Information Systems (IS) in the Management of Occupational and Environmental Risks.

Robin D. Smith,
Micromedex, Inc., Englewood, CO. USA
& Department of Environmental Sciences,
University of Colorado at Denver, Denver, CO. USA.

Recent developments in environmental management in the United States and other parts of the world have produced a shift in the perception of business leaders. Compliance with environmental laws and regulations is no longer the focus of companies. Industry is now considering the impact of environmental practices on the health and profits of companies. In the move to integrate business and environmental issues, a significant number of companies are looking to systems-based environmental management practices. The systems approach prioritizes issues by considering the technical, environmental, engineering and scientific aspects of Environmental Health and Safety (EHS) concerns as well as the business concerns. Management, therefore, shifts from a reactive, compliance-oriented mode of operation to a proactive mode in order to maximize EHS investment returns.

This overall change in approach has been driven by 3 basic changes in the regulatory environment. These are: 1) movement away from end-of-the-pipe solutions, 2) increasing importance of risk management and 3) global standardization. In order to be successful, environmental managment systems (EMS) must integrate two distinct components. The first is EMS itself, including the policies, objectives and procedures necessary for responsible EHS management. The second is/are Information Systems (IS) which are organized, easily accessible data on a wide range of issues, such as regulatory requirements, compliance status, worker exposures and EHS costs to identify only a few. In effect, IS serve as decision support tools for the EMS. Because the IS are an extension of the overall EMS goals, priorities and procedures, integrated development is cost-effective and saves resources.

Evaluation of IS must be approached with both the end-users and overall EMS integration in mind. With the recent rapid advancement of computer systems, the research, evaluation and management of environmental and occupational risks has become both easier and more difficult. The key to locating, interpreting and sharing knowledge is also something of a puzzle for many end-users of scientific, medical and technical information. Examination of the sources of information, applied software niche tools, technology and delivery platforms reveals that there is not a single universal solution. The overriding usefulness of EHS information for EMS is in an integrated strategy that allows ease of access, use and confidence in quality for protection of human health and the environment.

The problem for research scientists, occupational medicine practitioners, environmental health and safety officers and managers (EHS professionals) is access to information that will assist each individual in solving a specific problem or performing some aspect of a job. The types of information needed by each of these specific areas can be broad in nature or highly focused and specific. In the management of environmental health issues, the general types of information needed by end-users can include:

Toxicology
Occupational Medicine
Industrial Hygiene
Epidemiology
Environmental Engineering
Environmental Chemistry
Regulatory & Compliance
Material Safety Data Sheets (MSDS)
Exposure Assessment
Hazard Communication
Risk Management
Cost/Benefit Analysis
Standards & Certification
Risk/ Safety Assessment
Emergency Response

These types of information can be found through searching through an equally diverse set of sources. These sources are discussed below briefly with presentation of both positive and negative features.

Traditionally, print media formed the bulk of available information and included journals, monographs and reference books. While these sources are good for most types of information, the publishing cycles, timelines for acceptance of information and, therefore, currency of content may not be optimal for end users. Also, there is a problem with dissemination of information found in printed information. Many scientific and technical journals are now moving to cycles that are Internet-based and alleviate some of the above issues. There is still the problem of incorporating this type of information into a readily accessible, integrated EMS system.

Online sources, such as Medline and Toxnet, have been developed by large institutions, government agencies or even industry consortiums to address the need for disseminating and using EHS information. These sources can be costly to use on a regular basis and may not specifically address all EHS needs. Some of these sources are being discontinued or not maintained due to cost constraints of the agencies which administer them. Many are, however moving to more efficient platforms such as the Internet. As with many other sources, the online databases provide information that may or may not be the most current available.

The development and wide dispersal of CD-ROM has allowed for a wide diveristy of EHS information and niche: tools to be delivered at a relatively cost effective level. CD-ROM systems can be either individual users or group/internal network based and are, therefore, available to more users in an organization. Storage capacity is becoming an issue with CD-ROM causing many database offering to be contained on multiple disks. Many of the CD-ROM databases are on a quarterly or yearly update cycle and may lag behind developments in the field. The information on a CD-ROM may also be isolated in terms of overall access and integration with more organization-wide systems.

DVD-ROM (digital video or digital versatile disk) may be a partial solution to the issue of storage capacity in that larger amounts of information can be stored on a single disk. DVD-ROM is estimated to replace CD-ROM as the optical storage medium of choice by 2001.

The Internet is one of the most exciting developments in EHS/EMS information sources. Easy access to all types of information is the most attractive feature, as well as communication between professionals worldwide and ease of EMS integration.

Intranet (or internal internet) offers many of the advantages of Internet functionality, but also the internal control of information and security. The operation is similar to Internet navigation and decreases the costs of training by using a widely known approach to navigating databases and searching strategies.

In most cases, in the management of EHS risks, information or developments from one group of an organization (or between organizations) reach other groups only a small percentage of the time or in an untimely fashion. That is to say, the group conducting research & development is not able to access information about regulatory information that may directly impact them. In a similar fashion, management of a manufacturing company cannot trace the costs of occupational disease to the costs of doing business or to penalties for regulatory compliance. It is critical for all of these groups, to effectively manage and reduce impacts to human health and the environment, to share quality information among these disparate groups.

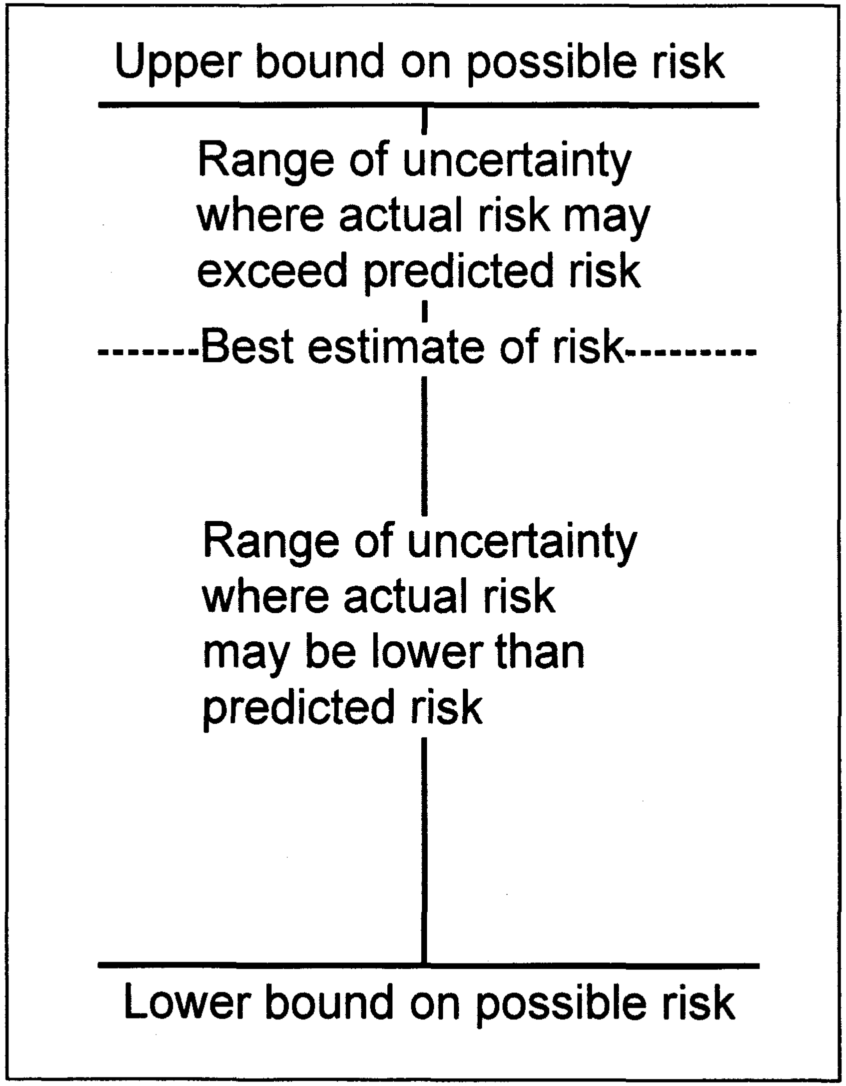
This is why obtaining information is no longer the primary goal of EHS professionals, it is the management of knowledge that is truly the goal. Integration of information from all parts of the organization, from research & development to senior management, under an EMS is a very effective method for providing efficient, high quality, cost-effective protection of human health and the environment.

UNCERTAINTY

"The dominant analytic difficulty (in risk assessment) is pervasive uncertainty…there is often great uncertainty in the estimates of the types, probability, and magnitude of health effects associated with a chemical agent, (and) of the economic effects of a proposed regulatory action…"

(*Risk Assessment in the Federal Government: Managing the Process, National Academy Press*, Washington, D.C., 1983, p.11).

UNCERTAINTY



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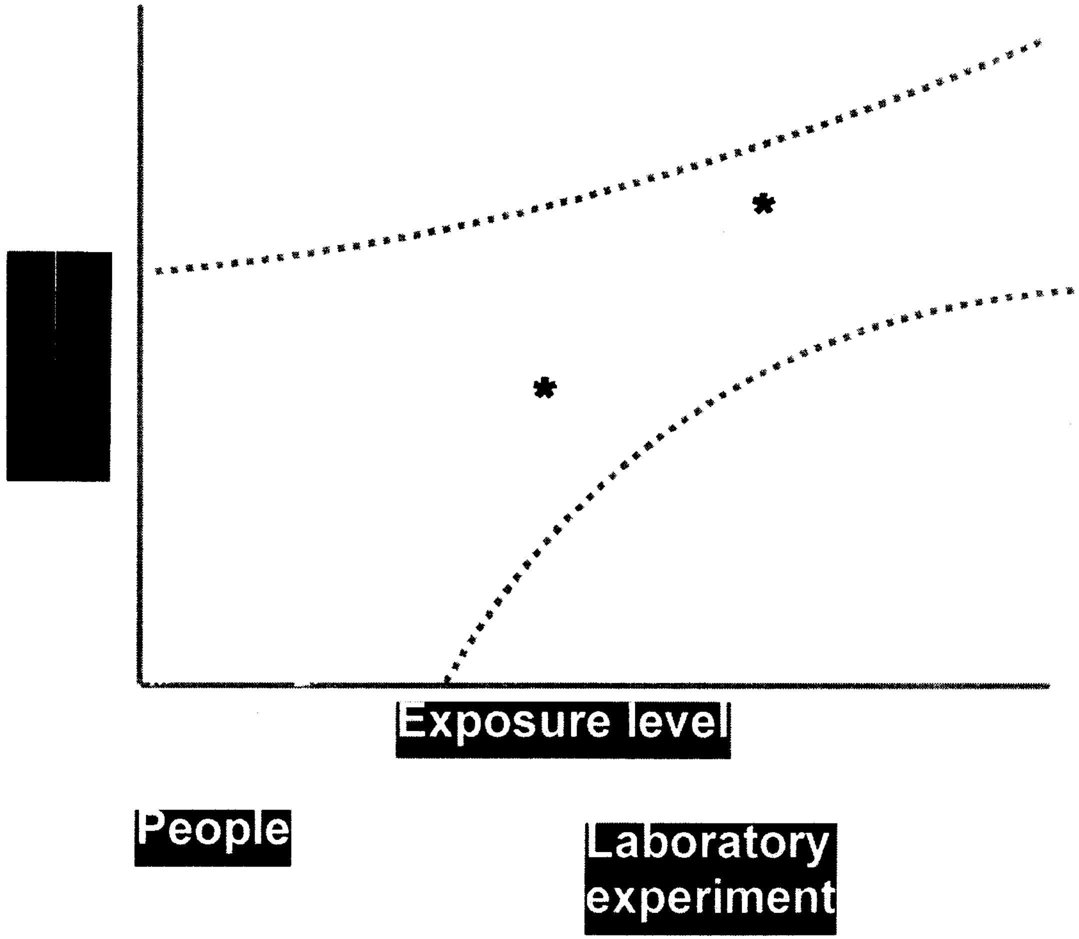
EXPOSURE-RESPONSE CHARACTERIZATION



DEFAULT ASSUMPTIONS

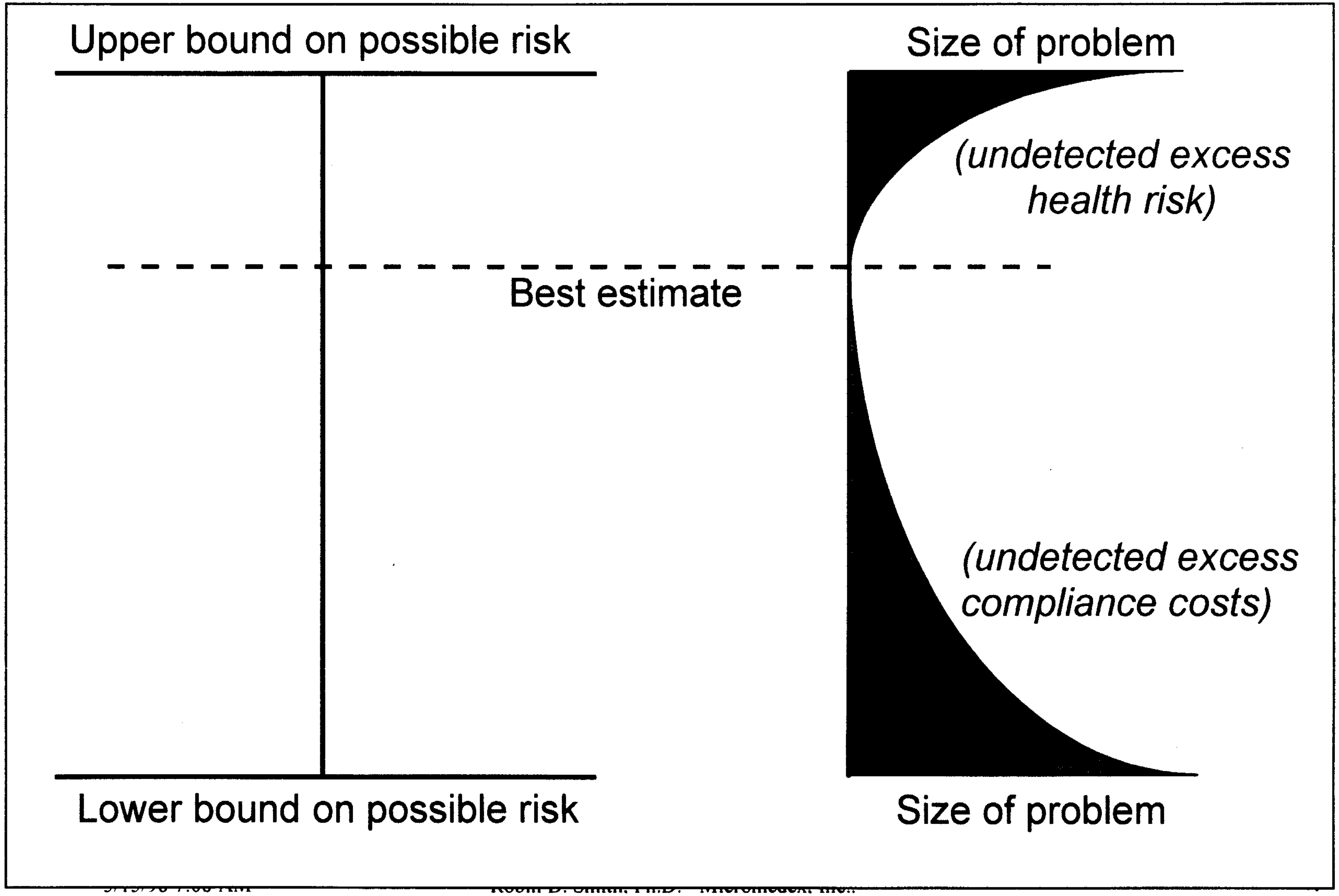
- Conservative assumptions used in the absence of data
  - laboratory animals are surrogates for humans
  - carcinogens
    - carcinogen dose-response is linear at low doses
      - LMS model describes dose-response curve
    - equivalent doses vary among species by $BW^{0.75}$
  - noncarcinogens
    - threshold dose-response
    - uncertainty factors of 10
      - between species
      - within a population
      - LOAEL rather than NOAEL
      - less than lifetime exposure
      - children

U.S. EPA CANCER RISK ASSESSMENT FOR CHLOROFORM DRIVEN BY DEFAULT ASSUMPTIONS

- **mouse and rat bioassays**
- **human equivalent dose calculation**
  - $bw^{2/3}$
- **linearized multistage model for low dose extrapolation**
- **data used**
  - exposure levels
  - animals/level
  - animals with tumor at each exposure level
- **uncertainty**

IF DEFAULTS PROTECT THE PUBLIC HEALTH IS THERE A PROBLEM?

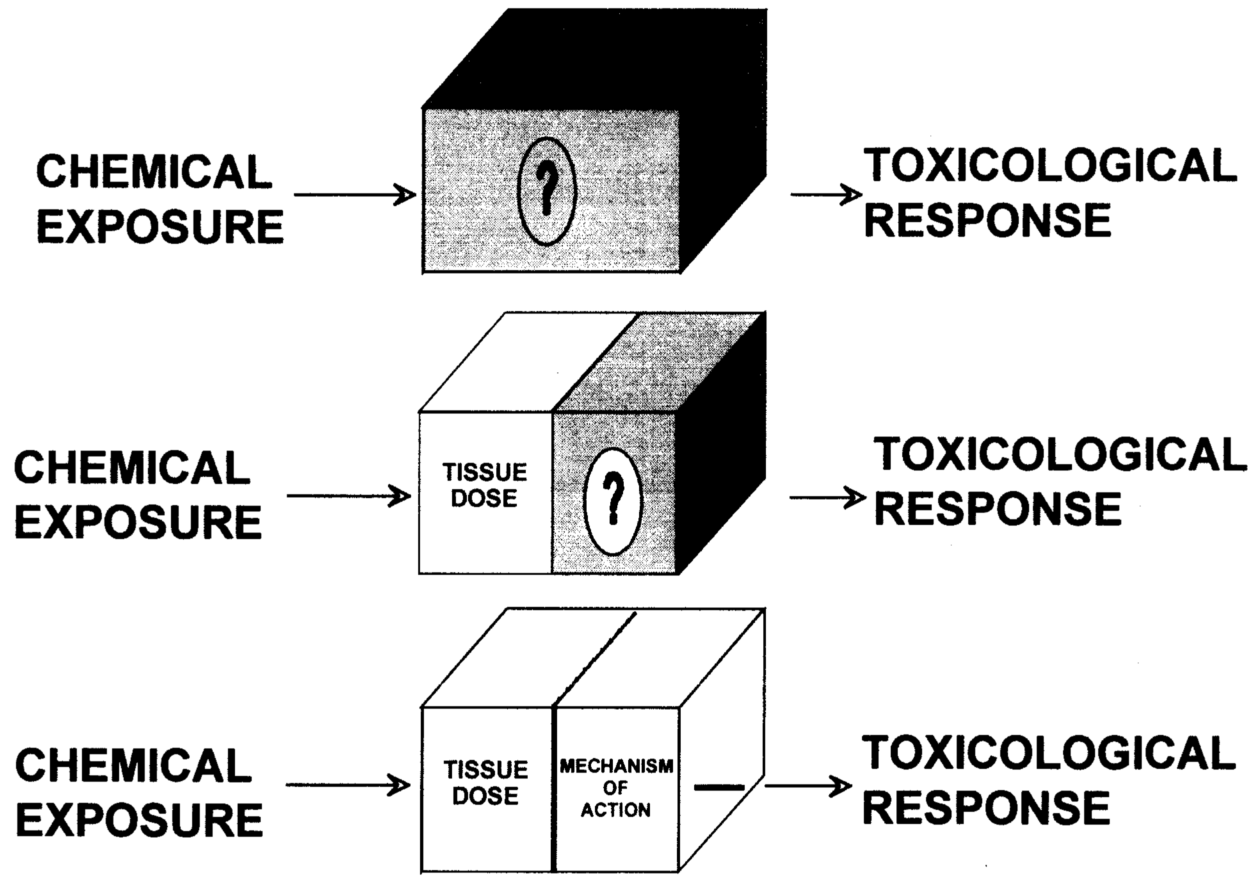
HOW DOES UNCERTAINTY AFFECT POTENTIAL HEALTH RISKS AND COSTS?



WHAT ARE THE SOURCES OF UNCERTAINTY?

- **lack of knowledge**
  - **exposure**
  - ***shape of dose-response curve***

WHAT DETERMINES THE SHAPE OF THE EXPOSURE-RESPONSE CURVE?



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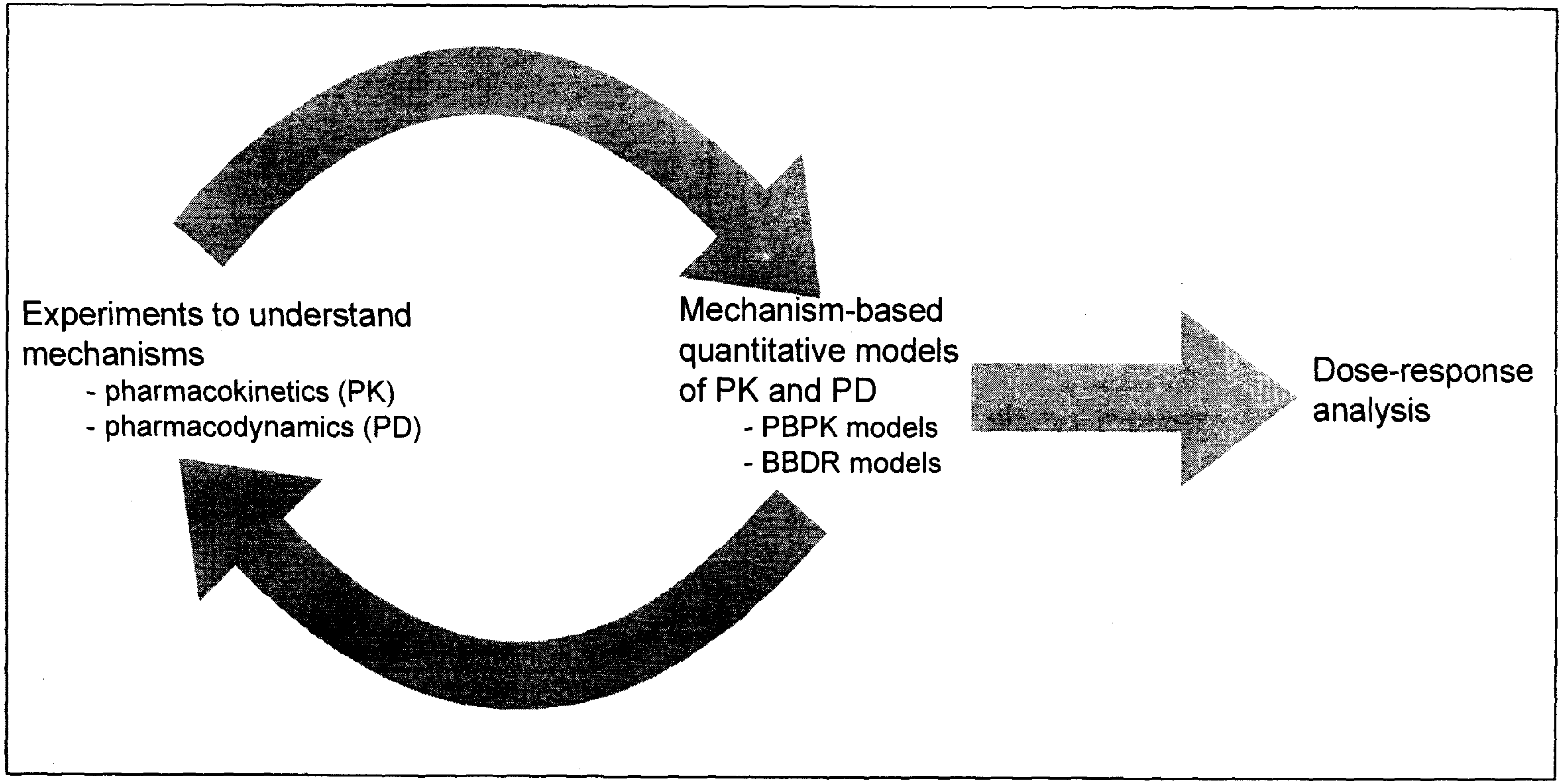
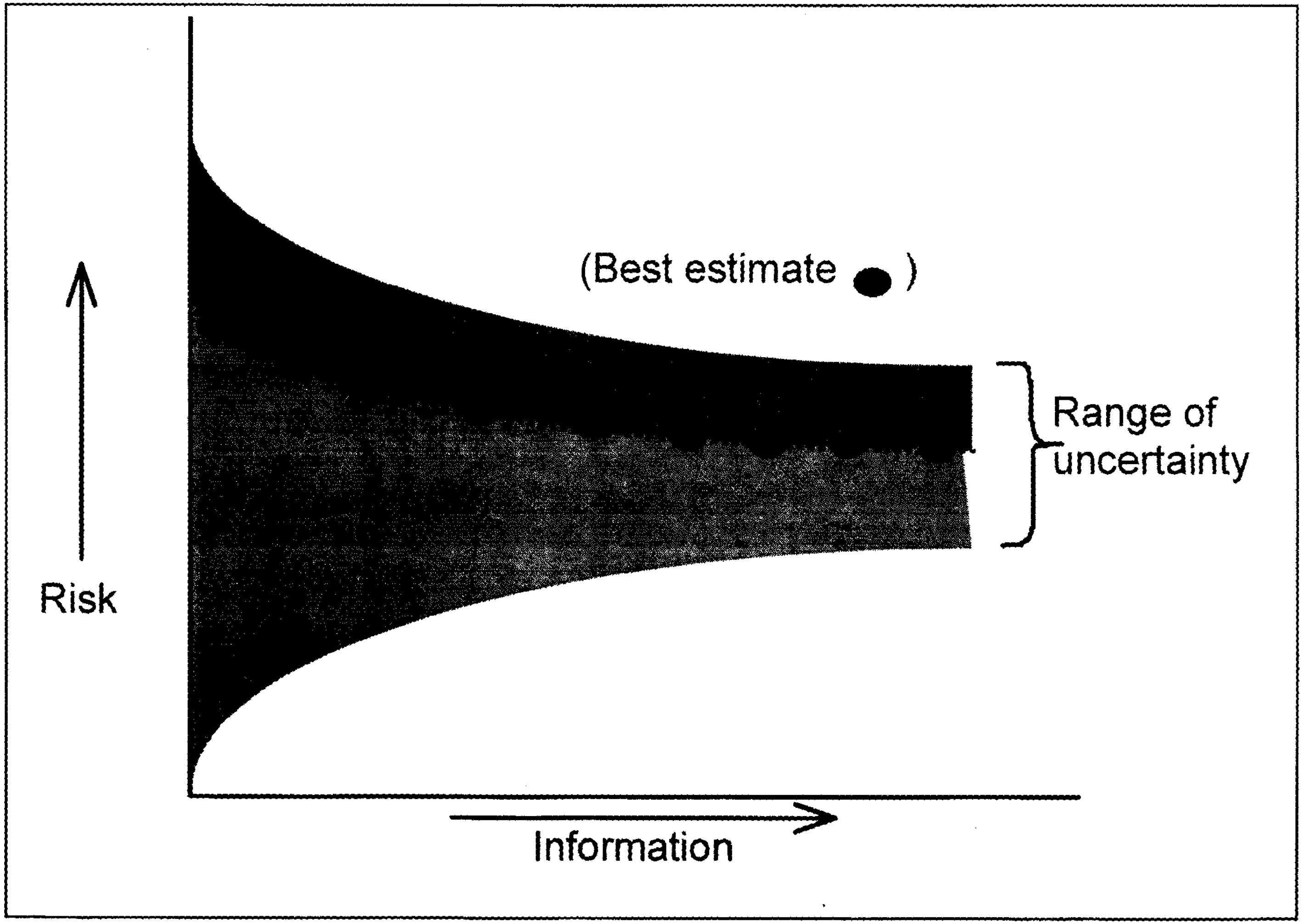
REDUCING UNCERTAINTY IN DOSE-RESPONSE ANALYSIS (I)



REDUCING UNCERTAINTY IN DOSE-RESPONSE ANALYSIS (II)

- **use mechanism-based quantitative models for dose-response analysis in place of default approach**
  - **not necessarily all-or-none**
    - ***e.g.,* replace interspecies UF but not sensitive subpopulations**

DOSE-RESPONSE MODELS INCORPORATING PK AND PD REDUCE UNCERTAINTY



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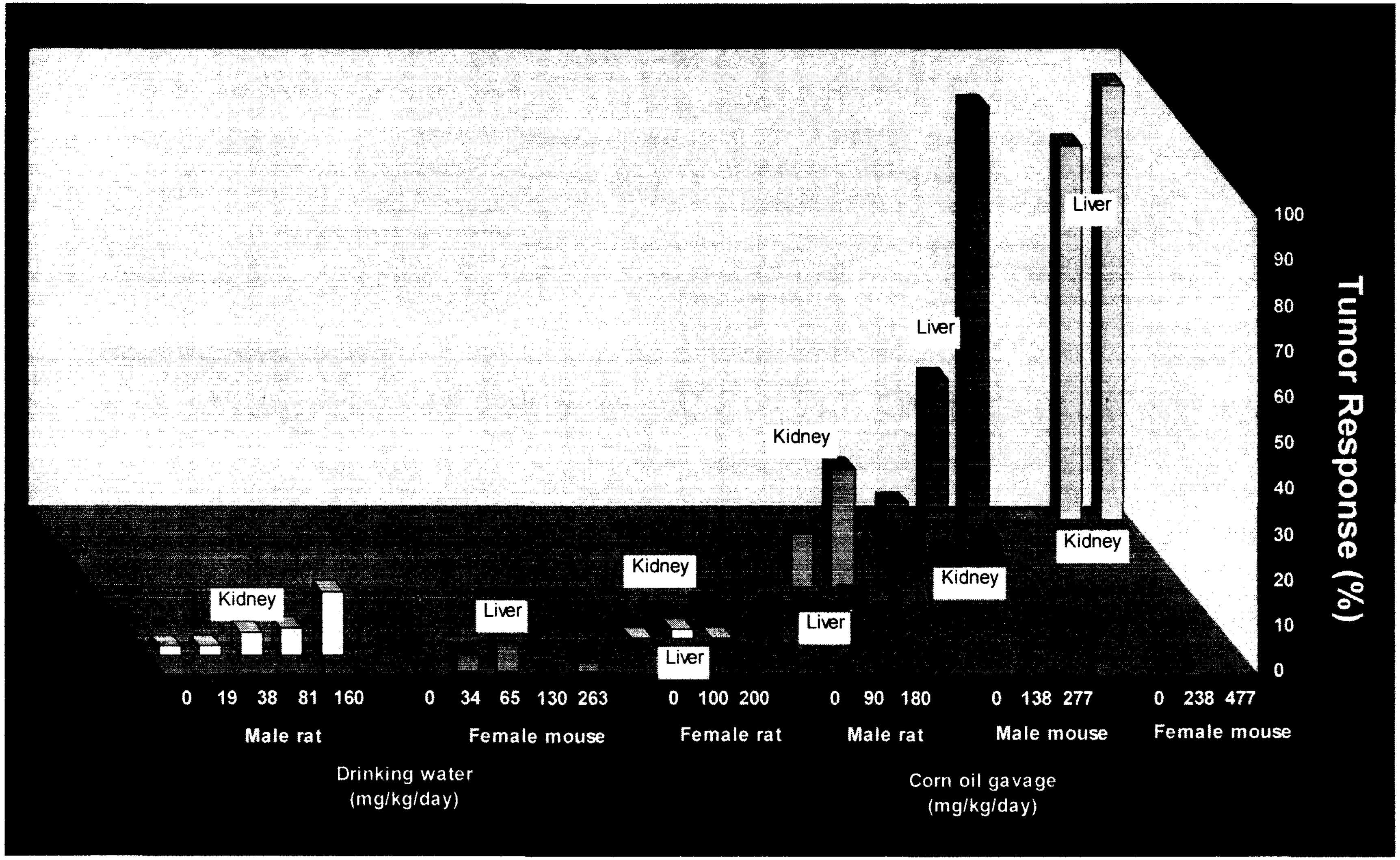
WHAT DO YOU GET FROM MECHANISM-BASED RISK ASSESSMENT?

- **reduced uncertainty**
  - **minimize chance that risk is significantly over- or under-predicted**
- ***probably* a prediction of less risk**
  - **due to conservative defaults**

- **CHLOROFORM**

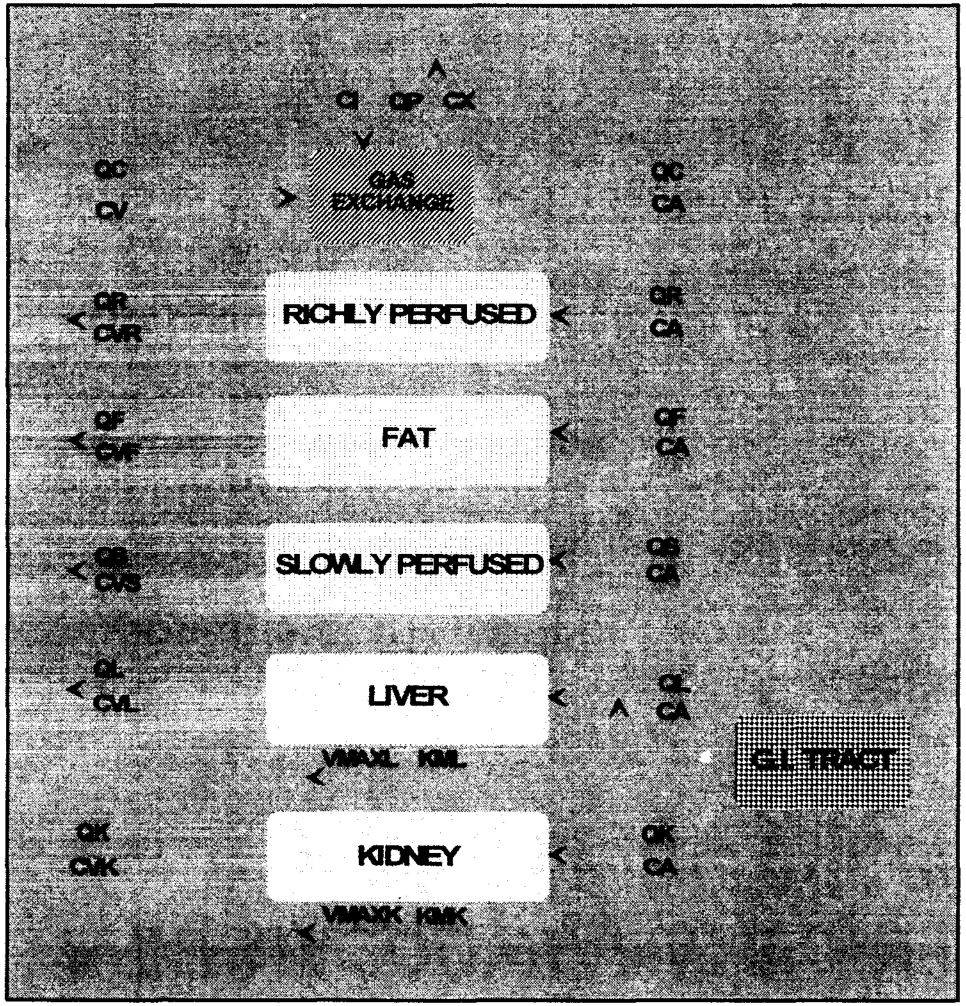
CHLOROFORM CARCINOGENICITY



CHLOROFORM: MODE OF ACTION

- **exposure-response curve for cytotoxicity predicts the curve for carcinogenicity**

PBPK MODEL (LINKAGE OF EXPOSURE WITH TISSUE DOSE)



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PHARMACODYNAMIC MODEL

(LINKAGE OF TISSUE DOSE WITH TOXIC RESPONSE)

- 3 components of PD model:
  - quantitative description of damage that links chloroform metabolism with cell killing
  - distribution of cellular sensitivity to the damage
  - linkage of cell killing with regenerative replication

COMPARATIVE UNCERTAINTY OF DEFAULT AND MECHANISM-BASED DOSE-RESPONSE MODELING FOR CHLOROFORM

Component	Default model *(1986 Guidelines)*[a]	Mechanism-based model *(1996 Proposed Guidelines)*[b]
Equivalent dose calculation	C X T with duration adjustment **(⇑ uncertainty)**	Target tissue dose from PBPK model based on physiology and mechanistic considerations. **(⇓ uncertainty)**
	$BW^{2/3}$ **(⇑ uncertainty)**	PBPK scale-up based on data, allometric relationships, and physiology. **(⇓ uncertainty)**
Drinking behavior	n/a **(⇑ uncertainty)**	Single bolus vs. sips (rate dependence) **(⇓ uncertainty)**
Cancer model	LMS **(⇑ uncertainty)**	Cell replication response surrogate **(⇓ uncertainty)**

SUMMARY

- Uncertainty and why we want to minimize it.
  - Underpredict risk --> public health threat
  - overpredict risk --> excess expense
- What determines the shape of the dose-response curve?
  - Pharmacokinetics
  - pharmacodynamics
- Chloroform
  - new approach vs. default-based risk assessment
  -