CAMRA
Center for Advancing Microbial Risk Assessment

Introduction to Risk Analysis and Risk Assessment Frameworks

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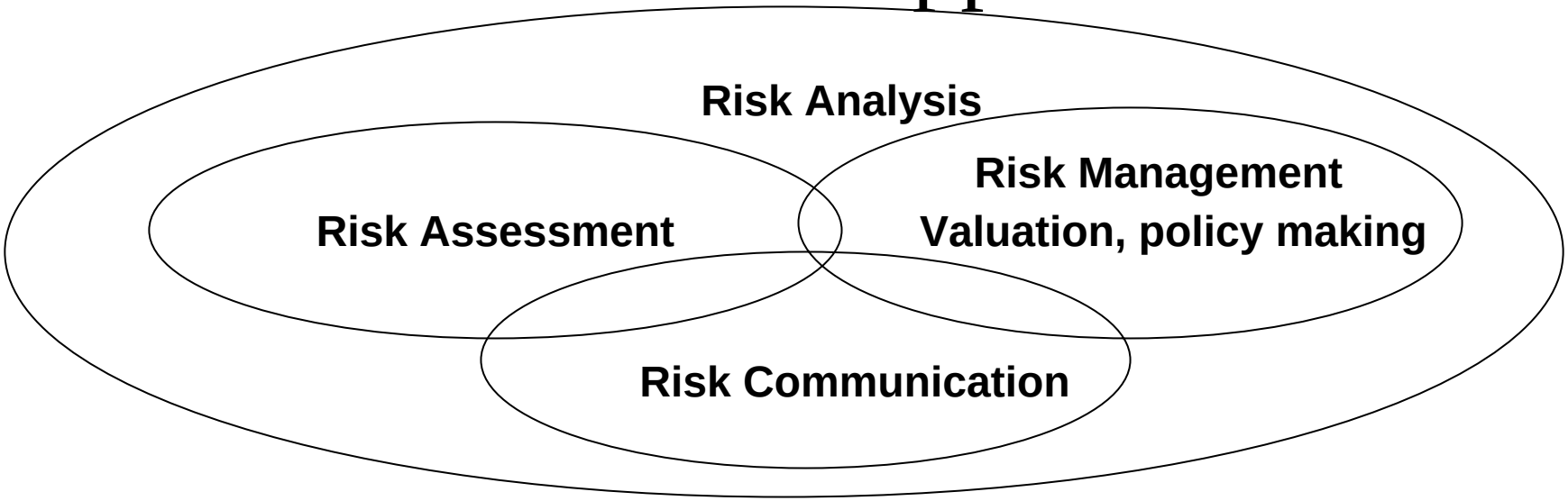
The definition chance*hazard*exposure*consequence

- Risk is the likelihood of identified hazards causing harm in exposed populations in a specified time frame including the severity of the consequences.

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.

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?**

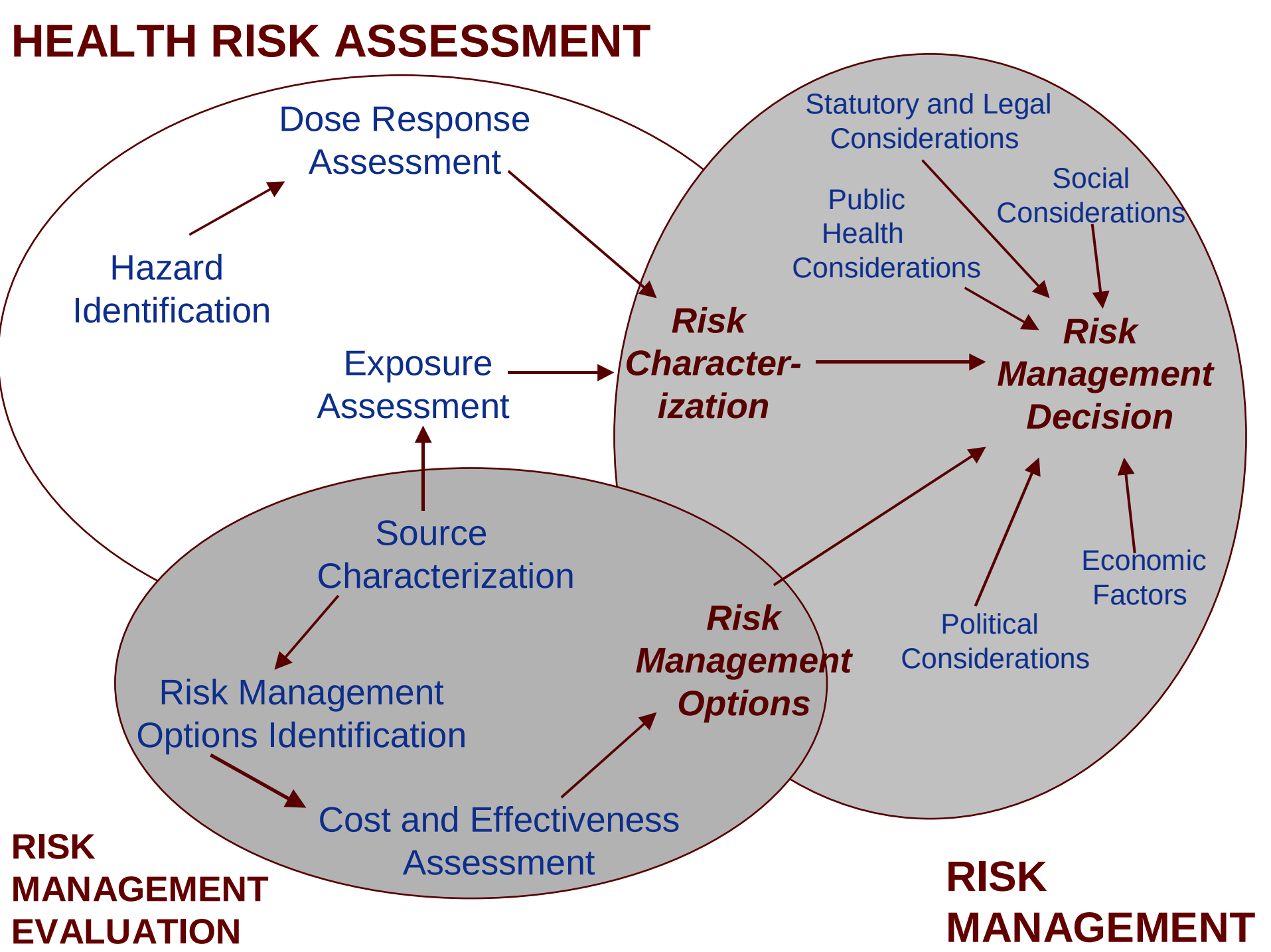
RISK Management

- **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 ISSUES

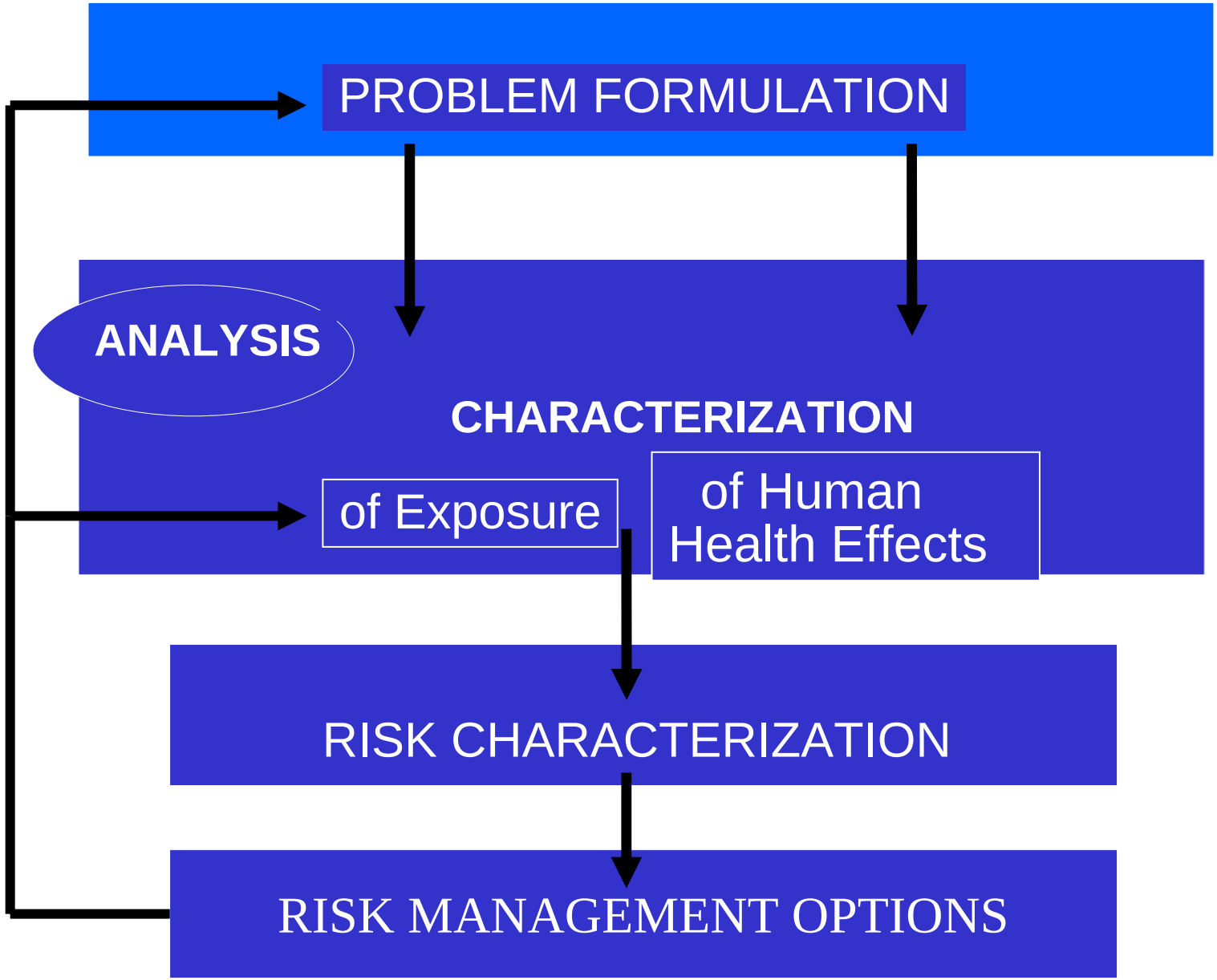
Acceptable risk (de minimis risk): EPA has suggested that 1/10,000 infection annually is an appropriate level of safety for drinking water.

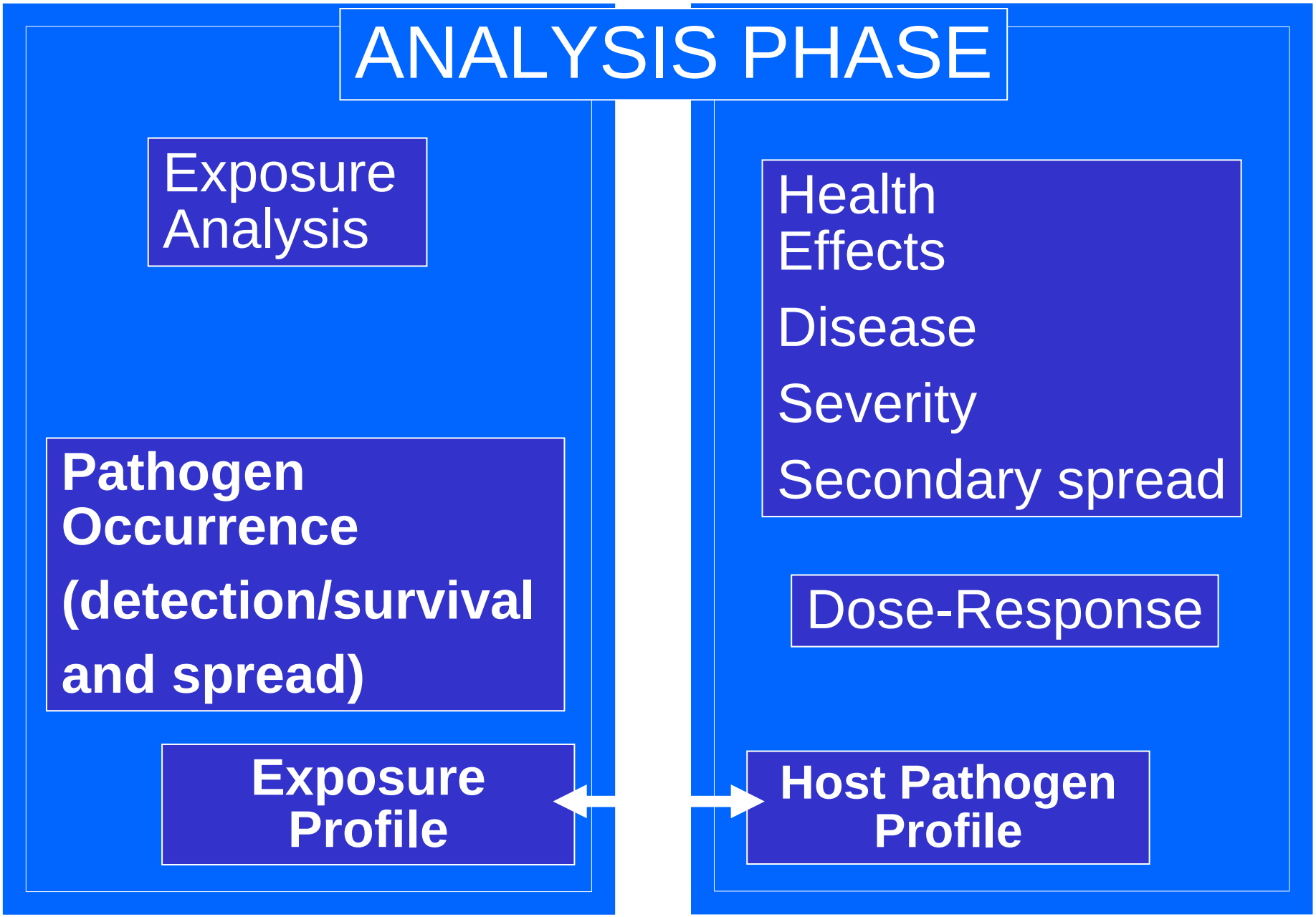
- What is acceptable for recreation? (1/500, single swimming event).
- Benefit and Cost: Cost for water treatment to reduce cost of disease (health care costs, productivity time lost and suffering)


HEALTH RISK ASSESSMENT
Dose Response Assessment
Hazard Identification
Exposure Assessment
Risk Character-ization
Statutory and Legal Considerations
Public Health Considerations
Social Considerations
Risk Management Decision
Economic Factors
Political Considerations
Source Characterization
Risk Management Options
Risk Management Options Identification
Cost and Effectiveness Assessment
RISK MANAGEMENT EVALUATION
RISK MANAGEMENT

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


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

Problem formulation

- Interaction risk manager – risk assessor
- Define the purpose of the QMRA
- Define the breadth of the QMRA
- Explore the context of the QMRA
- Develop a conceptual model
  - Route(s) of exposure for QMRA
  - System under evaluation
  - Pathogens (characteristics)
  - Exposed population; immunity
  - Health outcome
  - Data needs
  - Preliminary, exploratory assessment

Incorporate control alternatives (optional)

Analysis - Exposure assessment

- Pathogen characterization (relevant for exposure)
  - Die-off rate
  - Removal rate
  - Inactivation rate
  - Growth rates
- Pathogen occurrence
  - Frequency,
  - Concentrations,
  - Seasonality
  - Methodological issues

•Pathogen behavior in system

Removal/inactivation

System variability

Analysis - Exposure assessment 2

- Exposure analysis
  - Calculation of pathogen concentration in matrix
  - Consumption data
  - Combination of all information into exposure data
  - Include variability (ranges, probabilistic)
  - Include uncertainty analysis
  - Include sensitivity analysis

Analysis – Effect assessment

- Host characterization
  - Age, pregnancy, immune-status, nutritional status etc.
- Human health effects
  - Duration
  - Severity (morbidity, mortality, sequellae)
  - Secondary transmission

- Dose response
  - Human (or animal) dose-response data
  - Type of response: infection, morbidity, mortality,
  - Inoculum used (type, preparation, administration)
  - Study population characteristics
  - Strain variation
  - Statistical model

Risk characterization

- Risk characterization
  - Combine data from exposure assessment and effect assessment into characterization of risk
  - Include variability (probabilistic)
  - Discuss assumptions: include sensitivity analysis
  - Discuss how outcome answers problem formulation
  - (Compare control scenario's)
  - Identify data needs/improvements

Evolution of QMRA

<1950-70s — Indicator approaches used To develop dose-response for Recreational waters

<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

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.

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

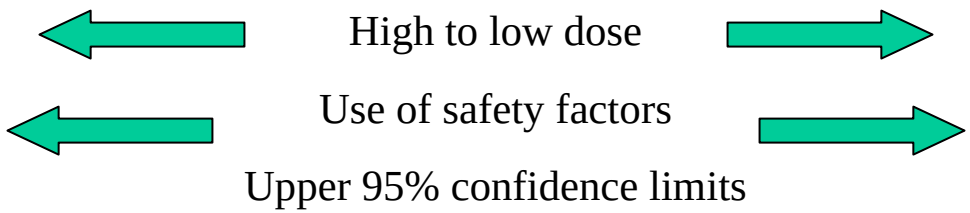
- EPA was required to regulated 83 contaminants by ’89
- Filtration and disinfection were required
- Monitoring for unregulated contaminants
- Lead ban – Corrosion Control Rule
- Ground Water Protection Programs

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:		

SDWA 1986 -- Concerns

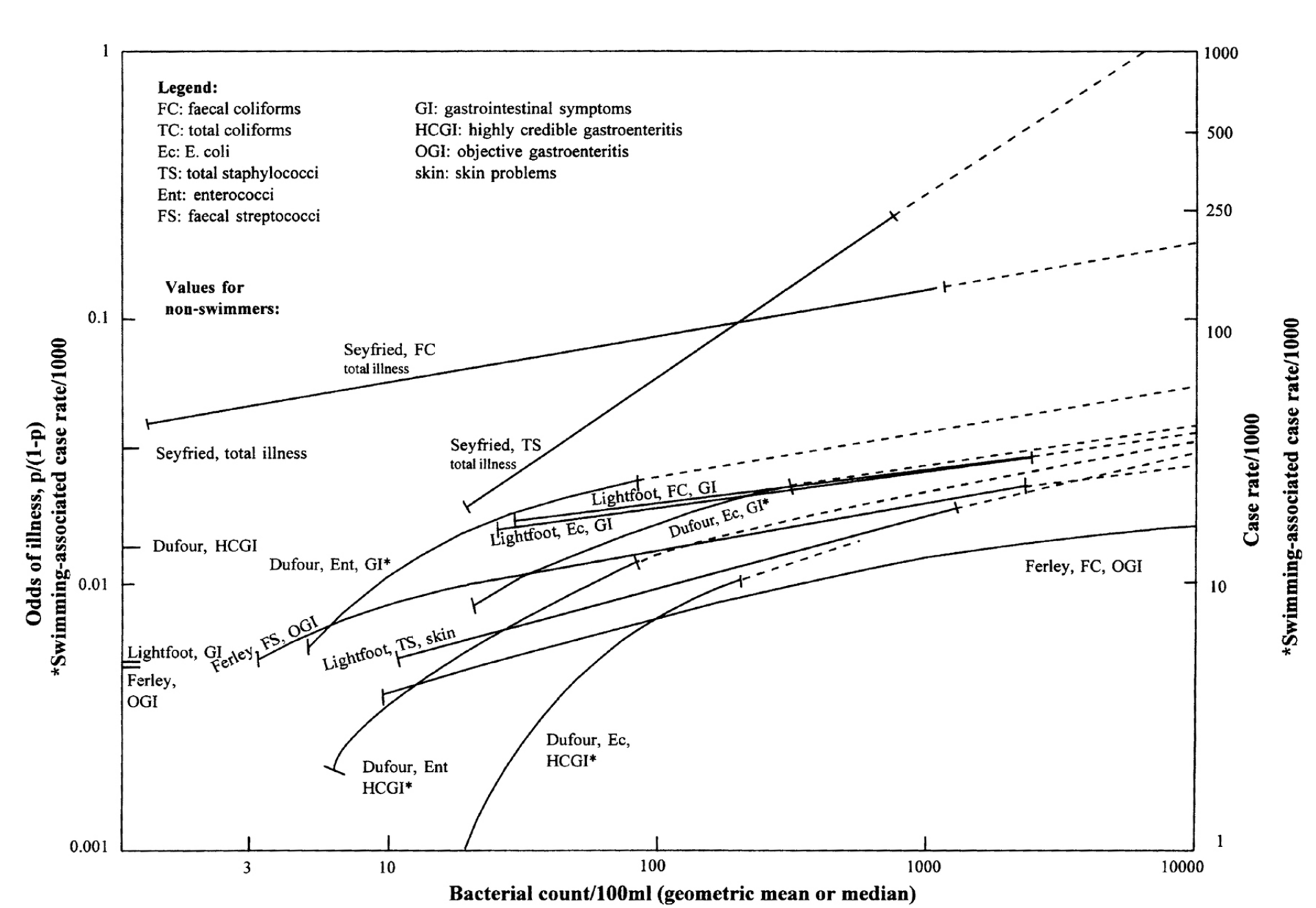
- High rate of non-compliance in small systems
- Funding shortages
- Deficiencies uncorrected
- 1991 outbreak of Cryptosporidiosis in Milwaukee

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

CLEAN WATER ACT: Health Data Associated with Swimming in Polluted Waters

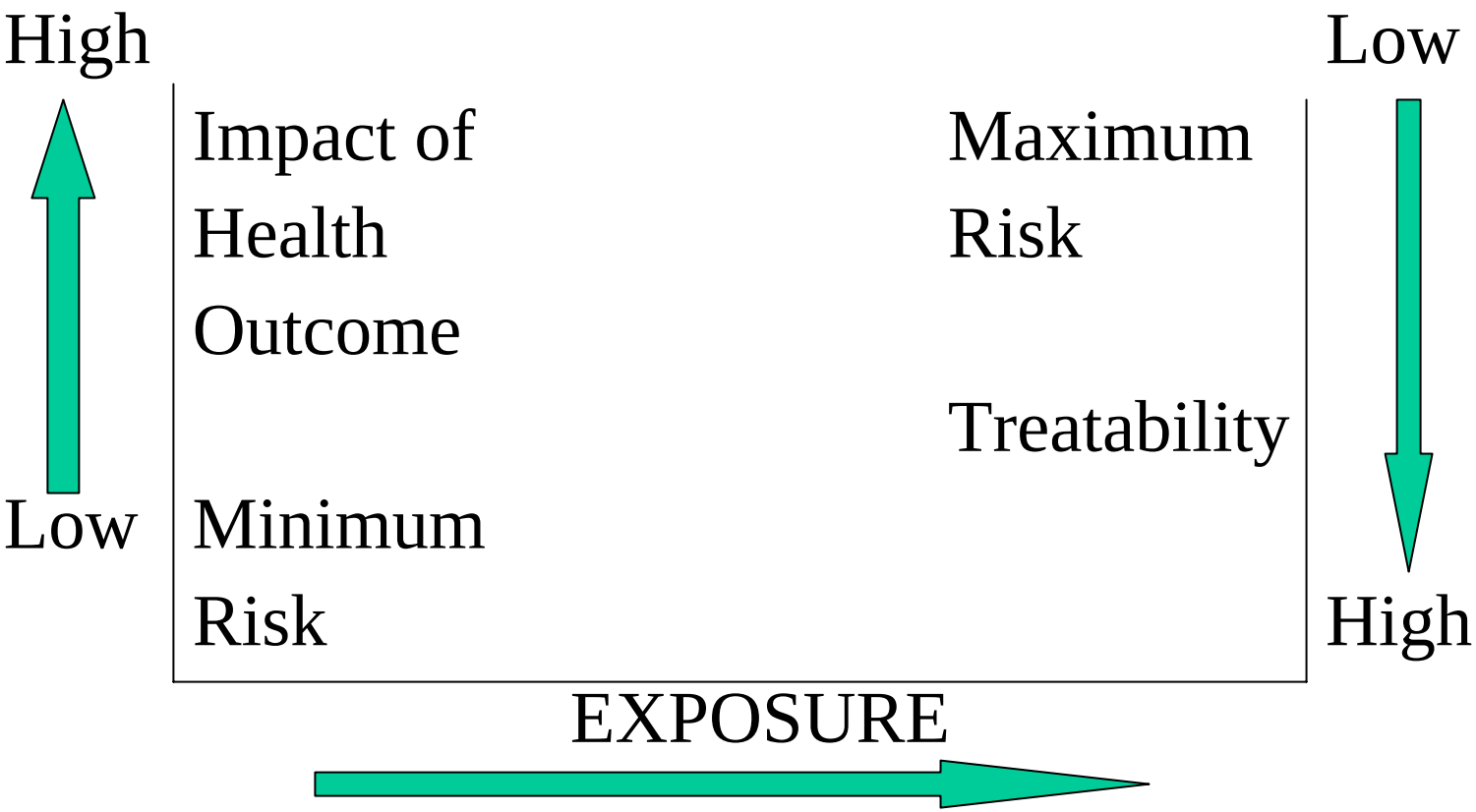
- **Disease endpoints: Respiratory, gastrointestinal, ear, eye, nose and skin infections.**
- **England: respiratory most common, 24% had one symptom.**
- **Santa Monica Bay, CA: gastrointestinal, 3.7%, associated with storm drains.**
- **Key West, FL: gastrointestinal most common, 33% associated with leaky sewer, liveaboards.**


Legend:
FC: faecal coliforms
TC: total coliforms
Ec: E. coli
TS: total staphylococci
Ent: enterococci
FS: faecal streptococci
GI: gastrointestinal symptoms
HCGI: highly credible gastroenteritis
OGI: objective gastroenteritis
skin: skin problems
Values for non-swimmers:
Seyfried, FC total illness
Seyfried, total illness
Seyfried, TS total illness
Lightfoot, FC, GI
Lightfoot, Ec, GI
Dufour, Ec, GI*
Dufour, HCGI
Dufour, Ent, GI*
Ferley, FC, OGI
Ferley, FS, OGI
Lightfoot, GI
Lightfoot, TS, skin
Ferley, OGI
Dufour, Ec, HCGI*
Dufour, Ent HCGI*
Odds of illness, p/(1-p)
*Swimming-associated case rate/1000
Case rate/1000
*Swimming-associated case rate/1000
1
0.1
0.01
0.001
1000
500
250
100
10
1
3
10
100
1000
10000
Bacterial count/100ml (geometric mean or median)

Meta Analysis
Jack Colford

- Recreational Epidemiological Studies
- Enterococci demonstrated the best statistical association in Marine Waters and was a good statistical fit in Fresh Waters
- E.coli was the best indicator of risk in Fresh Waters
- Coliphage and Enteric virus showed some relationship, however only a few studies.

Risk Matrix


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

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.

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

Populations at Greatest Risk

Infants

Aged

Pregnancy
(fetal and neonate)

Immunocompromized

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

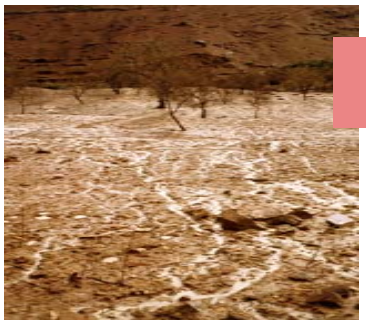
Occurrence Analysis for the Exposure process

- 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.

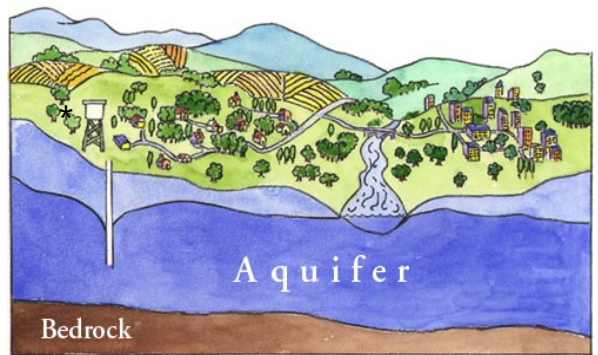


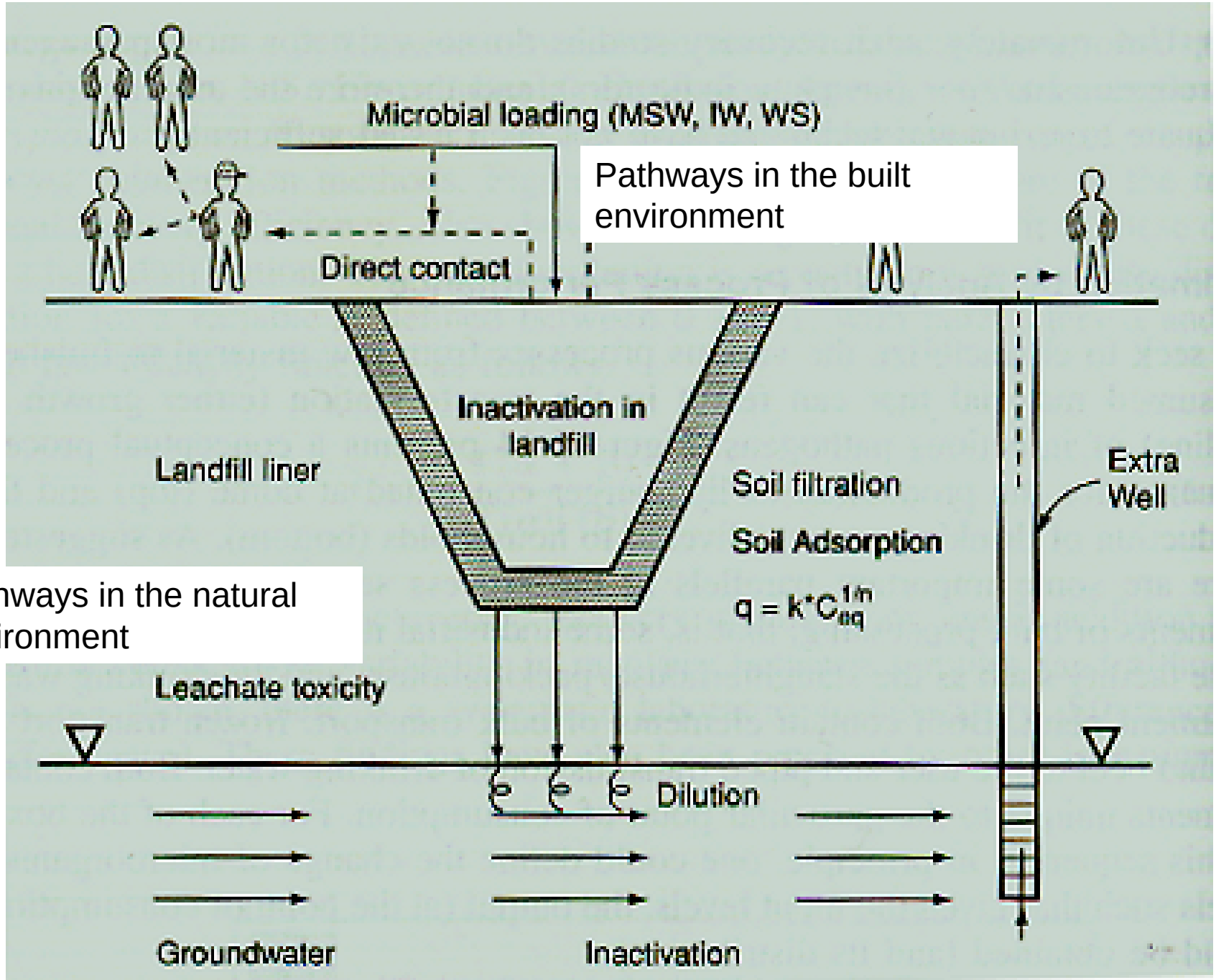
Overland

In-Stream

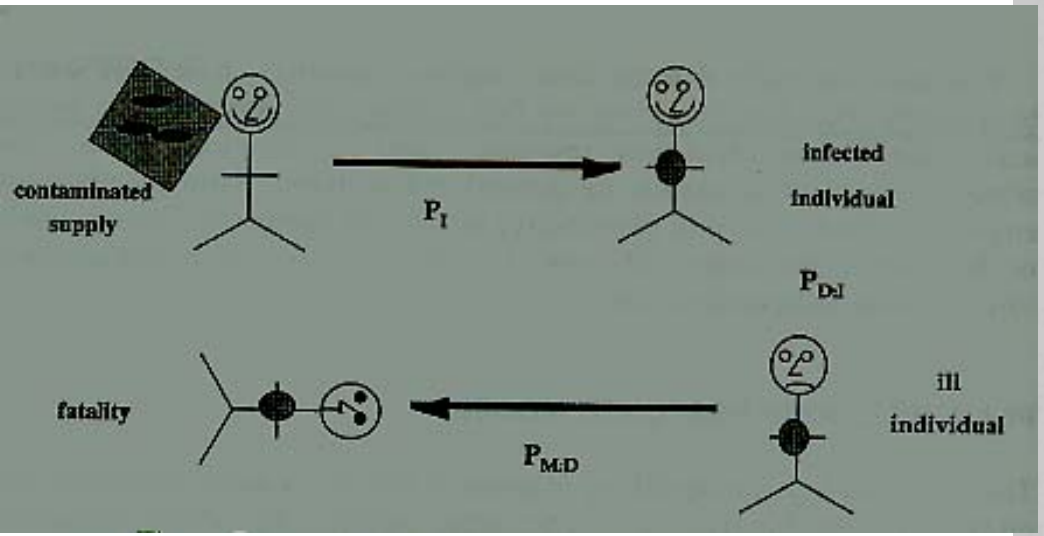
Near-Shore

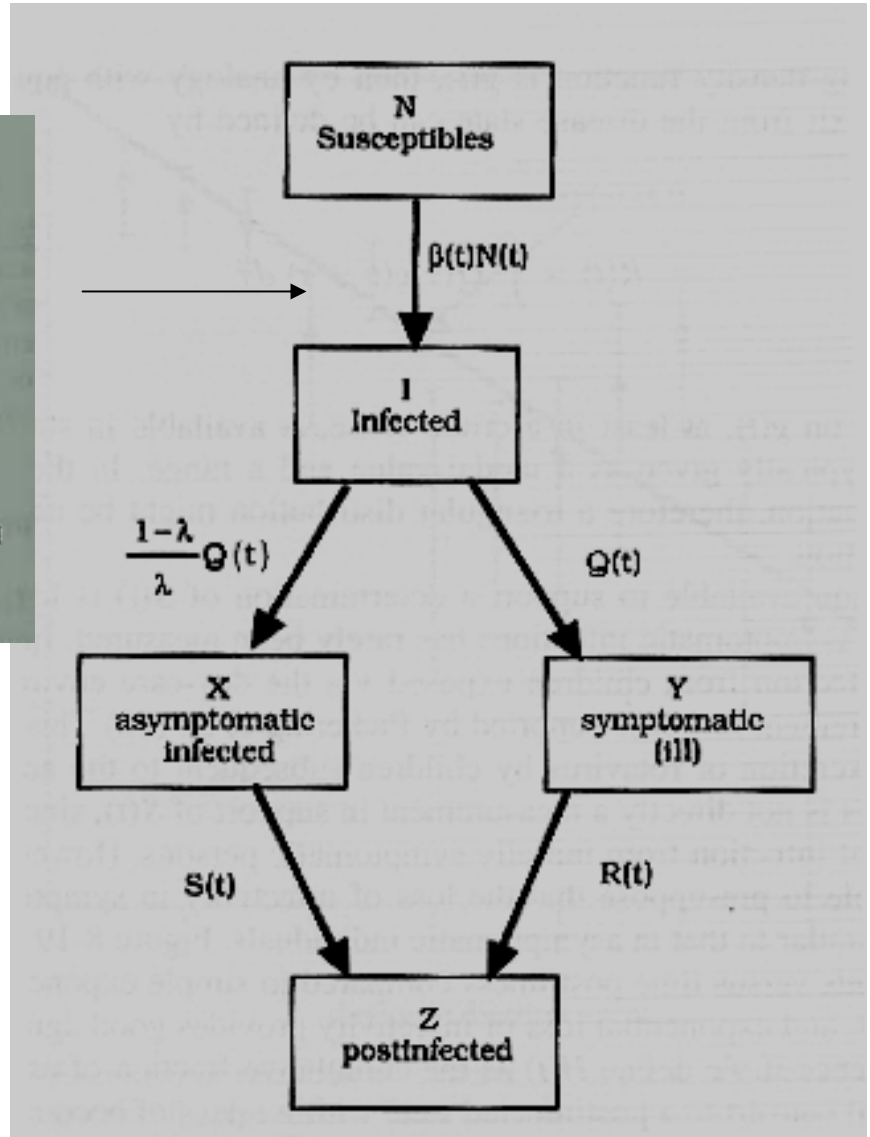
Sub-Surface



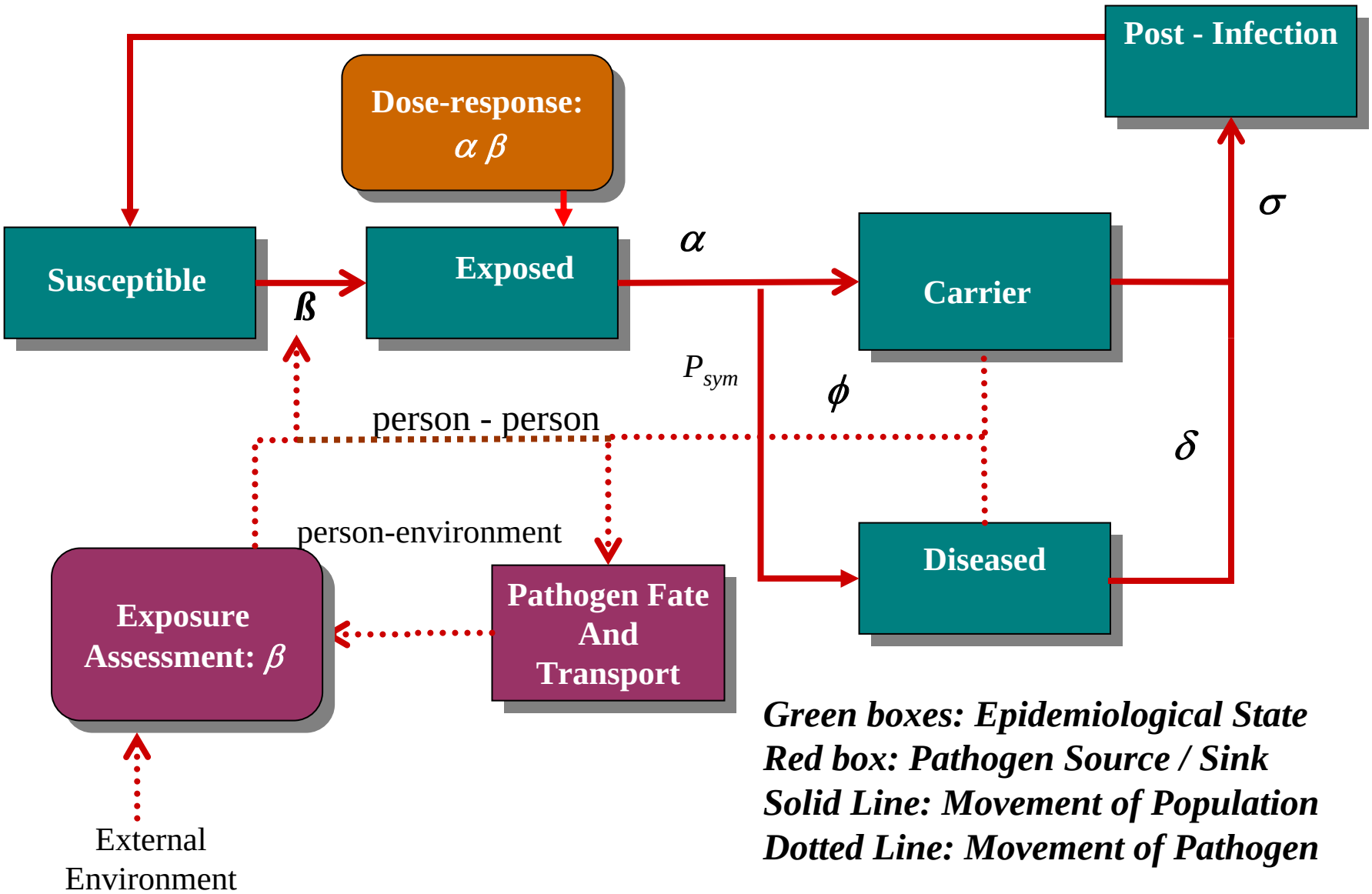

Microbial loading (MSW, IW, WS)
Pathways in the built environment
Direct contact
Inactivation in landfill
Landfill liner
Soil filtration
Soil Adsorption
$q = k^* C_{eq}^{1/n}$
Extra Well
Pathways in the natural environment
Leachate toxicity
Dilution
Groundwater
Inactivation

Linking probability of infection to population models





Interaction between Disease Transmission and the Environment

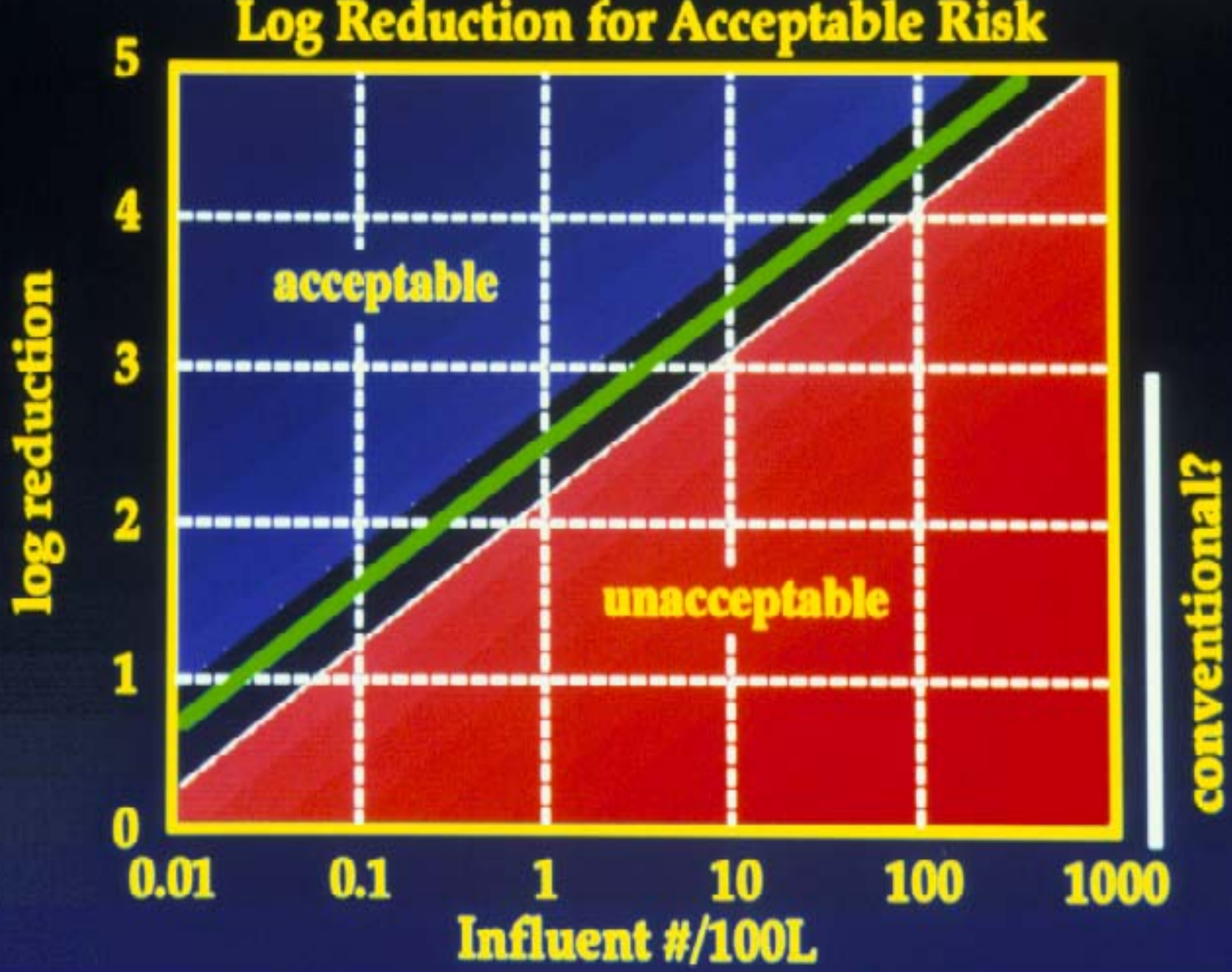


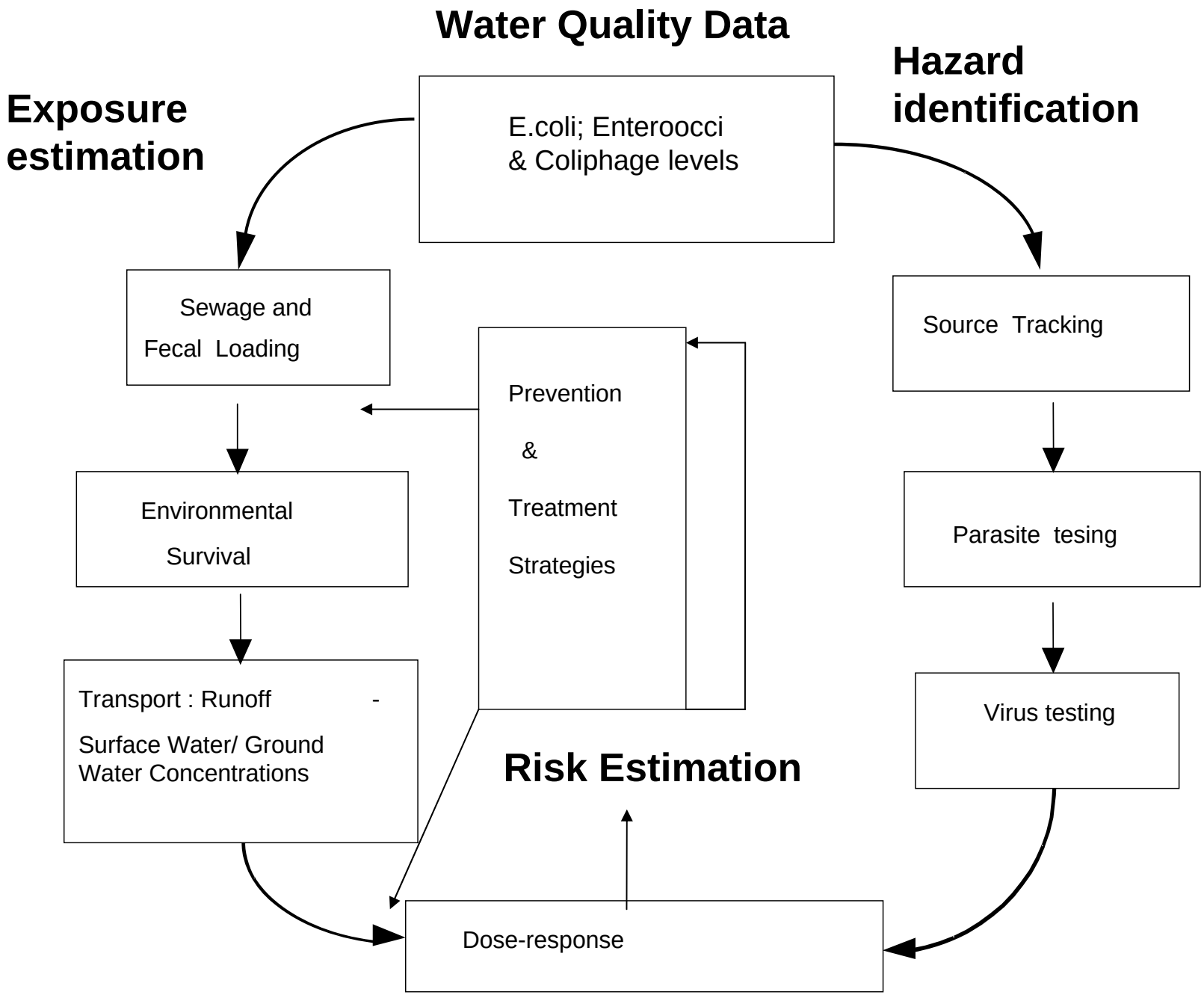
Green boxes: Epidemiological State
Red box: Pathogen Source / Sink
Solid Line: Movement of Population
Dotted Line: Movement of Pathogen

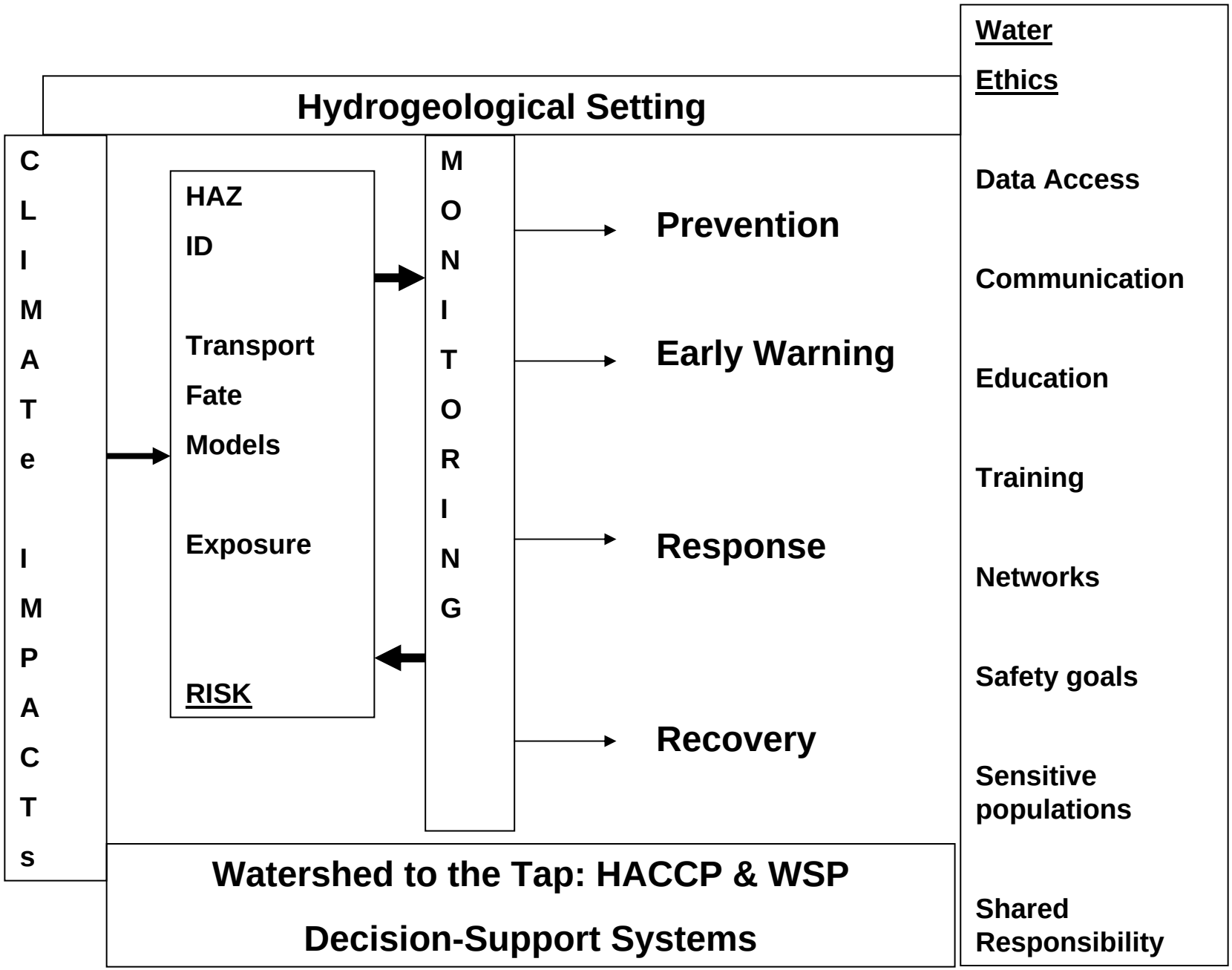
Applications for Microbial Risk Assessment

- 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




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


Water
Ethics
Hydrogeological Setting
CLIMATe IMPACTs
HAZ ID
Transport
Fate
Models
Exposure
RISK
MONITORING
Prevention
Early Warning
Response
Recovery
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

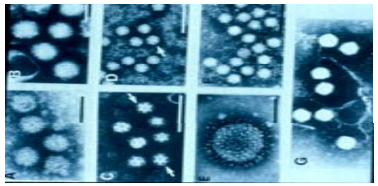
- Acceptable risk (Burden of disease)

Definition (infection) Acceptable/Tolerable Limit; Water Quality Goals for ambient waters.

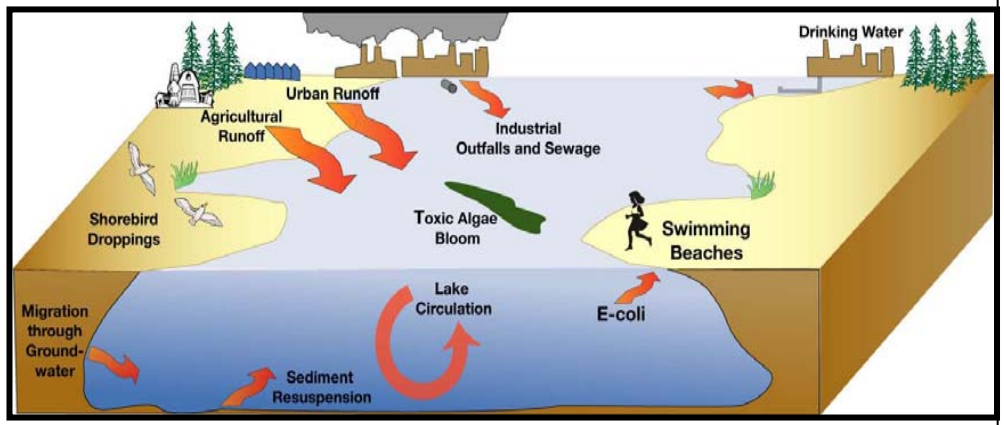
- Endpoints: Number of pathogens
- Critical control points: Identify areas for control and monitoring Efficiency.
- Treatment & Disinfection Needs

ADVANCING MICROBIAL RISK ASSESSMENT

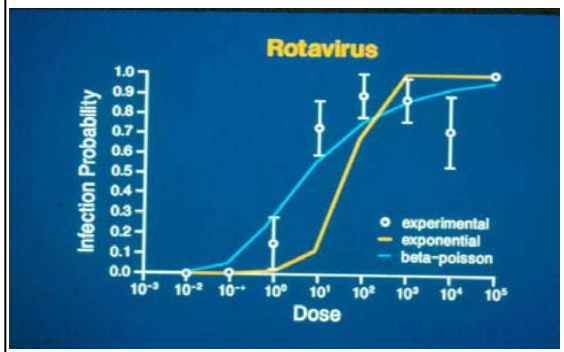
The Hazard



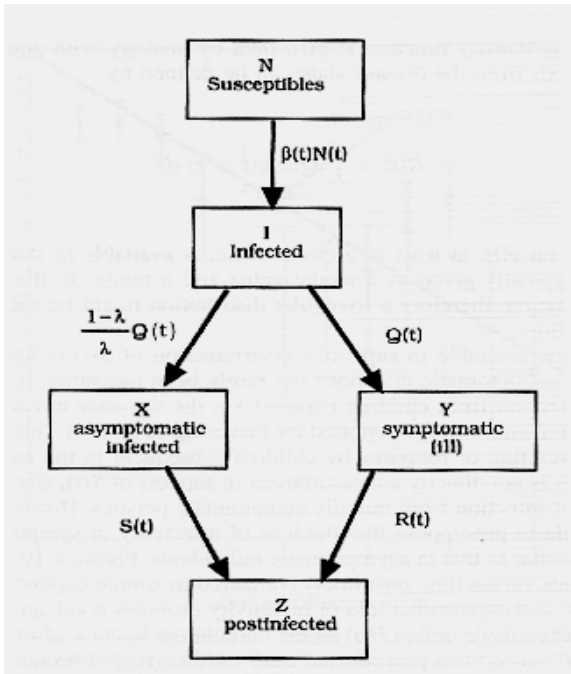
The Exposure



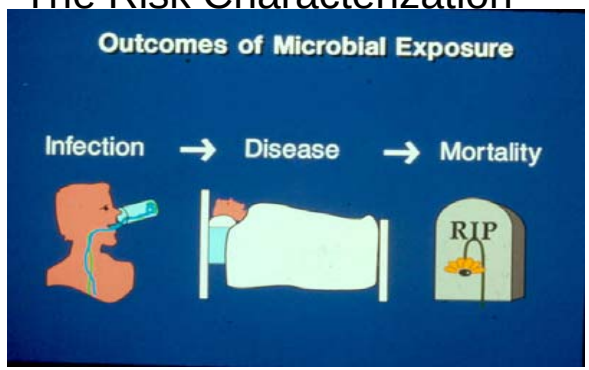
The Dose-response

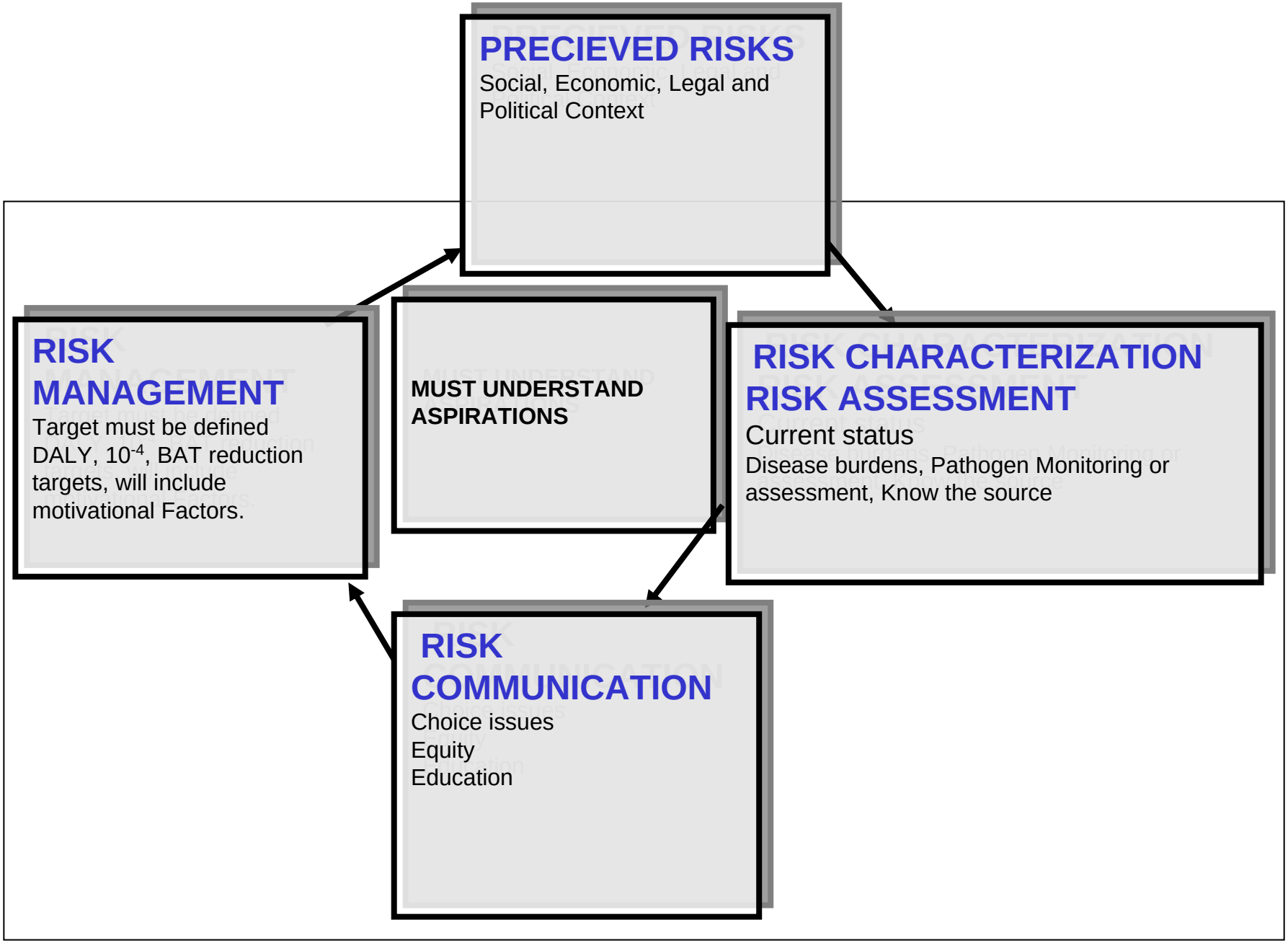


The Disease Dynamics



The Risk Characterization




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

Thank You
QUESTIONS?