

Risk & Remediation

Science and Decisions

Proper application of credible scientific information is critical to making sound public policy decisions.

Public policy decision making is a complex process that involves not only scientific components, but also issues of public perception, societal values, and costs. While such a decision-making process involves multiple iterative elements (see figure), the public is not well served by decisions that run counter to "sound science." General attributes of sound science are well-established and include: publication in scientific journals; peer review through scientific meetings, expert panels, and other venues; and replication of results among multiple investigators.

More specific attributes of sound science have been developed in public health evaluations, where two types of studies are used to establish a relationship between exposure and disease: epidemiological studies and animal studies. In the case of epidemiological studies, the "Hill Criteria" (see related article) provide a framework that can be used to evaluate data and make determinations about disease causation in human populations. In the case of animal toxicological studies, conclusions about disease potential due to

Although perception has always and will continue to play a role in the decision-making process, it is critical that decisions be firmly grounded in good science.

chemical exposure in humans are confounded by: the role of species-specific responses; exposure level and route in animals as compared to humans; and mode of action, or the biochemical and cellular basis by which toxicity is induced. For some chemicals, responses may occur only at high levels or with non-physiological exposure routes that would not be expected to occur in humans under typical exposure conditions. Even if a toxicity study is properly conducted and interpreted, a sound decision can still fall prey to policy considerations that do not have a basis in science. For example, U.S. EPA scientists recently concluded that chloroform-induced liver carcinogenicity occurs only when exposures exceed a "threshold" level. Thus, a Maximum Contaminant Level Goal (MCLG) of 300 µg/L for chloroform

continued on pg. 2

I N S I D E

<i>Science and Decisions</i>	1	<i>Role of Biomonitoring in Remedial Decision Making</i>	4
<i>Letter to our Readers</i>	1	<i>What's New at Gradient</i>	5
<i>Epidemiological Tools in Decision Making</i>	3	<i>Guest Editorial: Can Good Science at the EPA be Saved?</i>	6
<i>By The Way</i>	4		

Letter to our Readers

January 2000

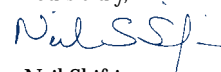
Dear Colleague,

With this issue of *Trends*, we usher in a new century and explore the role of science in decision making, particularly decisions concerning public health. Public policy decision making is a complex process that involves not only scientific components, but also issues of public perception, societal values, and costs. The public is not well served by decisions that ignore good science or that use scientific information improperly. In this issue, we examine the use and misuse of data from epidemiological studies and biomonitoring studies, and provide guidance to facilitate the appropriate use of such data to inform public health-related decisions.

Contributors to this issue include Dr. Barbara Beck, Gradient Principal and nationally recognized expert in toxicology and health risk assessment. Assisting her are Ms. Leslie Beyer, Senior Environmental Health Scientist and specialist in the toxicology of environmental contaminants, and Dr. Lorenz Rhomberg, Principal Scientist and expert in quantitative risk assessment, including pharmacokinetic modeling and probabilistic methods. We are pleased to welcome to this issue Mr. Chuck Elkins, former Director of the Office of Toxic Substances at the U.S. EPA and now President of Chuck Elkins & Associates. We thank him for his thought-provoking editorial on the marginalization of science in decision making at the EPA.

As we enter the 21st century, we hope this issue of *Trends* will help provide guidance on the proper use of scientific information in decision making.

Yours truly,



Neil Shifrin
President

Trends in Risk & Remediation is a quarterly publication of Gradient Corporation. As a national leader in risk assessment and negotiation of risk-based remediation, Gradient offers this publication free of charge to interested groups and individuals. If you have a colleague who would benefit from this publication - or if you have comments or suggestions - please contact Susan Hew at 617-576-1555 or email us at trends@gradientcorp.com.



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Science and Decisions

continued from pg. 1

would be health-protective. However, EPA policy dictates that the MCLG for carcinogens should be zero, and unfortunately, EPA managers ultimately chose to retain the MCLG of zero for chloroform, effectively discounting sound science.

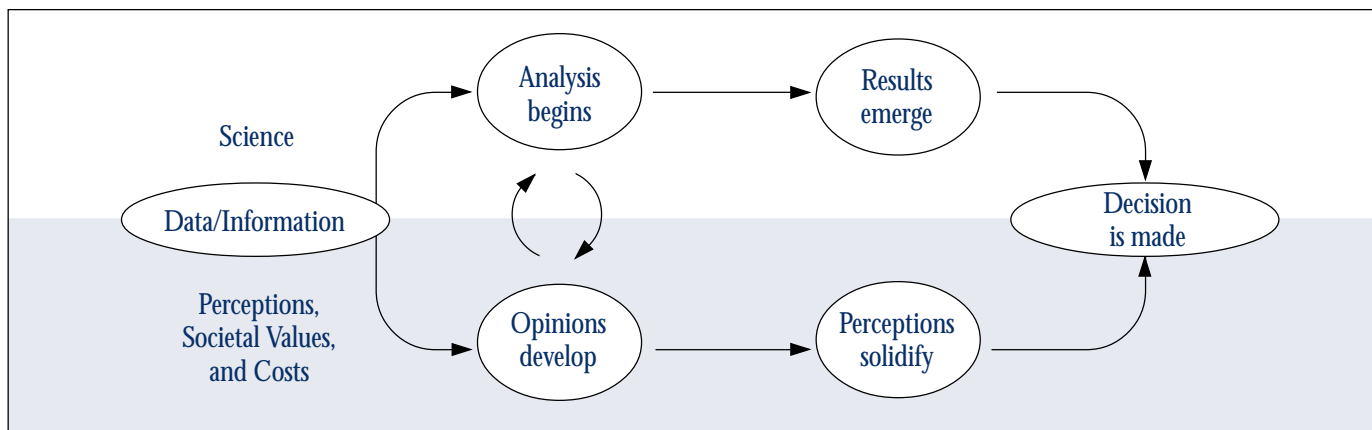
Poor decisions can also occur when scientific information developed for one purpose is misapplied to another purpose. For example, information collected from biological monitoring studies, in which chemicals are measured in biological media, such as blood or urine, when combined with appropriate environmental data can provide useful information about sources of chemicals in a community. However, because of individual variability and other factors, biological monitoring information can be difficult and sometimes impossible to interpret with respect to source identification or magnitude for an individual (see related article). Thus, environmental lead/blood lead studies performed at Superfund sites can provide useful information about the relative contribution of lead in soil to blood lead in the community, but identification of sources of lead for specific individuals (to the extent that it is feasible) usually requires the collection of additional information. As another example, disease incidence data from a state registry

may be useful in providing information about the general health of a community or in formulating hypotheses for further investigations. But, to use this information to infer causes of disease and then to make decisions based upon such inferences would represent an improper scientific use of the registry information.

Perhaps one of the most egregious recent examples of a decision not based on sound science concerns silicone breast implants. Staggering awards have been made in litigation despite the lack of any good scientific evidence from reliable peer-reviewed studies that women's health, particularly as reflected in auto-immune disorders, has been adversely affected by the implants.

Although perception has always and will continue to play a role in the decision-making process, it is critical that decisions be firmly grounded in good science. Decisions that are unduly influenced by perception or that are based on poor science do not necessarily result in satisfactory public health protection, and can set unwieldy precedents that adversely influence public policy for years to come. In contrast, public policy decisions that are grounded in sound science provide a framework for future actions that can optimize public health protection for the greatest number of individuals.

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The interaction between perception and scientific analyses provides the basis for an informed decision.

Epidemiological Tools in Decision Making

continued from pg. 5

more public health data becoming readily available, it is incumbent upon risk assessment professionals to review the available information rigorously, keeping in mind the Hill epidemiological criteria, before using this information as a basis for decision making.

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References:

- Blair, A., P.A. Stewart, P.E. Tolbert, D. Grauman, F.X. Moran, J. Vaught, and J. Rayner. 1990. Cancer and other causes of death among a cohort of dry cleaners. *British Journal of Industrial Medicine* 47:162-168.
- Caldwell, G.G. 1990. Twenty-two years of cancer cluster investigations at the Centers for Disease Control. *American Journal of Epidemiology* 132(Suppl., No 1):S43-S47.
- Ruder, A.M., E.M. Ward and D.P. Brown. 1994. Cancer mortality in female and male dry-cleaning workers. *Journal of Occupational Medicine* 36(8):867-874.

Epidemiological Tools in Decision Making

Well-established evaluation criteria must be applied to epidemiological studies before using the studies as a basis for action.

Epidemiology was pioneered in the study of occupational and infectious diseases as a means of determining their source. More recently, epidemiology has been used to study cancer incidence in communities and to quantify risk from exposures to chemicals in the environment. Using epidemiological studies as a basis for decision making requires establishing causation between the source of the risk and the disease state. Establishing causation in an epidemiological study, or in a group of studies,

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is difficult. It requires that rigorous standards be met. One of the most useful tools for evaluating the credibility of epidemiological findings is the “Hill Criteria” (see box).

Because of the complexity of conducting epidemiological analyses, incidence data (number of new cases) and other epidemiological evidence are often misconstrued. The following are two examples, cancer clusters and perchloroethylene carcinogenicity, where application of the Hill Criteria can be used to evaluate the credibility of study conclusions.

A cancer cluster is defined as a larger-than-expected number of cancer cases in a group of people who might share a common exposure. Historically, cancer clusters have been pivotal in identifying occupational carcinogens (*e.g.*, angiosarcoma in vinyl chloride workers). More recently, the term cancer cluster has been used to refer to excess cancer in specific geographical areas, often towns, where a common environmental exposure (*e.g.*, ingestion of contaminated water), has been identified as the possible cause. Upon discovery of a cancer cluster, public health officials investigate both the incidence/mortality data and possible exposures.

Frequently, clusters do not have statistically significant cancer increases and cannot be attributed to any particular cause. The Centers for Disease Control (CDC) has investigated 108 cancer clusters and no clear cause was found for any of them (Caldwell, 1990). The state of New Jersey also has investigated numerous cancer clusters. In 1990, they investigated the relationship between Hodgkin’s Disease among children in Pitman, NJ and the local Superfund site, and found no connection. The state investigation of groundwater contamination from two other Superfund sites found that the sites did not pose an apparent health risk and that the cancer rate in the surrounding community was below the state average, thereby not providing evidence of an association (Hill criterion one).

These results, which are typical, highlight the importance of conducting thorough investigations of cancer clusters using sound epidemiological principles, as articulated in the Hill Criteria.

The Hill Criteria are also useful when evaluating the carcinogenicity of perchloroethylene. Several epidemiological studies have investigated cancer and noncancer disease incidence and mortality in populations exposed to perchloroethylene — primarily laundry and drycleaning workers.

continued on pg. 5

THE HILL CRITERIA

1. **Strength of the Association** — is there a strong association as measured by the risk ratio?
2. **Specificity of the Association** — is the agent associated only with a specific disease outcome?
3. **Temporality** — does the exposure precede the event?
4. **Dose-Response** — is there a gradient of increasing risk with increasing duration or intensity of exposure?
5. **Biological Plausibility** — does the observation fit with what we know about the biology of disease mechanisms and toxicity of chemicals?
6. **Coherence** — does the observation from one study fit with what we know from other branches of science?
7. **Analogy** — is it analogous to other scientific experiences?
8. **Consistency** — are results consistent in repeated studies?
9. **Experimental Effect** — if the exposure is removed, does the disease go away?
10. **Internal Validity** — is each study free of bias and capable of providing a reliable, unbiased result?

* The Hill Criteria (adapted from A.B. Hill, President’s Address, “The Environment and Disease: Association or Causation?,” Proceedings of the Royal Society of Medicine, 1965.)

These ten criteria developed by Austin B. Hill, a medical statistician, are frequently used as guidelines for interpreting an association to see if it’s consistent with a causal explanation.

Role of Biomonitoring in Remedial Decision Making

Biomonitoring studies can be a useful tool to establish or refute exposure to a specific chemical constituent.

In the usual risk analysis for contaminated sites or pollution sources, data on chemicals of concern are provided as concentrations in local air, water, and soil. Exposures and consequent potential health risks to the surrounding population are then projected based on estimates of the amounts of a particular chemical(s) that local residents might be expected to take up

Interpretation of biomonitoring results is clearest when one can link the exposures to the original source of contamination...

from such an environment. Such projections are hypothetical and, for a variety of reasons, may overstate the actual degree of exposure and the health consequences. Thus, it can be valuable

to conduct surveys of the actual exposures and health effects among residents in the surrounding community — that is, to perform a community health evaluation.

One key tool in such community health evaluations is biomonitoring, the analytical measurement of a chemical or its metabolites in the body or in biological materials (See *Trends*, Fall 1998). Samples of blood, urine, expired air, or even fingernail clippings can be analyzed for the presence of chemicals or their metabolites. Finding a chemical in such samples provides good evidence that exposures have occurred, but it does not by itself identify the source (or sources), nor does it establish the timing of such exposures. Because the effects of most past exposures are eventually cleared from the body, biomonitoring often reflects relatively recent exposure. However, biomonitoring of more biologically persistent compounds reflects both current and historical exposures.

Interpretation of biomonitoring results is clearest when one can link the exposures to the original source of contamination, when there are few such sources that could contribute to each person's exposure, and when the effects of timing and duration of exposure relative to the sampling period can be interpreted. When these conditions exist, information can be gleaned not only on the average level of exposure, but also on how exposure varies among people with different exposure characteristics, such as their distance from the source.

Unfortunately, such idyllic conditions rarely exist. Because of variation in lifestyles and sources, results in a given individual are hard to interpret. However, people with particularly high levels (*e.g.*, a child with a blood lead level over 20 µg/dL) can be singled out for attention and perhaps treatment. If biomonitoring finds a general prevalence of elevated levels of a contaminant

in a potentially exposed group (*e.g.*, blood lead levels greater than 10 µg/dL in many children in a neighborhood), precautionary public health interventions can be considered.

Despite these limitations, biological monitoring can allay fears by demonstrating that actual exposures are low. For example, there was concern that U.S. soldiers in the Gulf War and its aftermath were being exposed to high levels of polycyclic aromatic hydrocarbons (PAHs) as a result of the many oil well fires. In fact, however, measurements of DNA-adducts in their blood cells (which vary with PAH exposure) showed lower values while the soldiers were in the Gulf than when they were stationed in Germany (Poirier *et al.*, 1998).

The U.S. EPA has expressed support of biomonitoring, as reflected in its recommendations to use blood lead data to identify site-specific exposure pathways and highly exposed individuals (U.S. EPA, 1998). Because biomonitoring is a direct indication of actual exposure, appropriate biomonitoring data should play a significant role in site characterization and remediation decisions.

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References:

- U.S. EPA, Office of Solid Waste and Emergency Response. 1998. *Clarification to the 1994 Revised Interim Soil Lead Guidance for CERCLA Sites and RCRA Corrective Action Facilities*. OSWER Directive # 9200.4-27; EPA/540/F-98/030; NTIS PB98-963244. August.
- Poirier, M.C., A. Weston, B. Schoket, H. Shamkhani, C.F. Pan, M.A. McDiarmid, B.G. Scott, D.P. Deeter, J.M. Heller, D. Jakobson-Kram, and N. Rothman. 1998. Biomonitoring of United States Army soldiers serving in Kuwait in 1991. *Cancer Epidemiology, Biomarkers & Prevention* 7(6):545-51.

BY THE WAY...

Prof. James Bridges, head of the European Union's Scientific Committee on Toxicity, Eco-Toxicity, and the Environment, recently stated that the emergency ban by the European Commission on the sale of children's plastic toys containing phthalates is not scientifically supported.

Source: *Wall Street Journal*. November 12, 1999.

What's New at Gradient

Gradient Moves to New Office Space

Effective the end of January, Gradient will be located at 238 Main Street, Cambridge, MA 02142. The new email site for *Trends* will be trends@gradientcorp.com.

Recent and Upcoming Presentations

Cambridge, MA. November 16, 1999. Barbara Beck. "Recent trends in childhood blood lead levels: evidence and implications," presented at MIT Center for International Studies, Program on Regulation and the Environment; Federal Environmental Policymaking: Responding to New Evidence.

Rocky Hill, CT. February 3, 2000. A. Dallas Wait. "Environmental forensic chemistry — tools for discerning site liability," presentation at the IT Technology & Information Exchange Breakfast Seminar.

Philadelphia, PA. March 20-23, 2000. Barbara Beck and Mara Seeley. "Variations in cancer classification between European countries and organizations," poster presentation at the Society of Toxicology (SOT) 39th Annual Meeting.

Philadelphia, PA. March 20-23, 2000. Teresa Bowers. "Recent trends in childhood blood lead levels," poster presentation at the SOT 39th Annual Meeting.

Philadelphia, PA. March 20-23, 2000. Lorenz Rhomberg. "Mode of action as a guide to quantitative analytical approaches," presentation at the SOT 39th Annual Meeting, Symposium on Harmonization of Cancer and Noncancer Risk Assessment: Moving Beyond the NRC Red Book.

Philadelphia, PA. March 20-23, 2000. Mara Seeley and Barbara Beck. "European differences in derivations of occupational exposure levels," poster presentation at the SOT 39th Annual Meeting.

Washington, DC. March 28, 2000. Barbara Beck. "Blood lead trends after NHANES III," presentation at the Lead Industries Association 2000 Annual Meeting.

San Francisco, CA. April 26, 2000. Lorenz Rhomberg. "Principles of toxicology," presentation at an American Chemical Society course.

Recent Articles

Brand, K.P., L. Rhomberg, and J.S. Evans. 1999. Setting non-cancer adjustment factors: are ratios of NOAELs informative? *Risk Analysis* 19(2):295-308.

To request copies of articles or presentations, please contact us at trends@gradientcorp.com or telephone Susan Hew at (617) 576-1555.

Epidemiological Tools in Decision Making

continued from pg. 3

In the two studies considered to be the most comprehensive (Blair *et al.*, 1990, and Ruder *et al.*, 1994), findings were inconsistent, thereby not meeting the Hill consistency criterion. For example, Ruder *et al.* found significant excesses of esophageal, bladder, and intestinal cancer in the drycleaning workers studied. However, in the subcohort (subgroup) of workers exposed only to perchloroethylene, the only cancer found in excess was esophageal cancer, which could be related to risk factors other than occupational exposure to drycleaning solvents (*e.g.*, smoking, alcohol use, and socioeconomic status). Blair *et al.* found significant excesses of esophageal cancer, cervical cancer, and emphysema. But for the cervical cancer, there was no association between the level of exposure and mortality. Moreover, the risk of esophageal cancer was

significantly associated with cumulative exposure to drycleaning solvents, but not with level or duration of exposure to perchloroethylene, thereby not meeting the Hill dose-response criterion.

Therefore, these human epidemiological studies do not provide convincing evidence that perchloroethylene causes cancers in human populations. This finding is consistent with the results of the animal bioassays, which indicate that while perchloroethylene exposure is associated with excess cancer in mice and rats, the mechanisms that result in these cancers do not operate in humans, and therefore biological plausibility (Hill criterion five) was not established.

A properly designed and executed epidemiological study can form the basis for regulatory decisions. However, with more and

continued on pg. 2

T R E N D S • I N

Risk & Remediation

Guest Editorial: Can Good Science at the EPA be Saved?

The former Director of the Office of Toxic Substances at the U.S. EPA offers practical guidance on how to preserve the use of sound science.

Former Congressman Jamie Whitten (D-Alabama) often opined that U.S. EPA's Administrator had "more power than a bad man should have or a good man should want." If one accepts the notion that "good science" is needed to hold the EPA's discretion in check in both directions, then there is cause for concern now. There is a growing sentiment both within the EPA and outside that the use of good science at the EPA is in jeopardy. Of course, individuals disagree about the baseline (*i.e.*, "was it ever really good science") or how serious the losses are (*i.e.*, "that's only one example"), but the warning signals are clear.

The recent uproar over Administrator Carol Browner's overruling of EPA scientists on the cancer risk from chloroform was a real wakeup call. There was a lot of scientific disagreement in that case, but most of the protagonists seemed to want

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the decision made on the basis of good science. It is not clear that it was.

It's not too late to reverse the trend. All scientists who are concerned can do their part to ensure that good

science continues to provide the basis for informed decisions. Here are some suggestions:

For scientists inside the EPA,

- Insist on rigorous procedures for science within the EPA.
- Invite input from knowledgeable scientists outside the EPA without regard to who pays their salaries. Good scientific ideas are not dangerous, no matter where they come from.
- "Just say no" to program managers — and even Administrators — who ask you to deviate from good scientific methods in order to favor a particular outcome.

For scientists in the "scientific community,"

- Actively serve on peer review panels and demand scientific rigor no matter how "urgent" or "important" the program. Insist that the EPA respond fairly and in writing to peer review comments.
- Challenge misinterpretations of the underlying science by the EPA's risk managers. Good science shouldn't be confined to the laboratory.

For public interest group scientists,

- Insist on sound science even if an EPA decision maker is willing to cut corners. Good science is "sustainable" while policy-only decisions are not.

For industry scientists,

- Set the right example. Resist the temptation to tell the EPA only half the story on the theory that EPA scientists can figure out the counter-arguments. Instead, demonstrate scientific integrity in your company's interactions with EPA scientists and expect the same in return.
- Become involved in the EPA's science processes across the board, not just when your company's products are threatened. Your credibility and effectiveness will be immeasurably enhanced.
- Form a "science watch" consortium with fellow scientists to call attention to poor scientific practices in the EPA and to provide input to the EPA's agenda for developing better science policies. Currently, no one is watching the EPA's science across the board. EPA scientists who want to lead and do the right thing need your professional support.

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In the next issue:

Consumer Product Risk Assessment

Product Testing Requirements

Measuring and Modeling Home Exposures

Guest Editorial: Product Stewardship

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