VALUE OF INFORMATION ANALYSIS IN RESEARCH PRIORITY SETTING

R. Jeffrey Lewis,[1] Mark J. Nicolich,[1] Kimberly M. Thompson[2]

[1]ExxonMobil Biomedical Sciences, Inc., 1545 Route 22 East, Annandale, NJ 08801, USA
[2]Harvard School of Public Health, 677 Huntington Ave., Boston, MA 02115, USA

Introduction

As with most environmental health issues, uncertainty surrounds the potential health risks associated with low levels of dioxin and other persistent bioaccumulative toxicants (PBT) in the environment. The uncertainty arises from our incomplete knowledge about the health effects of these compounds. Knowledge gaps and the resulting uncertainties present a complex dilemma for regulatory decision-makers and the research community. Should regulatory actions be deferred until further research is performed to address these gaps and possibly reduce uncertainty (an action clearly not devoid of costs)? If regulatory action is deferred in favor of additional research, what form should that additional research investment take (e.g., more animal studies, exposure data)?

Value-of-information (VOI) methods are a potentially useful tool for addressing and prioritizing among possible research investments to reduce uncertainty.[1,2] This paper provides a general description of VOI methods and their potential application to research priority setting questions and uncertainty reduction for environmental health risk estimation issues (see reviews by Yokota and Thompson[3,4] for depth).

Methods and Materials

Management of chemicals in the environment involves choices under uncertainty. The tools of decision analysis provide a basic framework for making such choices. The basic elements of a decision analysis problem include: a set of actions that the decision maker must choose between, a set of uncertain possible states of nature that might occur, and well-defined values of the decision maker that determine his or her preferences for the different potential outcomes. Decision analytic tools are designed to help inform the choice, in part by helping the decision maker see how the uncertainty impacts the decision and how much it would be worth to pay for information that would resolve the uncertainty prior to the choice being made.

Numerous examples of VOI applications exist in the published literature. These studies include analyses that focus on resolving uncertainty about toxicity, exposure or both. For example, Lave et al.[5-7] used VOI techniques to ask the question about the worth of the animal bioassay in the context of regulating carcinogens, which Taylor et al.[8] solved more generally. Thompson and Evans[9] provide one of the most comprehensive examples, which focused on decisions associated with regulating perchloroethylene exposures from dry cleaners.

General VOI framework
In the context of setting a research agenda for dioxin and other PBTs, it is critical to begin by framing the potential decisions to be made. Analysts must ask questions like the following:

- What is the overall goal or research question?
- What are the major decision points?
- What is the flow of information from exposure to health risk?
- What are the most significant uncertainties, and is it possible to obtain additional information to reduce the uncertainty of a decision?

We briefly address each of these questions here to explore the opportunities of using VOI techniques for prioritizing research on dioxin and other PBTs. The framework described below is based on the concept of a continuum from release of a substance to the environment up through the potential health effect(s) and the multiple opportunities along this continuum to obtain additional information and potentially reduce uncertainty as discussed by Brand and Small.[10]

What is the overall goal or research question?
The overall research goal and important decision points need to be specified. In the context of dioxin and PBTs a possible overall goal is to address the question of what is the health benefit associated with a reduction in dioxin exposure and what is the cost of a reduction?

What are the major decision points?
Some important decision points to be considered include the following:

- What are the sources of dioxin in the environment (e.g. natural, manmade)?
- What is the dollar cost associated with reducing each source by a specific amount?
- What is the mechanism of transport from dioxin source to an individual?
- What is the direct effect of an exposure of *x* units on an individual?
- What health risks are associated with those direct effects?
- What are the benefits of preventing potential adverse health outcomes?
- What are the ancillary (non-health) benefits associated with reducing dioxin exposure?

What is the flow of information from exposure to health risk?
At this stage, key decision points are arranged in a flow diagram to model the total exposure-health risk process, and associate modeled uncertainties (e.g., effect, benefit, cost) with each decision point (see Figure 1).

What are the most significant uncertainties, and is it possible to obtain additional information to reduce the uncertainty prior to making a decision?
A number of uncertainties exist for dioxin, such as the type(s) of potential health risks (cancer, reproductive, etc), potential toxicity of TCDD-like cogeners, estimation methods for cancer potency (e.g., extrapolation model form), exposure characterization, and the significance of biochemical changes at low exposures.[11] Inclusion of potential sources of uncertainty in the model allows for principles of decision analysis to be used to determine which sources have the greatest effect on the relationship between costs and benefits of additional data collection.

Results and Discussion

VOI methods promise to better inform the decision making process with regard to the value of additional research for chemicals. However, to ensure the success and usefulness of VOI analyses it is critical that these analyses be performed early in the health and regulatory debate. This generally means conducting analyses about a chemical either early in the regulatory decision process, or that the regulatory process must include sufficient flexibility to allow mid-course corrections if such are needed. In the current regulatory climate, where even suspicion that a chemical could be a carcinogen leads to regulatory implications, it is often not practical to expect major mid-course corrections.

Key strengths of VOI analysis include the ability to frame the problem and allow stakeholders to express their concerns; this will stimulate explicit analysis of the effects of social values, estimates of uncertainty and projected costs and efficiencies of control options on decisions. Also, VOI analyses facilitate the important public policy development process of open examination of the tradeoffs involved in deciding whether to perform additional research. However, to date there has been limited use of VOI methods in real world environmental health research priority setting.[3,4] This lack of a body of examples of real world applications likely reflects the complexity in modeling and solving VOI-type questions and the difficulties in valuing outcomes and characterizing the uncertain and variable model inputs.[3,4] But, advancements in analysis methods have improved the ability to perform complex actual applications. Another difficult task is valuation of health and other non-monetary outcomes; however, ongoing health outcome valuation research may help lessen this problem. Finally, in some instances additional research may actually increase the perceived uncertainty if the new research reveals more complexity and uncertainty than previously recognized. However, this information is valuable if the goal is to provide decision-makers with a complete characterization of the available scientific knowledge for regulatory decision making.[1]

References

1. National Research Council (1996) Understanding Risk: Informing Decisions in a Democratic Society. National Academy Press.
2. Office of Management and Budget (2003) Federal Register, 68,5492.
3. Yokota F, Thompson KM (2003) Risk Analysis (*In Press*).
4. Yokota F, Thompson KM (2003) Medical Decision Making (submitted).
5. Lave LB, Omenn GS (1986) Nature 324, 29.
6. Lave LB, Ennever FK, Rosenkranz HS, Omenn GS (1988) Nature 336, 631.
7. Lave LB, Omenn GS (1988) J Am Coll Toxicol. 7, 565.
8. Taylor AC, Evans JS, McKone TE (1993) Risk Analysis 13, 403.
9. Thompson KM, Evans JS (1997) Risk Analysis 17, 253.
10. Brand KP, Small MJ (1995) Risk Analysis 15, 719.
11. U.S. EPA (September 2000) Exposure and Human Health Reassessment of 2,3,7,8-Tetrachlorodibenzo-p-Dioxin (TCDD) and Related Compounds. EPA/600/P-00/001.

Figure 1 General Framework for Dioxin/PBT Value of Information Analysis