Quantitative Microbial Risk Assessment (QMRA) Workshop

108th American Society for Microbiology General Meeting
2008

Center for Microbial Risk Assessment

CAMRA
Center for Advancing Microbial Risk Assessment

U.S. EPA and DHS Center of Excellence

The CAMRA is an interdisciplinary research center stablished to develop scientific knowledge on the fate and risk of bioterrorist and other high priority infectious agents.

(Michigan State University, Drexel University, University of Michigan, Carnegie Mellon University, Northern Arizona University, University of Arizona and University of California Berkeley)

Homepage: http://www.camra.msu.edu/

Contents

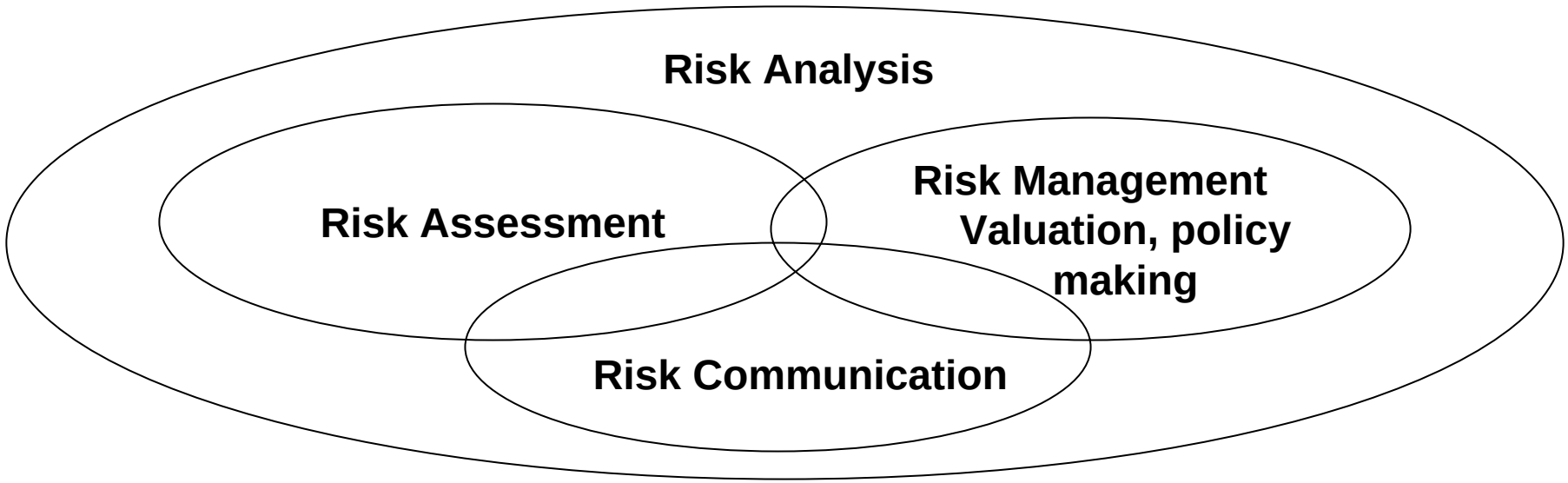
Time	Topics	Presenters
8:30 am	Check-in and Sign-in	
8:40 am	Introductory Comments	Dr. Joan Rose
8:45 am	Topic 1: Risk Frameworks, Data Sets and Integration of Microbiological Fields.	
9:30 am	Exercise 1	
10:00 am	Topic 2: Dose-Response	Dr. Charles N. Haas
11:00 am	Exercise 2	
12:00 pm	Lunch break	
1:00 pm	Topic 3: Exposure Assessment	Dr. Ryan Sinclair
2:00 pm	Topic 4: Risk Characterization & Management	Dr. Patrick Gurian
3:00 pm	Afternoon Break	
3:15 pm	Exercise 3	
4:45 pm	Workshop Summary Completion of Tests, Survey Forms, and Distribution of Certificates	Dr. Joan B. Rose
5:00 pm	Workshop Ends	

Introduction to Risk Analysis and Risk Assessment

Joan B. Rose, Ph.D.

Michigan State University

The National Academy of Sciences “Red Book” Approach



- More recent guidance stresses involving “interested and affected parties” throughout process (NRC 1996)

Definitions Used in Risk Analysis

Risk assessment	The qualitative or quantitative characterization and estimation of potential adverse health effects associated with exposure of individuals or populations to hazards (materials or situations, physical, chemical and or microbial agents.)
Risk management	The process for controlling risks, weighing alternatives, selecting appropriate action, taking into account risk assessment, values, engineering, economics, legal and political issues.
Risk communication	The communication of risks to managers, stakeholders, public officials, and the public, includes public perception and ability to exchange scientific information.

PRECIEVED RISKS

Social, Economic, Legal and Political Context

RISK MANAGEMENT

Target must be defined DALY, 10^{-4}, BAT reduction targets, will include motivational Factors.

MUST UNDERSTAND ASPIRATIONS

RISK CHARACTERIZATION RISK ASSESSMENT

Current status

Disease burdens, Pathogen Monitoring or assessment, Know the source

RISK COMMUNICATION

Choice issues

Equity

Education

- Risk assessment is a method to examine qualitatively or quantitatively the potential for harm from exposure to contaminants or specific hazards.

- Monitoring and data are some of the keys to establishing risks and therefore safety goals.

Quantitative Risk Assessment

- Tool used to estimate adverse health effects associated with specific hazards.
- Elicits a statistical estimate or probability of harm.
- Used for risk management decisions.
- Frame work for science-based assessment.

Risk Communication

- Messages/information.
- Who is providing the information?
- Who are the stakeholders?
- What format (s) are best?
- What education need is tied to the science?
- What are the choices associated with the risk?
- What will various stakeholders do with the information?
- Are the risks distributed equitably?

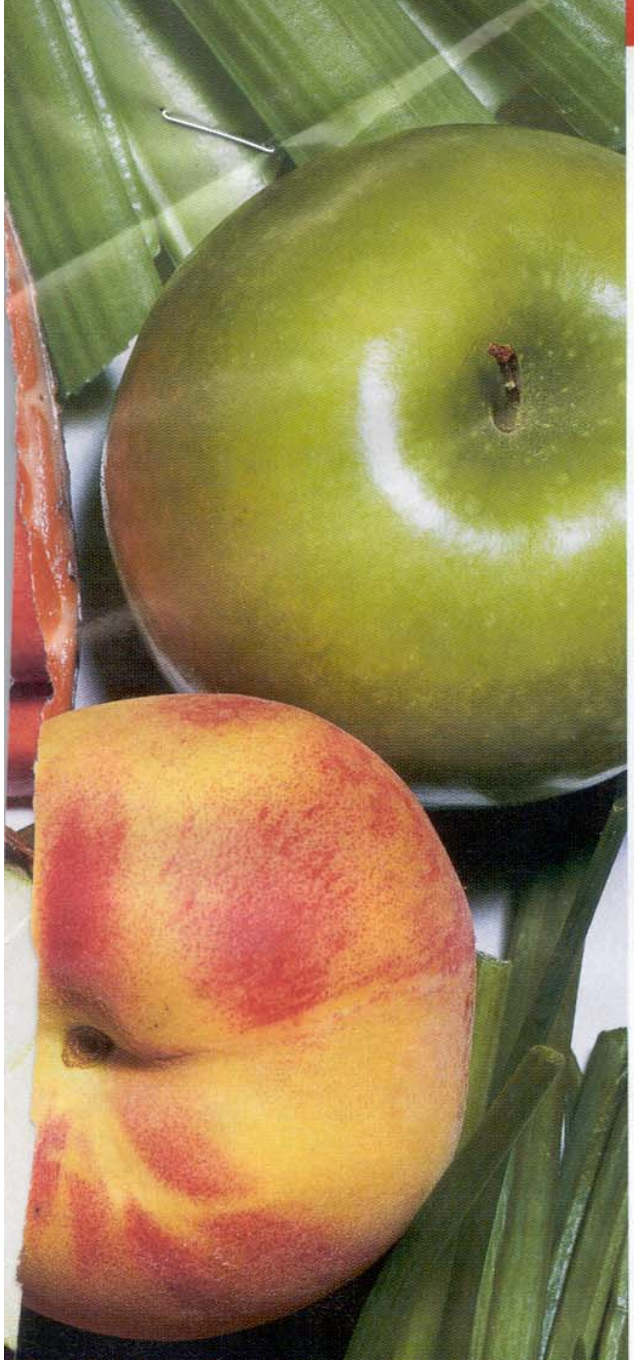
Risk Management

- Approaches for addressing control of the risk.
- Requires assessment and also choices of what people value and how they judge risks.
- Must decide what is the safety goal
- [judgment; ethics].
- Costs, feasibility, implementation important.
- Controls can be based on engineering approaches.
- Controls may be institutional; based on policies to limit exposures.
- Controls may be preventative.

Risk Management Issues

- Acceptable risk (de minimis risk): EPA has suggested that 1/10,000 infection annually is an appropriate level of safety for drinking water.

- Benefit and Cost: Cost for water treatment to reduce cost of disease (health care costs, productivity time lost and suffering)



They hoped it wouldn't happen here, then it did. Now U.S. officials are rewriting rules and assuring consumers that beef won't make them sick. Food safety's uncertain future.

MAD COW: WHAT'S SAFE NOW


MEATS
THE NEW FOOD LABELS ARE A BIT MORE CANDID, BUT DON'T LET THAT SCARE YOU.
PREPARE TO DIE
KIRK '72

Times-Union ★★★ E

ober 23, 1996 131st Year — Number 297 — 4 Sections — 44 P

Water banned, dozens taken ill

Eagle Harbor sickness

Clay County and state officials yesterday confirmed more cases of an

By Beau Halton
Times-Union staff writer

About 2,500 people have be

The Associated Press

Signs and tape warn visitors to stay out of the bacteria-infested water in Huntington Beach

Only bacteria ride waves in 'Surf City, USA'

USA TODAY

New consumer reports won't tell whole story

By Peter Eisler
USA TODAY

Beginning next year, consumers must be informed at least once a year by their water system of any violation of safe drinking water laws.

The congressionally mandated Consumer Confidence Reports will mark the first time that all consumers will learn whether their tap water has had too many contaminants, for example, or whether their water system is doing the right kind of quality testing.

"Thanks to these reports, contamination in (drinking) water will no longer be invisible,"

E. coli Death Toll Rises

September 12. 1999

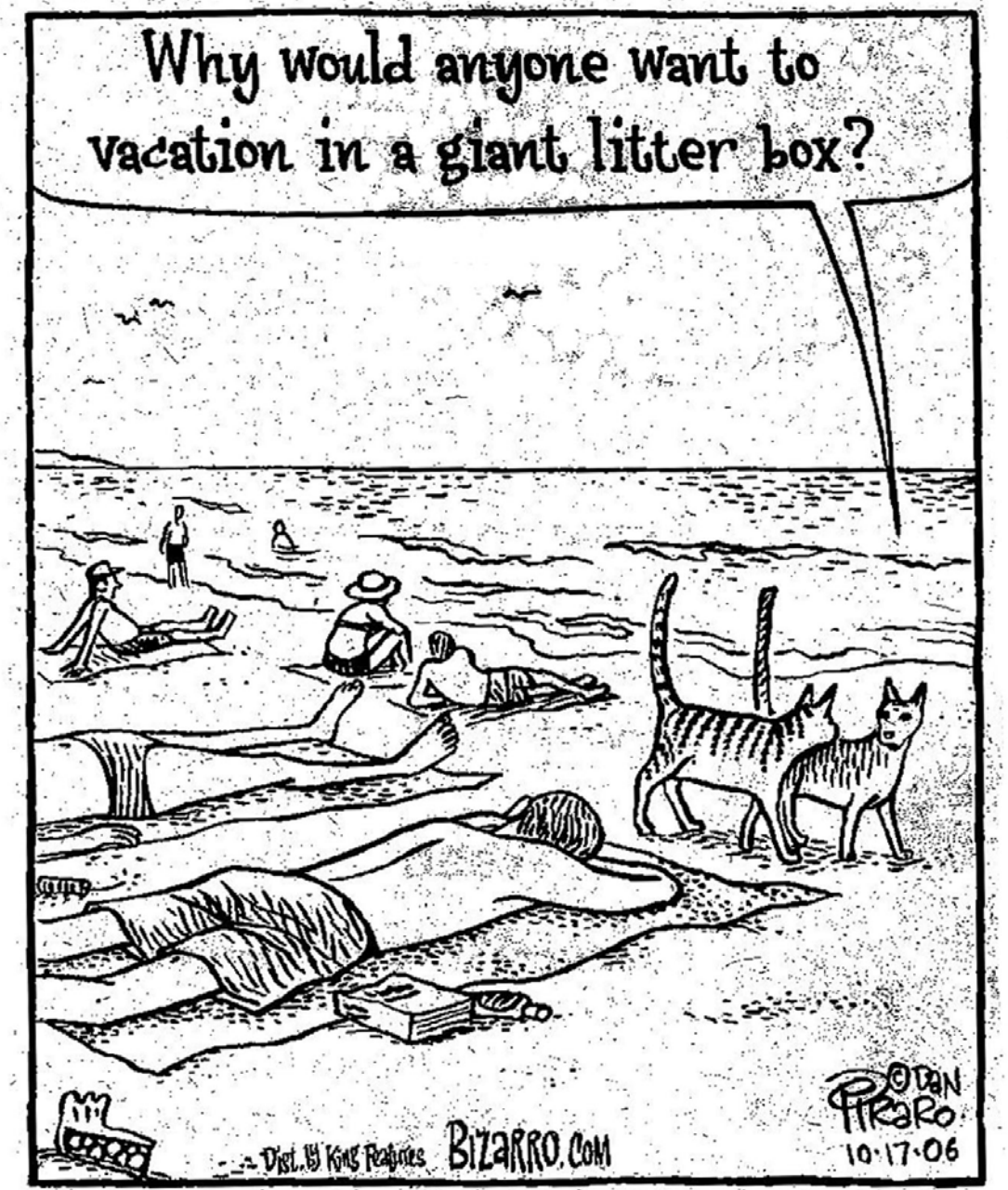
Over 750 People Sickened in N.Y., Two Die

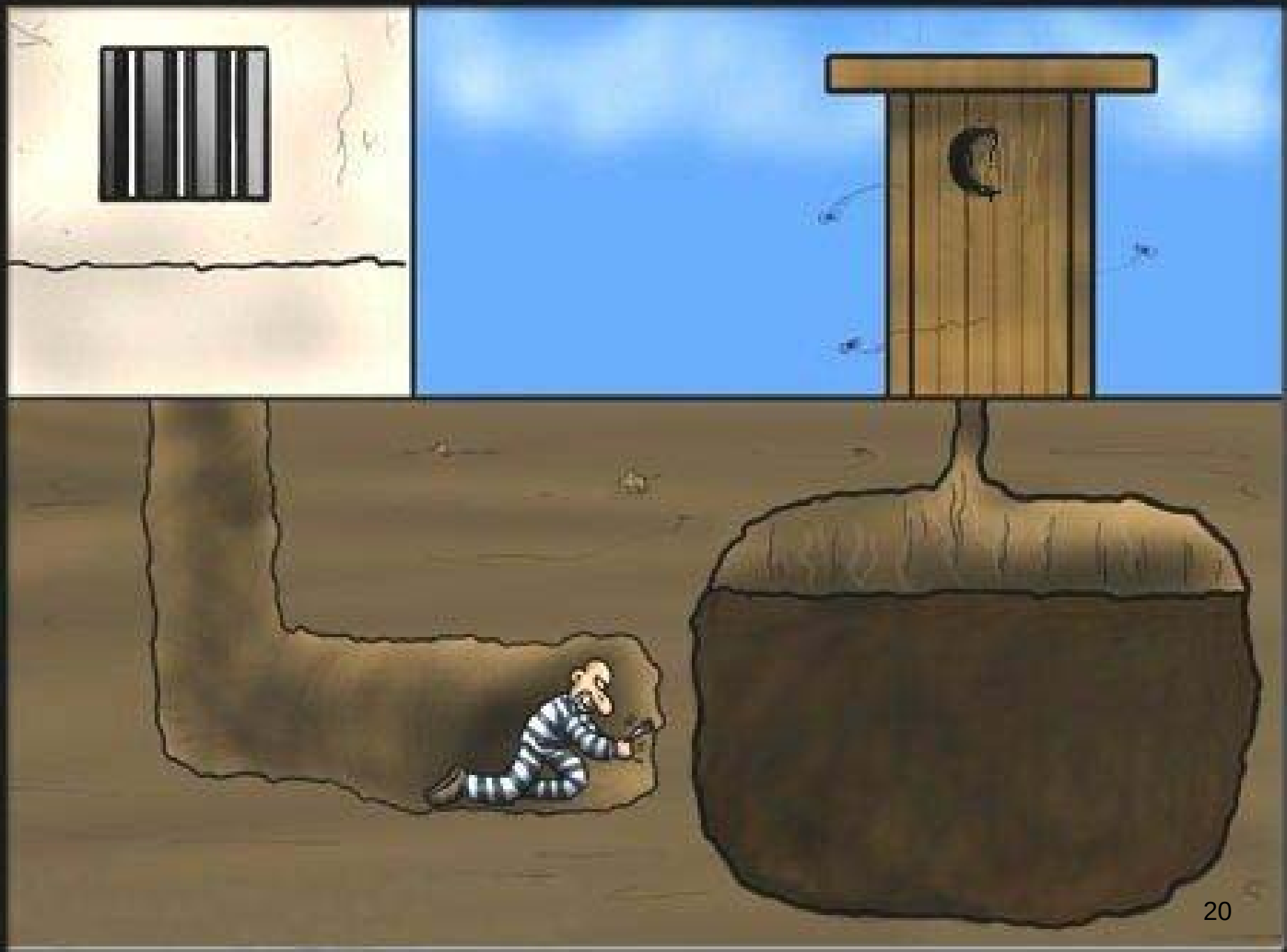
Hog Waste Polluting Water

Environmentalists, Hog Industry Continue to Battle

The hog industry brings in $1.3 billion in North Carolina. But the hogs produce a staggering 37 billion gallons of toxic waste, which festers in thousands of lagoons, or pools. (ABCNEWS)

Bizarro | *Dan Piraro*





- FDA Home Page | CFSAN Home | Search/Subject Index | Q & A | Help
- **September 16, 2006; Updated October 20, 2006**
- **Nationwide *E. Coli* O157:H7 Outbreak: Questions & Answers**

- FDA and the State of California announced October 12 that the test results for certain samples collected during the field investigation of the outbreak of *E. coli* O157:H7 in spinach are positive for *E. coli* O157:H7. Specifically, samples of cattle feces on one of the implicated ranches tested positive based on matching genetic fingerprints for the same strain of *E. coli* O157:H7 that sickened 204 people.

By kgw.com Staff

- **FAIRFAX COUNTY**

Senior Community Hit by Possible Norovirus

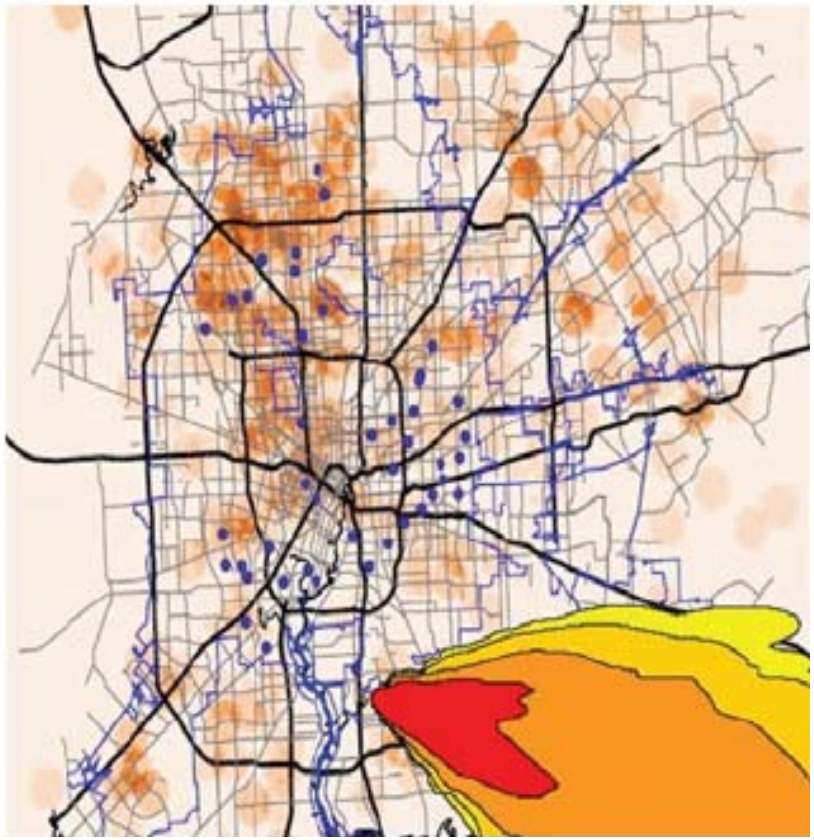
By **Leef Smith**
Washington Post Staff Writer
Saturday, March 10, 2007; Page B02

Washington-area hotel closes for cleaning after norovirus sickens dozens of guests

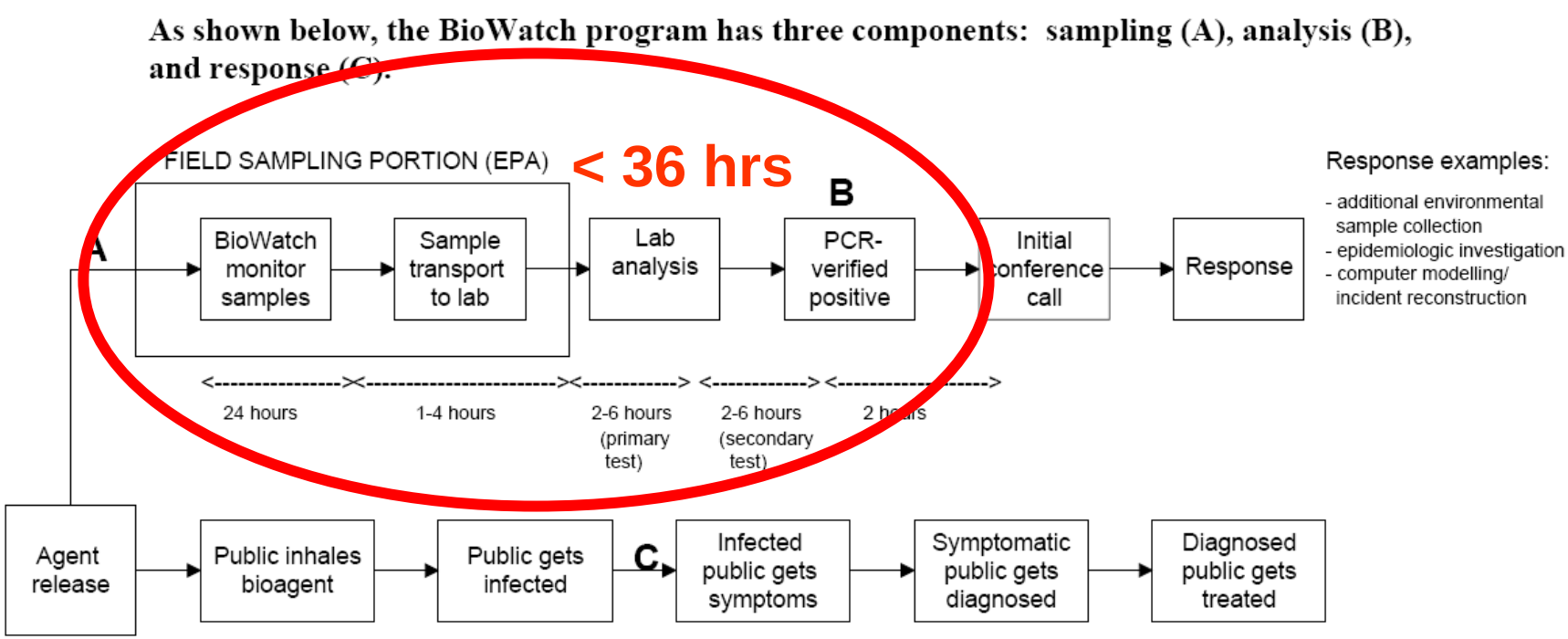
The Associated Press

Published: March 2, 2007 **ARLINGTON, Virginia:** A hotel near a Washington, D.C., airport was closed for cleaning after as many as 150 guests were sickened by the highly contagious norovirus, hotel and county health officials said.

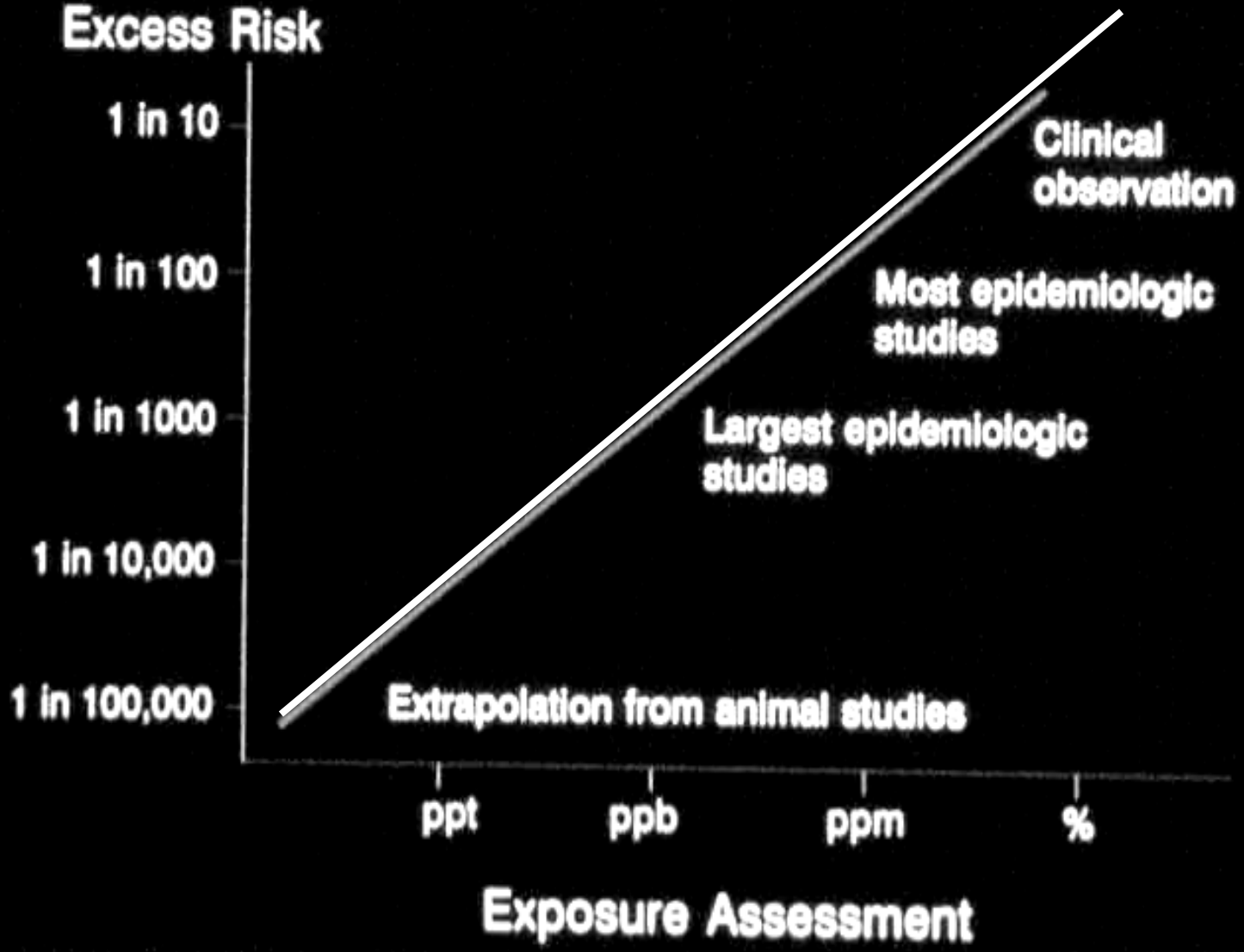
BioWatch Program



BioWatch Program Model



Sensitivity of Epidemiology in Detecting Risks of Regulatory Concern



HEALTH RISK ASSESSMENT

Risks and Water Quality Standards and Development of Management Strategy

U.S. EPA

Water Quality Standards

1. Set permissible levels of contamination (MCL)

2. Establish monitoring program, sample frequency, and sampling sites.

3. Standardize methodology, selectivity, sensitivity, accuracy and precision.

Performance Criteria

1. Specify the performance, treatment efficiency, and desirable end points.

2. Define the types of treatment.

3. Compliance monitoring, verification and reliability.

Early History of Federal Drinking Water standards

- 1914 First standards for *B. Coli*
- 1925 revised the coliform standard based on feasibility
- 1942 required coliform monitoring in the distribution system, added metals.

1962 US Public Health Service Standards

- 19,000 municipal water supplies
- Increased concern for industrial pollution
- Added nitrate, some crude organic parameters
- Binding at the federal level on 700 systems; 50 states accepted

1969 Community Water Supply Study

- 41% of the 969 systems surveyed did not meet standards
- U.S. PHS released report in 1970
- This generated congressional concern

Increasing Concern Leads to A Federal Mandate

- As a result of the 1969 CWSS, bills were introduced in 1970
- 1972 EPA report on Mississippi River, 36 organic compounds
- 1973 GAO reports only 60 of 446 systems surveyed were in compliance
- Trihalomethanes, a chlorination by-product, are discovered.

The Safe Drinking Water Act of 1974--Roles

- Federal = standard setting, research and oversight of states
- States = could adopt primacy for implementation/enforcement.
- Local = must monitor and comply (responsible for capital and O & M cost)

Safe Drinking Water Act 1986

- Congressional concern over the rate of regulation

- Oversight hearings began in 1982.
- Increasing reports of organic contamination
- Concern for uncorrected violations
- Red Book for Risk Assessment and it’s role in policy produced by the NAS.

SDWA 1986 -- Implementation

- EPA was required to regulated 83 contaminants by ’89
- Filtration and disinfection were required
- Monitoring for unregulated contaminants
- Lead ban – Corrosion Control Rule
- Ground Water Protection Programs

Evolution of QMRA

< 1980: Indicator approaches used suggesting that some level of contamination below which one is safe

1980's: Initial Dose Response concepts application in development of EPA Rules

1988 : Dose-response for *Giardia*, viruses in Water.

1990 : Adoption for food safety; WHO food and water consultations; Dynamic model applications; ILSI framework documents

2000's: Air and Home Land Security applications

Reg framework development

Population sensitivities

U.S. EPA Surface Water Treatment Rule 1988

- Identified *Giardia*, Viruses and *Legionella* for control using performance criteria.
- 1/10,000 risk identified in the preamble
- Cryptosporidium identified in the preamble
- QMRA used for *Giardia*
- Required 99.9% reduction of *Giaridia* and 99.99% for Viruses
- BMP filtration (turbidity)
- Disinfection: CT concept required for Viruses, Bacteria and Viruses. (However, DBP influencing this).

Comparative Risks

	Microorganisms in Water	Chemicals in Water
Acceptable risks:	10^{-4} Annual	10^{-6} Life-time
Exposures:	Intermittent acute	Continual chronic
Types of agents:	Hundreds of different pathogens	Less than 50
End points:	Infections, death (YLL), disease (acute +chronic), secondary spread	Death (YLL) Disease
Extrapolations:	Equal susceptibility	Animal dose-response data
Uncertainty:	← High to low dose → ← Use of safety factors → Upper 95% confidence limits	

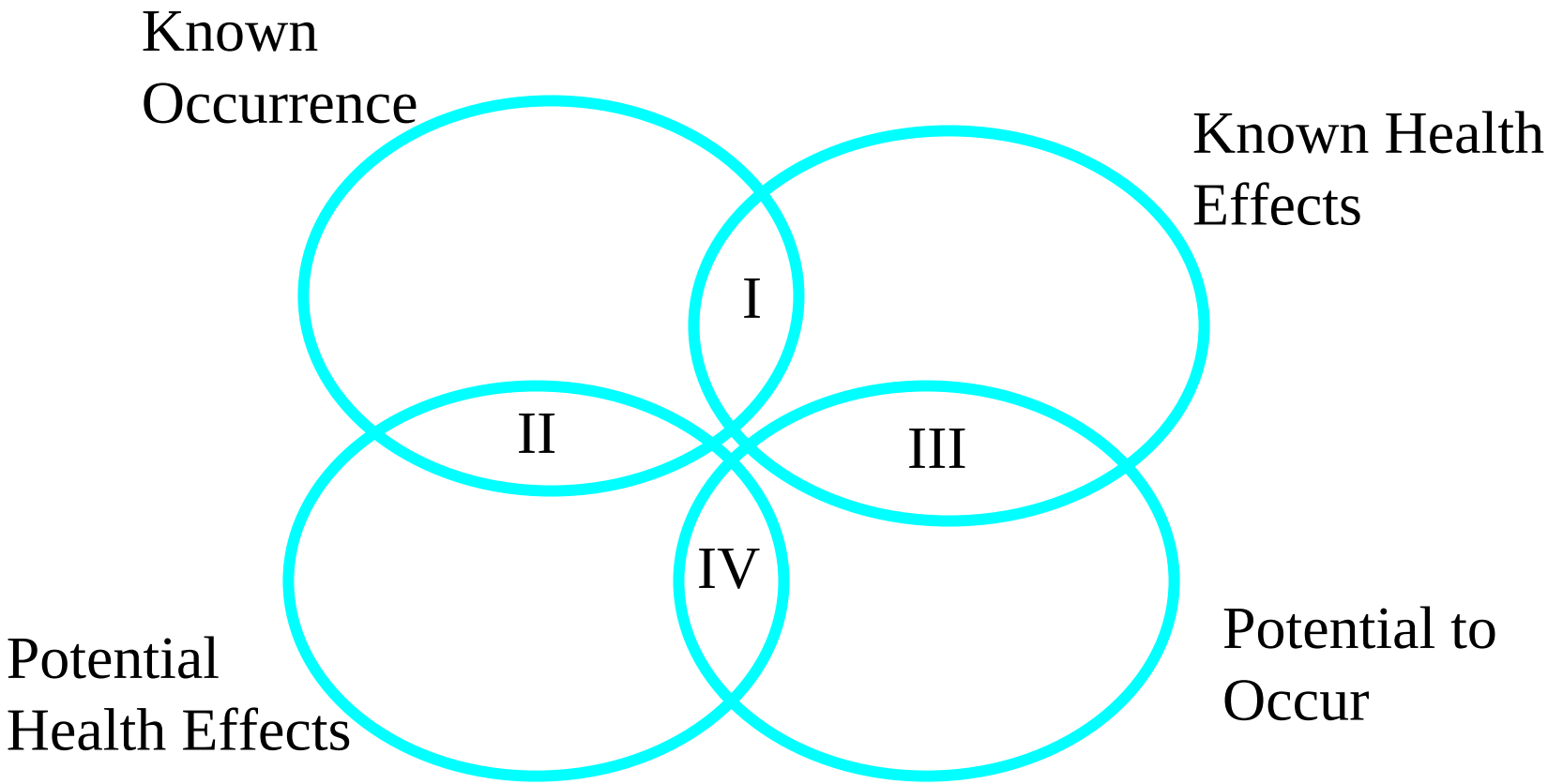
SDWA 1986 -- Concerns

- High rate of non-compliance in small systems
- Funding shortages
- Deficiencies uncorrected
- 1991 outbreak of Cryptosporidiosis in Milwaukee

SDWA 1996 -- Changes and New Programs

- Still required 83 standards
- Eliminated 25 new regulations every 3 years
- Revised process for listing contaminants **Contaminant Candidate List CCL**
- Required cost-benefit analysis
- National occurrence data base
- Created state revolving loan fund
- Required consumer confidence reports

The Universe of Potential Water Contaminants

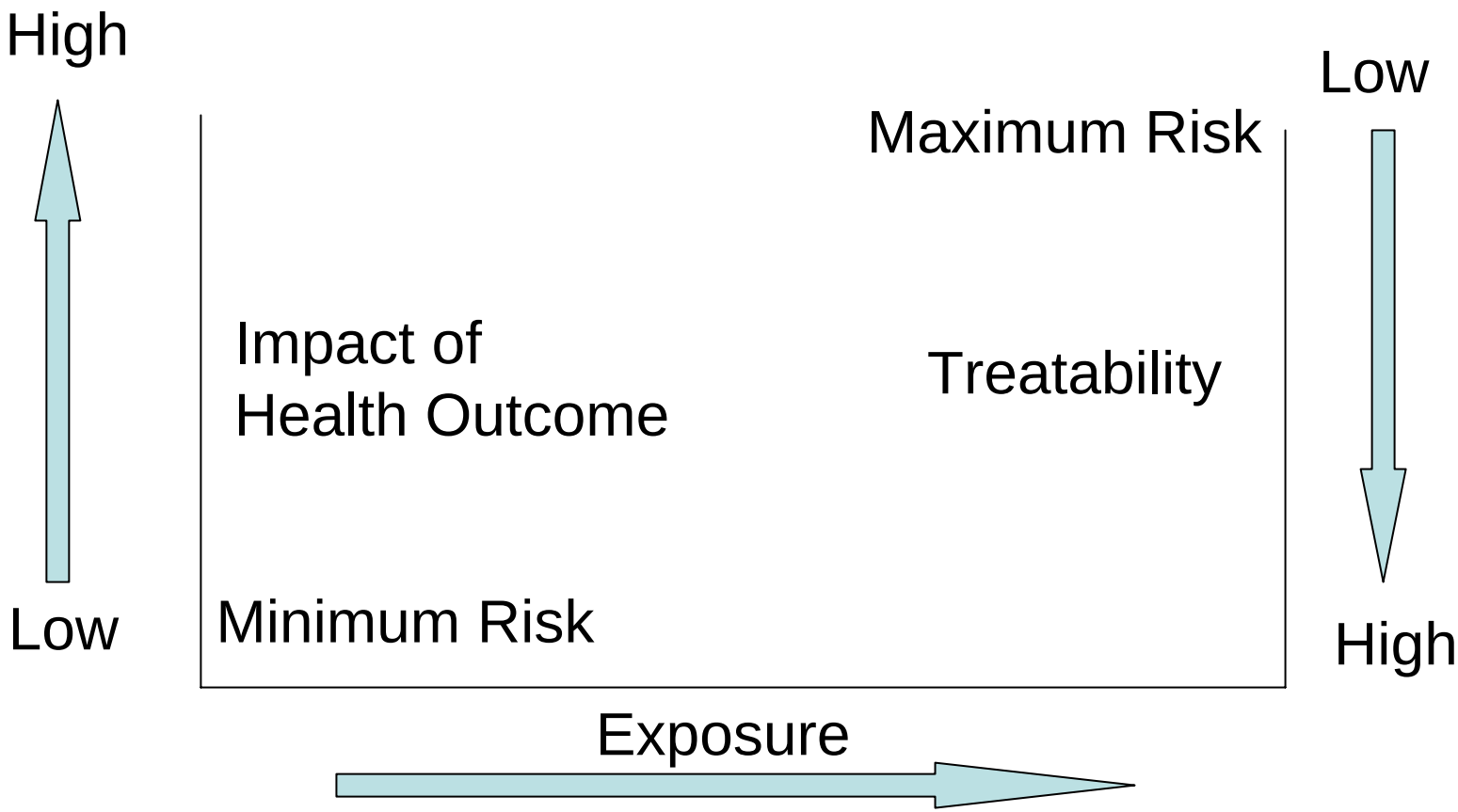


U.S. EPA
Contaminant Candidate List

- **Identify contaminants that have known or potential health effects AND**
- **Have a known or potential for occurrence in water**.

- **Develop health effects information**
- **Develop methods for detection**
- **Develop occurrence data base**
- **Develop rules**
- **HAS NOT ADDRESSED A QMRA FRAMEWORK.**

Risk Matrix


High
Low
Maximum Risk
Low
Impact of
Health Outcome
Treatability
Minimum Risk
High
Exposure

Risk Issues

- Acceptable risk (de minimis risk): EPA has suggested that 1/10,000 infection annually is an appropriate level of safety for drinking water.

- What is acceptable for recreation? (1/500, single swimming event).
- Benefit and Cost: Cost for water treatment to reduce cost of disease (health care costs, productivity time lost and suffering)

Current Regulatory Climate

- Major advances have been made in pollution control in the last 60 years.
- Further gains will require increasingly discriminating assessment and control of risks.
- Costs of the controls increase as high risks are controlled and attempts are made to control marginal risks
- Methods are now available to measure small levels of contaminants in the environment.
- Still need a framework for application of QMRA for microbials within EPA.

National Academy of Sciences Risk Assessment Paradigm

- HAZARD IDENTIFICATION
  - Types of microorganisms and disease end-points
- DOSE-RESPONSE
  - Human feeding studies, clinical studies, less virulent microbes and health adults
- EXPOSURE
  - Monitoring data, indicators and modeling used to address exposure
- RISK CHARACTERIZATION
  - Magnitude of the risk, uncertainty and variability

Four Step Risk Assessment

- Hazard Identification: To describe acute and chronic human health effects; sensitive populations, immunology need to be understood.
- Dose-Response: To characterize the relationship between various doses administered and subsequent health effects; have human data sets but lacking appropriate animal models to increase assessment.
- Exposure Assessment: To determine the size and nature of the population exposed and the route, amount, and duration of exposure. Temporal and spatial exposure with changes in microbial populations a concern.
- Risk Characterization: To integrate the information from exposure, dose response, and health steps to estimate magnitude of health risks. Monte Carlo analysis to give distribution of risks and population/community models needed.

Tools & Data Needs for Microbial Risk Assessment

- Disease surveillance
- Clinical studies
- Epidemiological studies
- Methods for detection of microbials
- Transport models
- Regrowth and die-off models
- Development of occurrence data bases
- Dose-response models

Human Health Effects

- Microbial virulence and pathogenicity factors
- Symptomatic and symptomatic infection
- Severity (duration, medical care & hospitalization)
- Mortality
- Host immune status (role in outcome)
- Susceptible populations

Hazard Reporting

- Sequence of events before an individual infection can be reported
  - Individual is infected
  - Did illness occur?
  - Did the ill person seek medical care?
  - Was the appropriate clinical test (stool, blood) ordered?
  - Did the patient comply?
  - Was the laboratory proficient?
  - Was the clinical test positive?
  - Was the test result reported to the health agency?
  - Was the report timely?
  - What did the health agency do with the report?

Populations at Greatest Risk

Infants

Aged

Pregnancy
(fetal and neonate)

Immunocompromized

Acute and Chronic Outcome Associated with Microbial infections

	Acute disease	**Chronic disease**
Microorganism	**Outcomes**	**Outcomes**
Campylobacter	Diarrhea	Gullain-Barre' syndrome
E. Coli 015H7	Diarrhea	Hemolytic uremic syndrome
Helicobacter	Gastritis	Ulcers and stomach cancer
Salmonella, *Shigella, & Yersinia*	Diarrhea	Reactive arthrititis
Coxsackievirus B	Encephalitis, aseptic Meningitis, diarrhea, respiratory disease	Diabetes
Giardia	Diarrhea	Failure to thrive, lactose intolerance, chronic joint pain
Toxoplama	Newborn syndrome, hearing and visual loss	Mental retardation, dementia, seizures

Dose Response Issues

- Human data sets (healthy volunteers)
- Vaccine strains or less virulent organisms
- Low doses often not evaluated
- Doses measured with mainly cultivation methods for bacteria and viruses (CFU; PFU) for parasites counted under the microscope.
- Response: excretion in the feces, antibody response and sometimes illness.
- Human subjects concerns for filling in data gaps

Exposure Assessment and Risk Characterization

- Exposure and levels of contamination the most important aspect for providing input to risk characterization.
- Need better monitoring data, better transport models.
- Will need new methods, QPCR, for better assessment of non-cultivatible but important viruses and bacteria.
- Essential for Good Risk Management Decisions

Occurrence Analysis for the Exposure Process

- Concentrations
- Frequency
- Spatial and Temporal Variations
- Regrowth and Die-off
- Transport

New Microbiological Methods to Inform Risk Assessment during Exposure Assessment

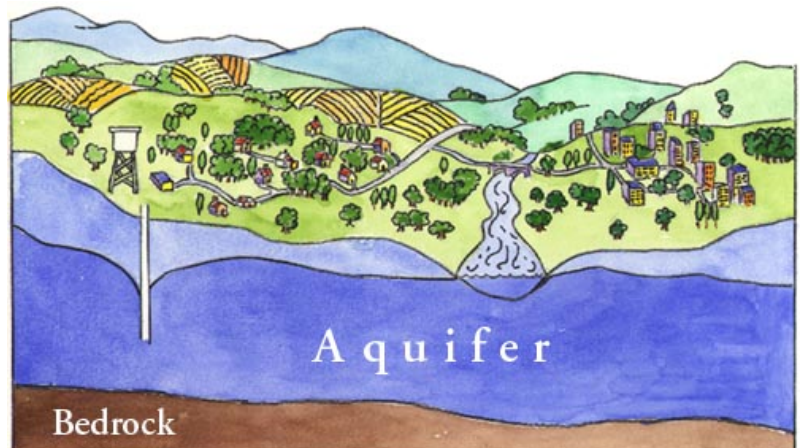
- Alternative Indicators
- Pathogen Monitoring
- Source Tracking

Watershed assessment, Flow, Transport, Integration with Water Quality and Thus Exposure.

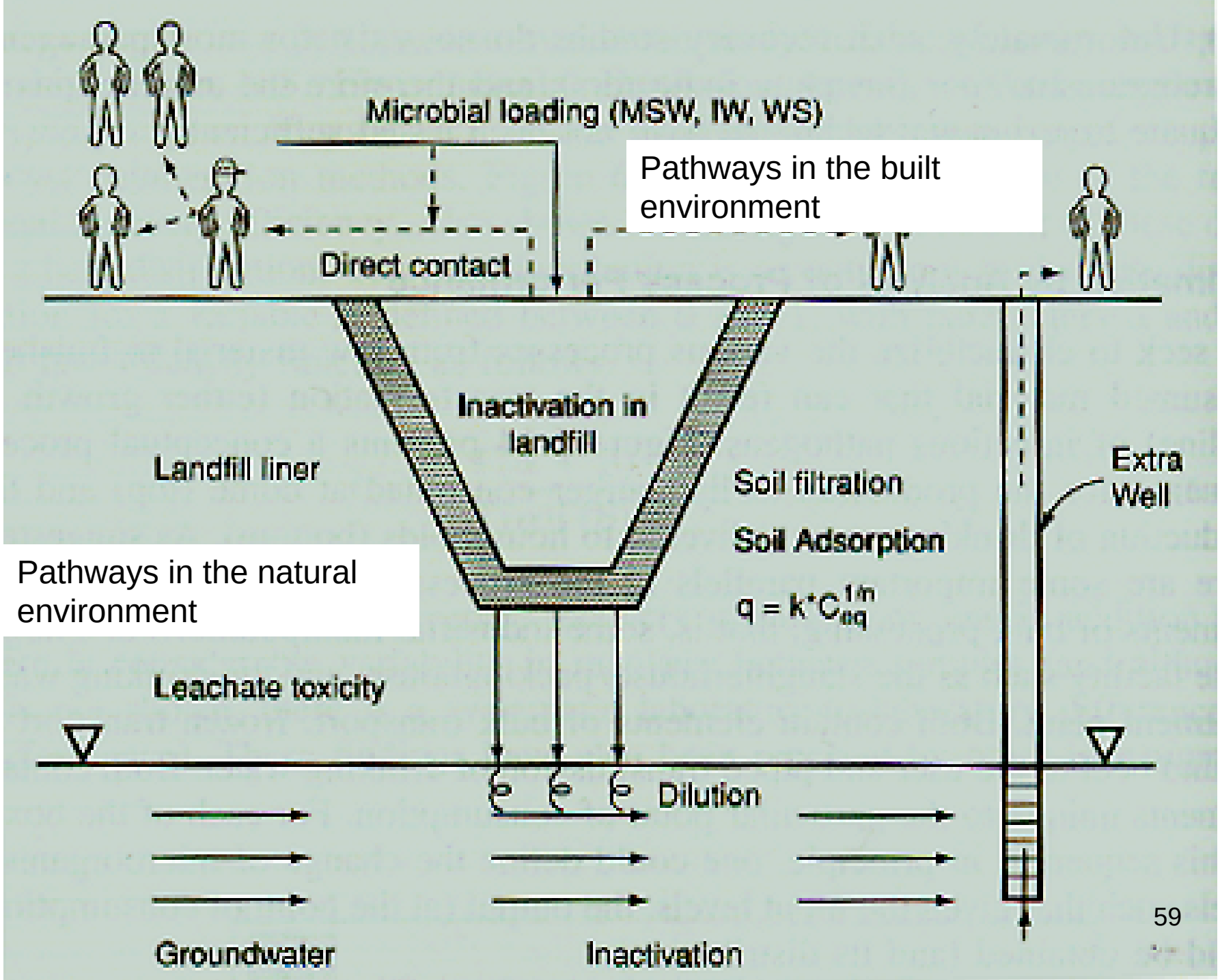
Overland

In-Stream

Near-Shore



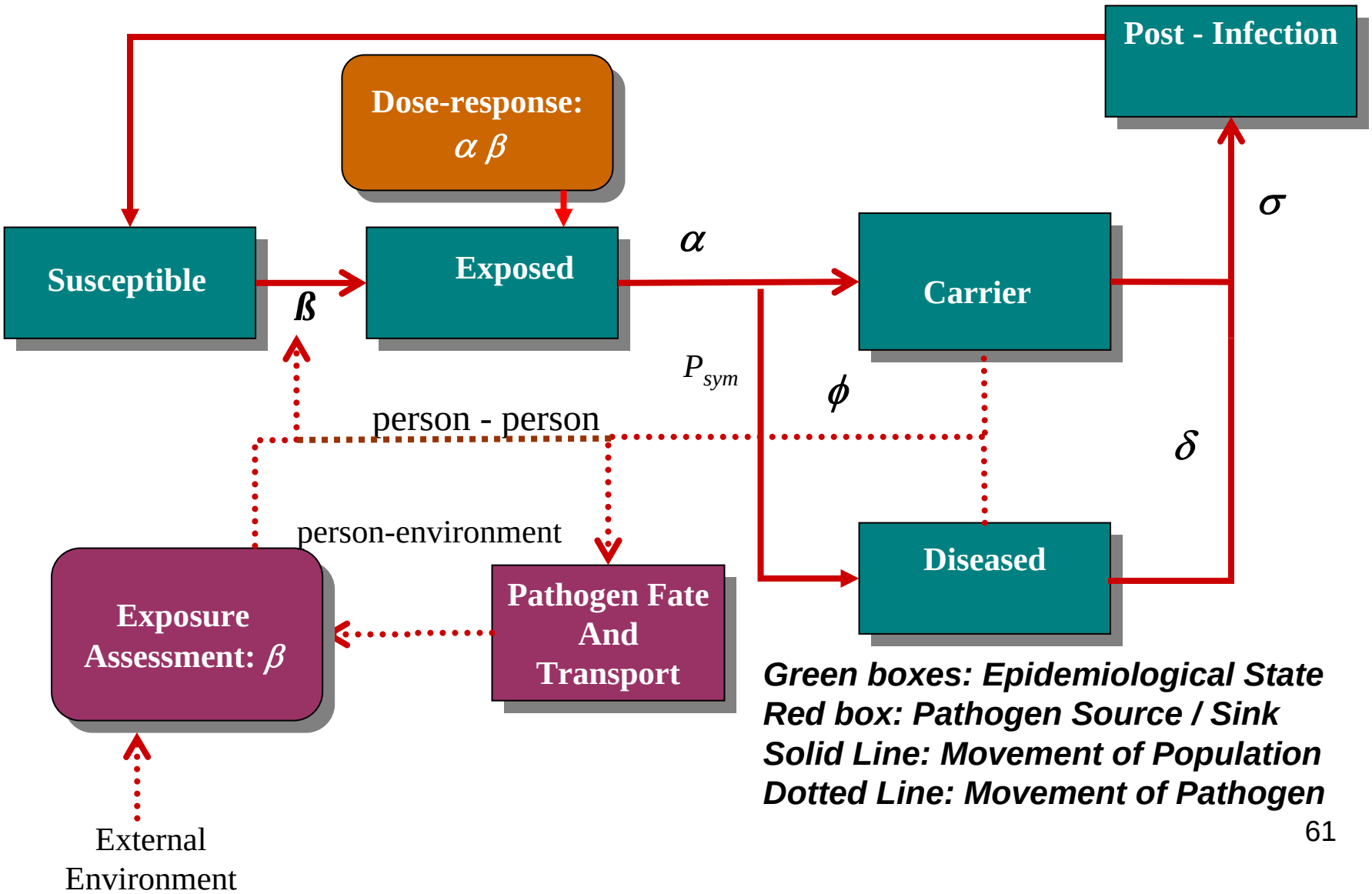
Sub-Surface


Microbial loading (MSW, IW, WS)
Pathways in the built environment
Direct contact
Inactivation in landfill
Landfill liner
Soil filtration
Soil Adsorption
$q = k^{*}C_{eq}^{1/n}$
Extra Well
Pathways in the natural environment
Leachate toxicity
Dilution
Groundwater
Inactivation

Risk Characterization

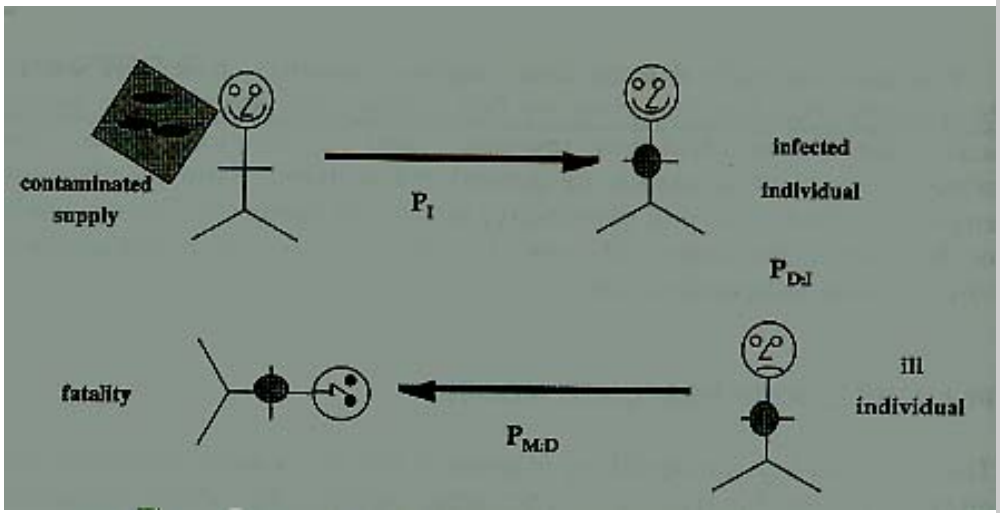
- Individual risk versus population risks.
- Static Models used predict infection NOT illness, thus are conservative.

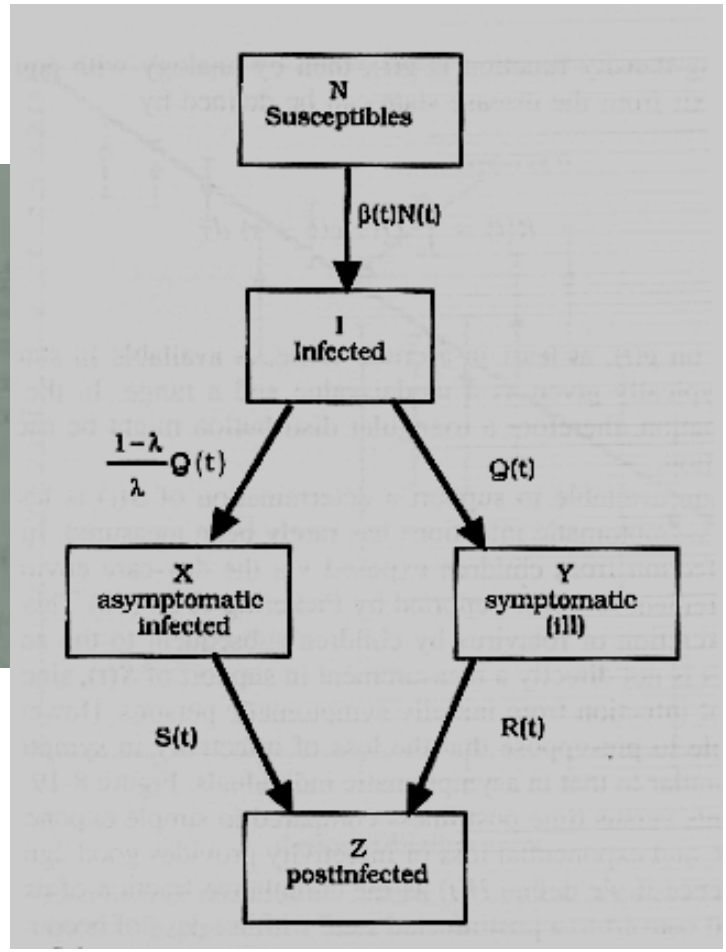
Interaction between Disease Transmission and the Environment



Green boxes: Epidemiological State
Red box: Pathogen Source / Sink
Solid Line: Movement of Population
Dotted Line: Movement of Pathogen

Linking Probability of Infection to Population Models

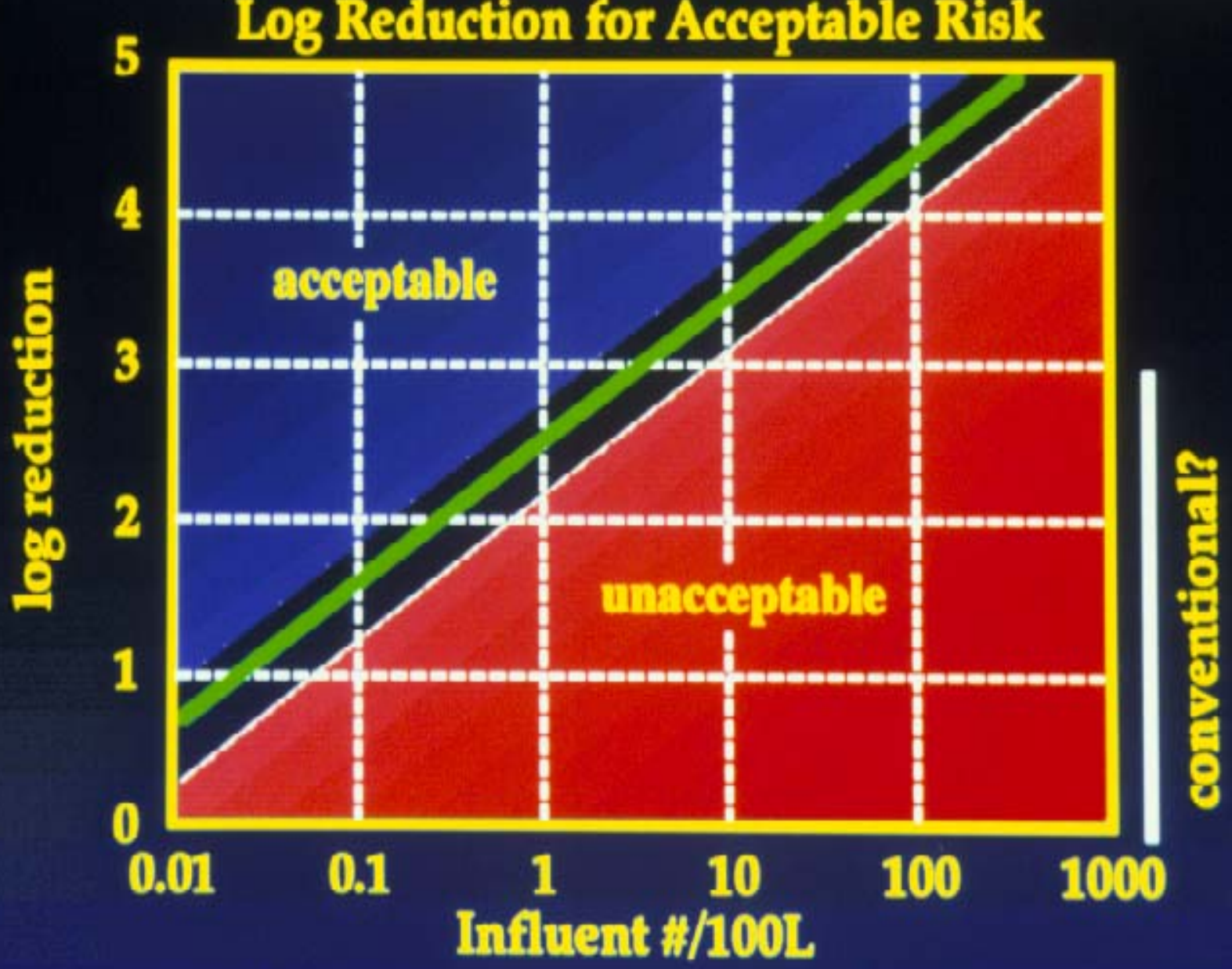


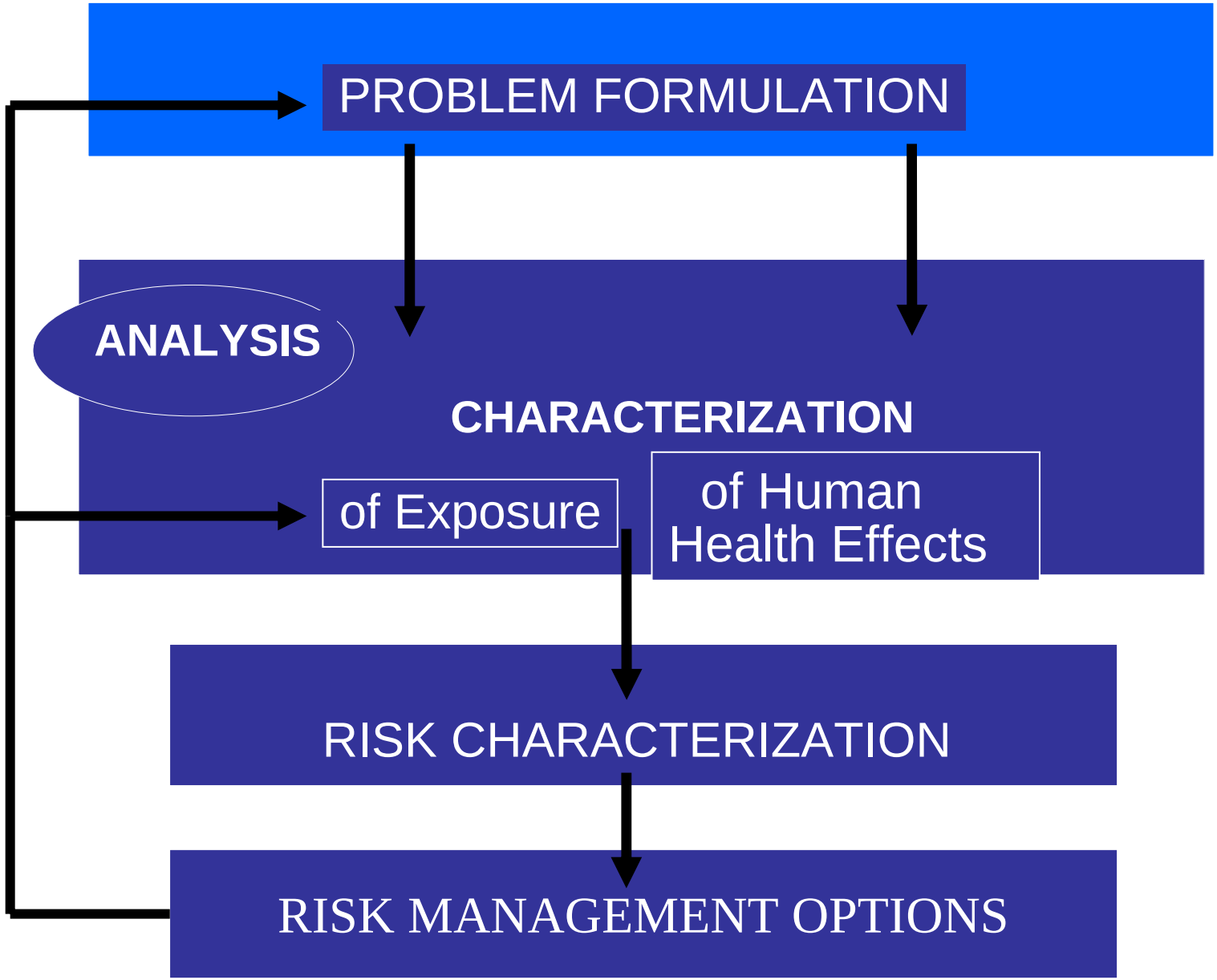


Applications for Microbial Risk Assessment

- Establish policies for protection of health using standards or performance based criteria
- Compare risks
- Evaluate alternative solutions
- Prioritize risks
- Identify scientific data gaps
- Develop protocols for monitoring

Treatment vs. Influent: Endemic Risk




PROBLEM FORMULATION
ANALYSIS
CHARACTERIZATION
of Exposure
of Human Health Effects
RISK CHARACTERIZATION
RISK MANAGEMENT OPTIONS

ANALYSIS PHASE

Exposure Analysis

Health Effects

Disease

Severity

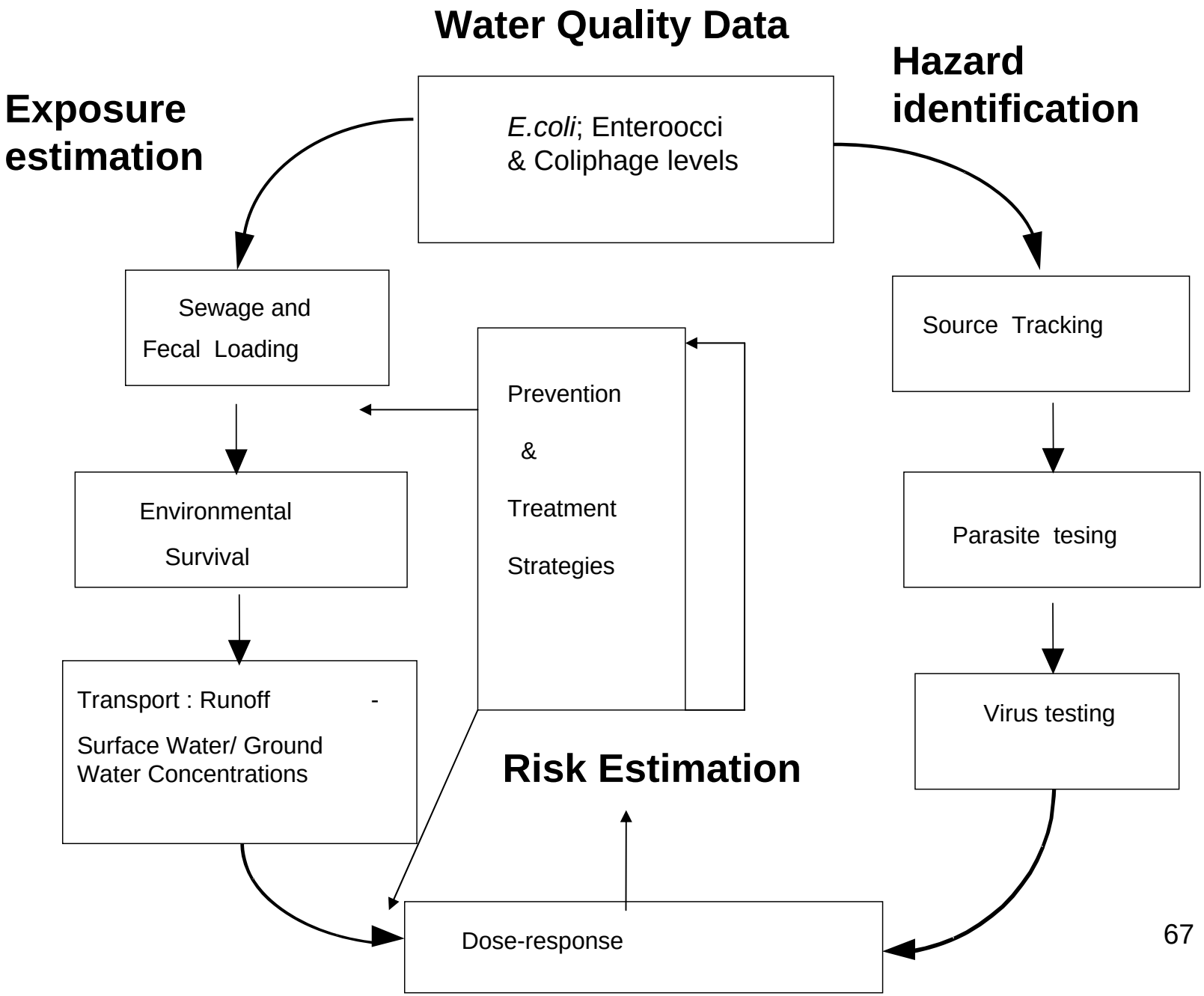
Secondary spread

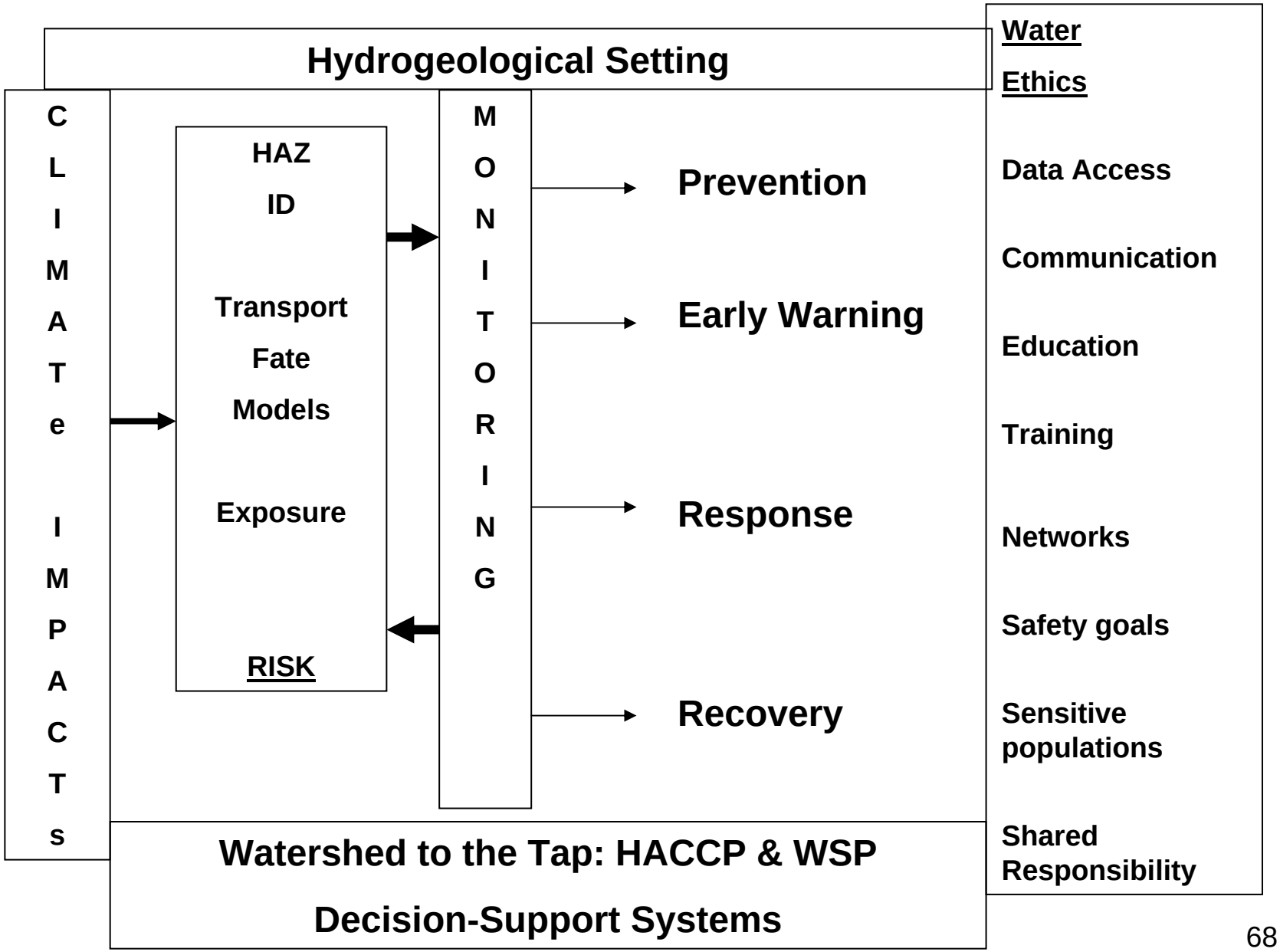
Pathogen Occurrence (detection/survival and spread)

Dose-Response

Exposure Profile

Host Pathogen Profile


Water Quality Data
Exposure estimation
Hazard identification
E.coli; Enteroocci & Coliphage levels
Sewage and Fecal Loading
Source Tracking
Prevention & Treatment Strategies
Environmental Survival
Parasite tesing
Transport : Runoff -
Surface Water/ Ground Water Concentrations
Virus testing
Risk Estimation
Dose-response


Hydrogeological Setting
CLIMATe IMPACTs
HAZ ID
Transport
Fate
Models
Exposure
RISK
MONITORING
Prevention
Early Warning
Response
Recovery
Water
Ethics
Data Access
Communication
Education
Training
Networks
Safety goals
Sensitive populations
Shared Responsibility
Watershed to the Tap: HACCP & WSP
Decision-Support Systems

HACCP

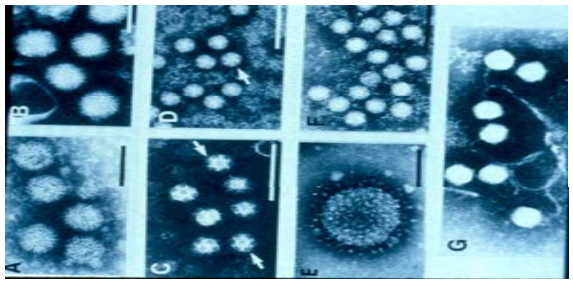
- Hazards (Haz ID).
- Critical points of contamination (part of the exposure pathway; product end point but chain from source and raw materials through to finished product).
- Controls; Processes to achieve safety.
- Critical Control Points (monitoring) assurance monitoring.

Challenges Water Safety Plans WHO

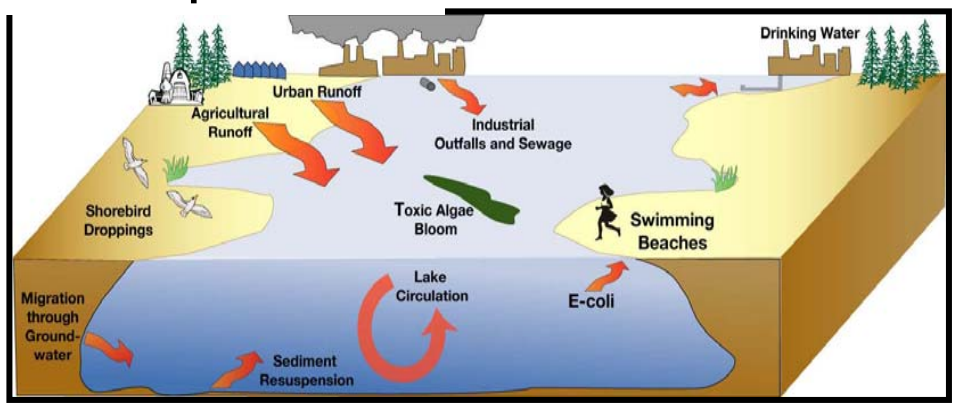
- Acceptable risk (Burden of disease)
- Definition (infection) Acceptable/Tolerable Limit; Water Quality Goals for ambient waters.
- Endpoints: Number of pathogens
- Critical control points: Identify areas for control and monitoring Efficiency.
- Treatment & Disinfection Needs

Advancing Microbial Risk Assessment

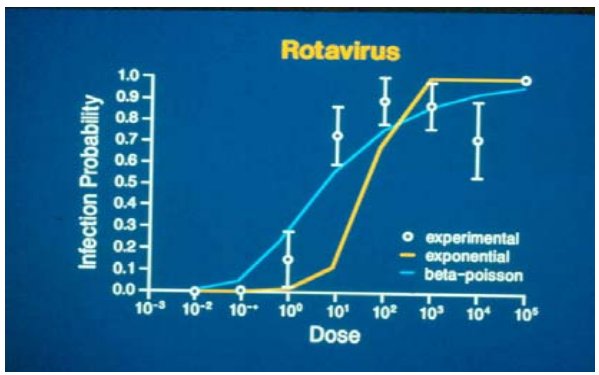
The Hazard



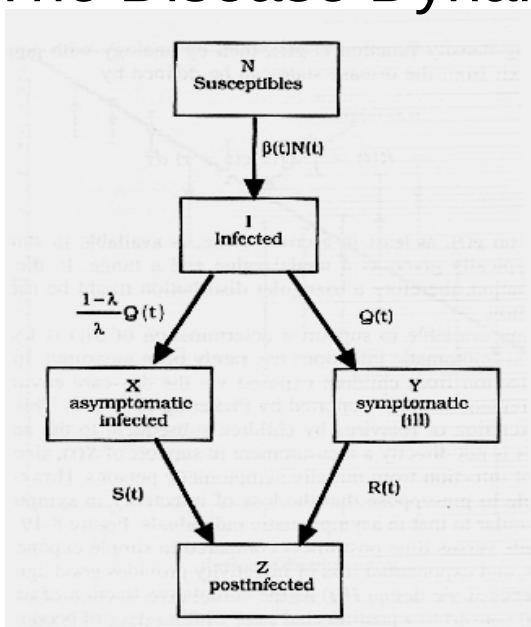
The Exposure



The Dose-response



The Disease Dynamics



The Risk Characterization