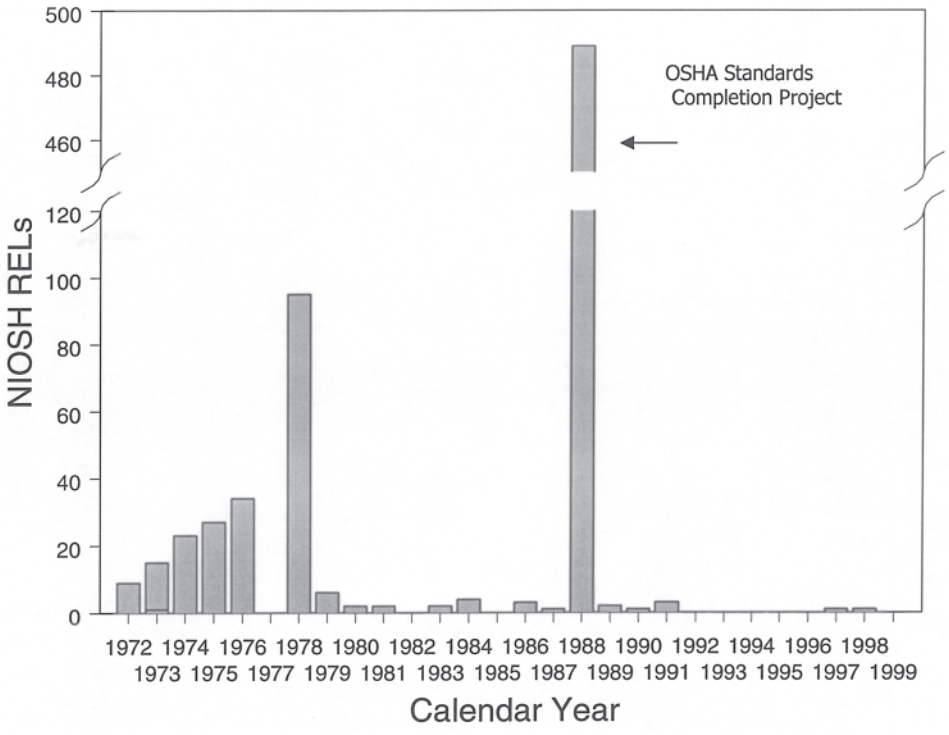


Figure 3: Number of NIOSH RELs set since passage of the Occupational Safety and Health Act in 1970



The extremely large amount of resources and time that agencies have had to invest in developing risk assessments has led some to question the utility of risk assessments for regulatory decision making (Silbergeld 1993). Recent environmental legislation in the European Union has emphasized the use of what has been referred to as the "precautionary principle" as an alternative to risk assessment for setting regulations (Epstein 2000). Simply put, the precautionary principle emphasizes that when there is insufficient evidence to characterize risk then one should set standards that err on the side of protecting the public health. This is really not a new concept, and in fact is essentially the philosophy that was the basis for much of the regulatory action in the U.S. prior to the development of the formal requirements for risk assessment in the 1980s. Some in the U.S. risk assessment community have reacted negatively to the precautionary principle as a substitute for risk assessment, in part because it does not provide either information needed to juxtapose expected costs and benefits of different policy options, or to judge the fairness (equity) of the distributions of benefits and risks to different parties that are expected to result from different public policy choices (Hattis and Anderson 1999; Graham 1999).

Finally because risk assessment often spans several different disciplines with different analytical paradigms and different traditions for what counts as "good" information, there have been important philosophy of science and even ethical disputes as scientists trained in different fields have misunderstood or misinterpreted work and the information standards used by others (Hattis and Smith 1987; Hattis 2000).

OPPORTUNITIES

Given what some might consider a crisis in the current state of affairs of risk assessment and risk management in our country, it seems an appropriate time to consider what as researchers we could do to resolve some of the issues discussed above. In order to identify the research opportunities that would address these issues, a workshop was convened on August 16 to 18th, 2000, in Aspen, Colorado, on "Future Research for Improving Risk Assessment Methods." The primary objective of this workshop was to bring together prominent scientists in the field of risk assessment and related sciences (*e.g.*, epidemiology, toxicology, industrial hygiene and statistics) to assist in the development of a national agenda for research that would enhance risk assessment methodology. The first few papers in this journal were from presentations intended to identify issues with current risk assessment methods, and to broadly identify opportunities for research solutions to these issues. The last set of papers in this issue are from three workgroups on mice (toxicology), men (epidemiology), and models (toxicokinetics and dose-response). These workgroups were charged with developing specific research ideas that could improve our ability to perform risk assessments in the future that better reflect our scientific understanding, and are more helpful and informative for decision making.

It would be misleading to suggest that further research is all that is needed to solve our problems with risk assessment. Nonetheless, there are significant research opportunities that may improve the current situation. The most significant new development is the burgeoning new area of genomics which was the subject of one of the

presentations in this special issue (Morgan 2002). The recent announcement of the successful mapping of the genome (Lander *et al.* 2001) is clearly going to usher in a whole new era in our understanding of the molecular basis for diseases including those induced by environmental agents. Future risk assessments will need to address how the risk associated with a particular agent are modified by genetic characteristics. Current mechanistic models for cancer (*e.g.*, multistage and 2-stage clonal expansion) will need to be modified to fit our increasingly complex knowledge of the carcinogenic process. Toxicologic bioassays may be improved so that they more accurately predict human risk, and require less time and resources to perform. Handling the vast amount of information generated from the high output DNA assays will present a challenge for risk assessors, and will require the development of new methods.

The explosion of information available for risk assessments in the future will also provide an even greater burden on risk assessors to develop methods that are not overly complex. Silbergeld (2002) has a clear warning to the risk assessment community that current risk assessments are already too complex, which contributes to distrust on the part of the general public. In developing new methods we should bear this warning in mind and remember the principle of Ockham's razor, which for risk assessment might state that the simplest model that adequately explains a phenomenon is probably the most useful. On the other hand, we might also consider that Einstein reportedly said that theories should be as simple as possible, but no simpler. The balance between faithfulness to our mechanistic understanding and simplicity in describing limited available data is addressed by Krewski *et al.* (2002) in these proceedings. Clearly, with the explosion of genetic and other mechanistic information that will be available to us, striking this delicate balance is probably the greatest challenge that risk assessors will face in the future.

REFERENCES

Albert RE. 1983. Comparative carcinogenic potencies of particulate from diesel engine exhausts, coke oven emissions, roofing tar aerosols and cigarette smoke. Environ Health Perspect 47:339-41

Albert RE, Pasternack BS, Shore RE, *et al.* 1979. Identification of occupational settings with very high risks of lung cancer. J Natl Cancer Inst 63:1289-90

Ames BN and Gold LS. 1990. Too many rodent carcinogens: Mitogenesis increases mutagenesis. Science 249:970-1

Bailer AJ, Stayner LT, Smith RJ, *et al.* 1997. Estimating benchmark concentrations and other noncancer endpoints in epidemiology studies. Risk Anal 17(6):771-80

CFR (Code of Federal Regulations). USA29CFR 1910.900. Office of the Federal Register. Government Printing Office. Washington, DC, USA

Crump K. 2001. Modeling lung cancer risk from diesel exhaust: suitability of the railroad worker cohort for quantitative risk assessment. Risk Anal 21:19-23

Crump K, Hoel D, and Peto R. 1976. Fundamental carcinogenic processes and their implications for low dose risk assessment. Cancer Research 36:2973-9

Crump KS, Guess HA, and Deal KL. 1977. Confidence intervals and test of hypotheses concerning dose response relations inferred from animal carcinogenicity data. Biometrics 33:437-51

Dawson SV, Alexeeff GV. 2001. Multi-stage model estimates of lung cancer risk from exposure to diesel exhaust, based on a U.S. railroad worker cohort. Risk Anal 21:1-18.

Epstein SS. 2000. Legislative proposals for reversing the cancer epidemic and controlling runaway industrial technologies. Int J Health Serv 30:353-71

Graham JD. 1999. Making sense of the precautionary principle. Risk Perspective 7:1-6

Hattis D. 1998. Strategies for assessing human variability in susceptibility, and using variability to infer human risks. In: Neumann DA and Kimmel CA (eds), Human Variability in Response to Chemical Exposure: Measures, Modeling, and Risk Assessment, pp 27-57. CRC Press, Boca Raton, FL, USA

Hattis D. 2000. Draft risk analysis ideals. Human Ecol Risk Assess 6:913-9

Hattis D and Anderson E. 1999. What should be the implications of uncertainty, variability, and inherent 'biases'/'conservatism' for risk management decision making? Risk Anal 19:95-107

Hattis D and Smith J. 1987. What's wrong with quantitative risk assessment? In: Humber JM and Almeder RF (eds), Quantitative Risk Assessment, Biomedical Ethics Reviews: 1986, pp 57-105. Humana Press, Clifton, NJ, USA

Hattis D, Banati P, and Goble R. 1999. Distributions of individual susceptibility among humans for toxic effects–for what fraction of which kinds of chemicals and effects does the traditional 10-fold factor provide how much protection? Annals NY Acad Sci 895:286-316

Hattis D, Baird S, and Goble R. 2002. A straw man proposal for a quantitative definition of the RfD. Drug Chem Toxicol (*in press*)

Kolstad H and Olsen J. 1999. Why do short term workers have high mortality? Am J Epidemiology 149(4):347-52

Kreski D, Brand KP, Burnett RT, *et al.* 2002. Simplicity *vs.* complexity in the development of risk models for dose-response assessment. Human Ecol Risk Assess (*this issue*)

Lander ES, Linton LM, Birren B, *et al.* 2001. Initial sequencing and analysis of the human genome. Nature 409:860-921

Moolgavkar SH. 1993. Cell proliferation and carcinogenesis models: general principles with illustrations from the rodent liver system. Environ Health Perspect 101(suppl 5):91-4

Moolgavkar SH. 1994. Biological models of carcinogenesis and quantitative cancer risk assessment. Risk Anal 14:879-82

Moolgavkar SH and Knudson AG Jr. 1981. Mutation and cancer: a model for human carcinogenesis. J NCI 66:1037-52

Moolgavkar SH, Day NE, and Stevens RG. 1980. Two-stage model for carcinogenesis: Epidemiology of breast cancer in females. J Natl Cancer Inst 65:559-69

Morgan KT, Brown HR, Benavides G, *et al.* 2002. Toxicogenomics and human disease risk assessment. Human Ecol Risk Assess (*this issue*)

Silbergeld EK. 1993. Risk assessment: the perspective and experience of U.S. environmentalists. Environ Health Perspect 101:100-4

Silbergeld EK. 2002. An NGO perspective on risk assessment and scientific research. Human Ecol Risk Assessment (*this issue*)

Stayner L. 1999. Protecting public health in the face of uncertain risks: The example of diesel exhaust. Editorial. Am J Public Health 98(7):991-3

Steenland K and Stayner L. 1991. The importance of employment status in occupational cohort mortality studies. Epidemiology 2(6):418-23

Steenland K, Deddens J, Salvan A, *et al.* 1996. Negative bias in exposure-response trends in occupational studies: Modeling the healthy workers survivor effect. Am J Epidemiology 143(2):202-10

USEPA (U.S. Environmental Protection Agency) 1996. Proposed guidelines for carcinogen risk assessment. Fed Reg, April 23, 1996:1790-01