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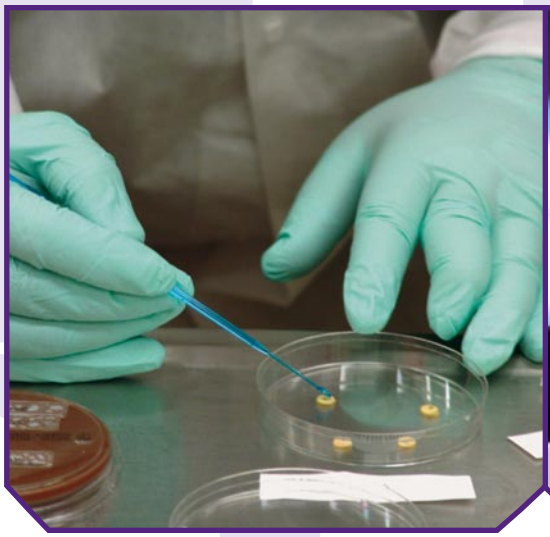
A Compendium of Prior and Current Microbial Risk Assessment Methods



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A Compendium of Prior and Current Microbial Risk Assessment Methods

For Use as a Basis for the Selection, Development, and Testing of a Preliminary Microbial Risk Assessment Framework

FINAL REPORT

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This document is a product of a collaboration between the American Association for the Advancement of Science (AAAS) Fellowship Program and EPA's National Homeland Security Research Center (NHSRC). It was prepared by AAAS Risk Policy Fellow Dr. Jennifer Choich; by Dr. Irwin Baumel (on detail to NHSRC from Edgewood Chemical Biological Center); by Ms. Cynthia Sonich-Mullin, Director, Threat and Consequence Assessment Division/NHSRC; and by Peter Jutro, Deputy Director of Policy, NHSRC.

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Executive Summary

Introduction

Following the events of September 11, 2001, EPA's mission expanded beyond safeguarding the natural environment – air, water, and land – from traditional sources of pollution. With the nation under continued threat from those who seek to harm it, EPA also has the important responsibility of helping to protect the environment from terrorist threats. Several Homeland Security Presidential Directives describe EPA's responsibilities, which are outlined in EPA's Homeland Security Strategy.

One of the most important issues facing EPA's National Homeland Security Research Center (NHSRC) is the development of a biological risk assessment methodology. No consensus-based methodology exists for evaluating biological threat contaminants and establishing cleanup levels. This Compendium of Prior and Current Microbial Risk Assessment Methods is one of the first steps toward establishing such a methodology.

The Compendium

NHSRC recognized that microbial risk assessment (MRA) methodology was at an early stage of development and that the methods applied in MRAs had not been systematically compiled, analyzed, and evaluated for their application to biothreat incident assessment.

NHSRC's Threat and Consequence Division (TCAD) therefore set out to acquire all existing information and research related to prior and current efforts regarding microbial risk assessment. They evaluated the information acquired, selected the most relevant literature, and prepared a compendium of the most applicable information on MRA methods.

The information gathered and presented here will be used to establish a preliminary framework and integrated methods to support threat incident-based biological risk assessments. The approaches described will be utilized in developing a future MRA methodology for biothreat agents, as well as in developing the procedures needed to establish appropriate cleanup levels following intentional contamination with biological hazards.

A great many studies were examined to ensure that the compendium would be a comprehensive review of the field. For the relevant studies, the references and summary information appear in Appendix A. The subsections of the appendix cover exposure assessment, dose-response, risk characterization, hazard identification, and excluded studies. Secondary references not reviewed are listed in Appendix B, and related references dealing with particle deposition are included as Appendix C.

The body of this compendium report gives an overview of the studies in the compendium, describes how these studies were selected for inclusion and then summarized, and presents the roadblocks and deficiencies encountered in the literature as regards TCAD's objectives, with approaches to circumventing or remedying them where possible.

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NOTE: To be useful in hard-copy form, this document requires the insertion of tab dividers before each of Appendix A / section A.1, sections A.2 through A.6, Appendix B, and Appendix C. (One of the sections is nearly 100 pages long.)

SECTION 1: Overview and Guide to the Compendium

1.1 Background

Shortly after September 11, 2001, the White House issued Homeland Security Presidential Directives (HSPDs) that communicated presidential decisions concerning national homeland security policy and tasked federal departments and agencies with specific activities. The HSPDs confer specific responsibilities upon EPA for building decontamination and water system infrastructure and protection. The HSPDs most relevant to EPA are:

HSPD 5: Management of Domestic Incidents
HSPD 7: Critical Infrastructure Identification, Prioritization, and Protection
HSPD 8: National Preparedness
HSPD 9: Defense of United States Agriculture and Food
HSPD10: National Policy for Biodefense

EPA's National Homeland Security Research Center (NHSRC) was established to conduct research in support of decontamination, water system and building security, and the rapid assessment of threat scenarios and consequences. The overarching issue of "How clean is safe?" has been a concern of several of EPA's program offices, but the attacks of September 11th led to more pressing demands for deeper understanding of risks and responses in this area. NHSRC must address critical new issues, one of the most important being the development of a biological risk assessment methodology.

1.2 Approach

Currently, there exists no consensus-based methodology for evaluating biological threat contaminants and establishing cleanup levels. NHSRC determined that a compendium of relevant existing studies, and their approaches to assessing biological risk, would offer its scientists a knowledge base that would enable them to direct their research most productively. This compendium includes 135 of the most relevant studies published between 1994 and 2004. (The criteria for inclusion, and the template used to summarize the information from each study, are described in Section 2.) Of the relevant studies, 44 were related to exposure assessment (EA), 31 to dose-response (DR), and 60 to risk characterization (RC). The roadblocks and data gaps encountered by the summarized studies' researchers are presented in Section 3, with recommendations for dealing with them.

1.2.1 Exposure Assessment

The Exposure Assessment section of Appendix A includes 33 studies on foodborne, 6 studies on waterborne, and 5 studies on airborne (inhalation) exposure methods. No dermal methods for EA were identified.

1.2.1.1 Foodborne Organisms

Most of the food-based approaches incorporated EA models that simulate the prevalence of pathogens and the dynamics of their growth and decline as the food moves from farm to table. The early models of this class relied heavily on two types of assumptions in areas that are very influential for microbial population dynamics in various media: first, computational convenience;

and second, the times and temperatures of food storage. In addition, most disease transmission models assumed discrete inputs or distributions for EA, since they were not process models that could describe the route of exposure or potential dynamics prior to ingestion or inhalation. There were many foodborne EA methods, particularly when it came to modeling changes in numbers of bacteria at the various stages prior to consumption. It is hoped that some of these methods for assessing the risk of foodborne exposure will be found to apply to scenarios that involve deliberate contamination at establishments that offer or process food.

1.2.1.2 Waterborne Organisms

Models' predictions of the inactivation of waterborne microbes (which are based on plant water-quality measures, treatment system characteristics, and human exposure factors) were consistent with measured concentrations in drinking water, suggesting that such models may also be useful for predicting EA for intentional contamination of water distribution systems. EA models for waterborne agents incorporated declining pathogen survival in water; this seems appropriate, since conditions in water distribution systems would rarely (if ever) permit significant growth. Several studies provided MRAs for pathogens in drinking water. Exposure scenarios included contact with untreated or raw water, as well as water that had undergone disinfection treatment. Poisson, negative normal, negative binomial, and beta-binomial distributions were used for the prediction of microbial exposure through drinking water under different scenarios.

1.2.1.3 Airborne Organisms

Size, density, and shape are key properties that influence particles' aerodynamic properties, the characteristics of their deposition within the respiratory tract following inhalation, and the characteristics of their clearance from the respiratory tract. One of the studies clearly demonstrated the importance of these particulate properties on the infectivity potential of airborne anthrax spores. Data on these properties of biological threat agents are likely to be useful in developing methods for assessing exposure and in analyzing exposure-response relationships, and where possible were included in the information compiled for the compendium. Knowledge of the mechanics of deposition and pathogenesis/infectivity of inhaled spores may permit extension of existing particulate methods to anthrax dosimetry modeling.

1.2.2 Dose-Response (Hazard Characterization) Information

The more relevant DR models presented in Appendix A were found primarily in food ingestion studies that included human clinical data for bacteria (*Campylobacter*, enterotoxigenic and enteroadherent *Escherichia coli*, *Plesiomonas*, typhoid and non-typhoid *Salmonella*, *Shigella*, *Vibrio cholera*), protozoans (*Cryptosporidium*, *Entamoeba*, *Giardia*), and viruses (rotavirus, echovirus 12, polio virus, norwalk virus). Data from outbreak investigations were also used for DR modeling for two bacterial pathogens (*Listeria* and *E. coli* O157:H7), and animal data were used for DR modeling for a blue-green alga (*Cyanobacterium*), a bacterium (*Listeria*), and a protozoan (*Cryptosporidium*). Typically, empirical models (exponential, beta-Poisson, Weibull-gamma) were fitted to the data. Only one study discussed mechanistic modeling. Analysis-of-variance models were developed for non-typhoid salmonellosis and shigellosis.

1.2.3 Risk Characterization

A large segment of the relevant literature addressed risk characterization (RC). Many tools were used to link EA and DR models so as to characterize risk. Monte Carlo simulation was the most common, but other types of models were also used, including Bayesian network, discrete spatial-temporal simulator, disease transmission, hierarchical-statistical, and statistical-

relational. To some extent, the choice of model type and tools depended upon the type and quality of the available data. (Of the 60 RC studies that appear in Appendix A, 26 describe disease transmission.) Many of the models included in the RC section were hypothetical or theoretical. Several of the studies applied "what if" analysis and scenario analysis.

1.3 Application of Compendium to Methods Development

This compendium of most credible methods is intended to be the basis for developing a generalized Preliminary Microbial Risk Assessment Framework. This framework will include the following elements:

1. *Hazard characterization/health effects assessment* – This part will include (but not be limited to) information on infectivity, adverse effects through lethality, virulence, host specificity, infection mechanisms, and portals of entry.
2. *Exposure assessment* – This section will include at least transmission, persistence, detection, size of exposed population, spatial and temporal nature of exposure, symptomatology, and containment. All relevant pathways (inhalation, ingestion, dermal) and media (air, food, water, surfaces) will be specified.
3. *Risk characterization* – The framework will cover level of risk (e.g., probability statements, effective dose range), all relevant uncertainties for key factors (e.g., transmission, lethality, dose-response, detection, background, sampling), and attributable risk.

As can be seen in Appendix A, the study summaries in this compendium include the material that will make it possible to develop the framework.

SECTION 2: How the Compendium Was Developed

2.1 Development of Literature Search Strategy and Criteria

The initial step in the compendium development process was the design of a search strategy for identifying relevant methodologies and approaches in microbial risk assessment. The search strategy needed to reveal pertinent information in scientific publications, technical reports, presentations given at scientific meetings, workshop reports, and so on. The information would then be cross-referenced with sources of additional information identified in documents, and reports would be pursued as appropriate. In the case of scientific abstracts presented at meetings and workshops, presenters would be contacted as necessary to secure copies of relevant publications or supporting reports.

A list of criteria, given below, was used to conduct the world literature search. The sources included information published in the open literature, provided via the Internet, or made available through other public avenues – for example, technical reports released on federal agency Web sites, publications in peer-reviewed journals obtained through libraries (e.g., MEDLINE, TOXLINE, NTIS, Agricola, Biosis, SciSearch), professional society publications and technical reports (e.g., ASM, ILSI, SOT, SRA, NAS), publications obtained directly from researchers in academia or in federal laboratories, reference listings in technical and workshop reports, and other material considered reliable.

Literature Search Criteria

- "Biological" agents are taken to mean only microbial, infectious agents, such as viruses and bacteria.
- Each candidate method or piece of material must address some aspect of microbial risk that could lead to formulation of a methodological approach.
- The hierarchy of sources shall include, but not be limited to, peer-reviewed journals, the private sector, the federal government, military organizations, professional societies, academia, and international research and professional organizations.
- The literature search is to go back 10 years.
- In all cases, the method or approach identified does not necessarily have to be associated with a threat organism of concern to NHSRC. Methods and approaches associated with any other microbial organism will qualify as long as they are useful and can be directly applied to one or another of the NHSRC threat organisms.
- Air, water, and/or food matrices qualify for consideration.
- The method may assess any type of exposure route (dermal, inhalation, ingestion).
- The method must fall into at least one of the following categories:
    - Approach has developed or applied models for transmissibility, host persistence, or biomarkers of infectivity or other endpoints.
    - Approach deals with the use of epidemiologic, breakout, or other unique datasets to fashion a dose-response curve for a microbial agent.
    - Approach has designed a process for developing exposure assessments on the basis of breakout or epidemiologic data and/or aerosol behavior and deposition of a microbial agent.

Over 1700 citations and more than 50 links to Web documents were considered, and 267 citations met these criteria for potential inclusion in the compendium.

2.2 Selecting Relevant Biological Risk Assessment Methods

A two-step process was used to screen the gathered references for further review and consideration for inclusion in the compendium. First, two overarching inclusion criteria for method selection were applied.

Inclusion Criteria

- Any reference will be included in the compendium if it provides a full description of a method for assessing the risk of bacterial and/or viral hazards by any human exposure route (dermal, inhalation, or ingestion).
- Any information source will be included in the compendium if it describes a method for secondary transmission of any microbial hazard contained in the source.

The most relevant MRA efforts described in the publicly available literature, irrespective of the basis and application of the method (e.g., assessment of risk of foodborne, airborne, or waterborne organisms; exposure assessment; dose-response; model development), were thus selected for review.

Second, specific exclusion criteria were used to further screen the citations, so as to generate a final list of most desirable references.

Exclusion Criteria

- chemical hazards and microbial toxins (clostridia, staphylococci, ...)
- biological agents other than bacteria and selected viruses
- rickettsial agents (Q-fever, typhus, ...)
- parasites (*Cryptosporidia*, *Giardia*, ...)
- fungi (mildew, spores, human disease agents, ...)
- prion agents (BSE, TSE, ...)
- sexually transmitted diseases
- pathogens requiring transmission by arthropod vectors
- influenza, hepatitis, HIV viruses
- animal and plant pests
- non-pathogenic agents
- genetically modified foods
- environmental modeling (surface water, ground water, agricultural, solid waste)
- antimicrobial-resistant microorganisms
- general modeling techniques applied to non-microbial hazards
- hazard identification methods
- principles, guidelines, definitions, and frameworks without pertinent examples
- food safety objectives
- economics and risk management methods (cost-benefit analysis, HACCP, ...)
- risk communication
- commerce and trade
- medical procedures and pharmacological studies

The application of these two sets of criteria reduced the 267 references to 135 studies to be evaluated (a total of 132 templates). Of these 135 studies, 44 were related to exposure assessment, 31 to dose-response, and 60 to risk characterization of MRA methods. (They can be found in sections A.1 (EA), A.2 (DR), and A.3 (RC) of Appendix A to the compendium.)

Methods that did not meet the inclusion and exclusion criteria are more likely to represent marginal or weak studies that lack the necessary scientific rigor to support future EPA decision making.

2.3 Evaluation and Presentation of Compendium Results

Once the most desirable references had been extracted from the results of the literature search, a template (shown in Table 1) was developed for summarizing and critiquing the data presented in the chosen documents. It serves as the general structure for the content of most of Appendix A. As Table 1 shows, the template presentation provides a brief introduction to each of the literature sources, including items such as source type (report, publication) study type (exposure assessment, dose response), publication attributes (author, sponsoring organization), experimental design, observed data gaps and possible solutions, weight of evidence, plausibility of the authors' conclusions, applicability to microbial risk assessment, and inclusion in other sources.

The studies presented in sections A.1 through A.3 represent an overview and evaluation of recently published studies whose methods could support the development of the methods needed for NHSRC's purposes. Within each section the studies are presented in alphabetical order, with a complete list of the references at the start. The template in Table 1 is also used in section A.5 of Appendix A, which presents the studies that were considered to be hazard identification rather than useful approaches, and A.6, which summarizes the studies that did not meet the other exclusion criteria described above. (Section A.4 is a list of all the sources discovered by the study.)

Appendix B lists the secondary search results, which were not reviewed and evaluated. Appendix C gives a complete list of citations for particulate deposition. Both of these listings may merit future examination.

The template summaries were designed to emphasize not only gauging the quality of the data presented, but also evaluating its utility. Guidelines for rating data utility were established (see Table 2 below) to assist with deciding how well the information in the document could be extended and applied to incident-based risk assessment of biothreat agents in buildings and water distribution systems.

Table 1. Sample Study Summary Template

Section Title	Section Content
A. Study Identification *(tailored by type and group)*	Complete reference (author, title, journal, etc.) or URL
B. Objectives and Type of Study	1. purpose 2. type (EA, DR, RC, etc.)
C. Publication Attributes	1. sponsors/affiliations 2. peer-review mechanism (e.g., journal)
D. Data and Study Design	1. type of data 2. source 3. extent of data 4. sampling plan 5. sample size 6. performance characteristics 7. relevance
E. Method/Model/Approach	1. general characteristics (e.g., experimental, observational, simulation) 2. specific characteristics (e.g., error structure for analytical data; repeatability; reproducibility; adequacy of analytical and statistical methods; completeness of study) 3. assumptions 4 limitations 5. relevance
F. Study Conclusions and Extended Applications	1. conclusions (supported by the data) 2. authors' extrapolations from the observed data
G. Data Gaps and Proposed Solutions	1. data gaps 2. proposed solutions
H. Weight of Evidence	1. robustness of method 2. representativeness of data 3. generalizability or external validity 4. soundness of study conclusions or internal validity 5. defensibility
I. Criteria for Exclusion From Compendium	e.g., review study, or insufficient data quality or quantity to support rigorous science-based modeling
J. Reviewer Comments	e.g., description of most appropriate uses of method
K. Cross-References	additional data from same study summarized in other sections of the compendium

Table 2. Key to Ratings of Utility of Study Data and Methods for EPA's Purposes

Template Section and Subsection	Ratings Used	Definitions
Section D, item 7 (relevance of data)		
	high	meets all three data-relevance criteria (1. agent named on EPA list; 2. waterborne, foodborne, or airborne agent; 3. sound study based on description for items 3–6 of Section D)
	medium	meets two criteria
	low	meets one criterion or none
	NA	not applicable or not available
Section E, item 5 (relevance of method)		
	high	meets all method-relevance criteria (1. data rated high relevance; 2. directly describes aspects needed for incident-based scenario modeling for acute and residual effects, including fate and transport, dose-response, disease transmission, or risk characterization for airborne, waterborne, or foodborne hazards)
	medium	meets one criterion
	low	meets no criterion
	NA	not applicable or not available
Section H, item 1 (robustness of method)		
	high	method applied to multiple datasets of interest with consistent performance
	low	method applied sparsely or with inconsistent performance
	NA	not applicable or not available
Section H, item 2 (representativeness of data)		
	high	agent named on EPA list
	low	related or unrelated agent
	NA	not applicable or not available
Section H, item 3 (generalizability or external validity)		
	high	predictions of model consistent with other data sources and other studies
	low	sparse validation or predictions inconsistent with other data sources and other studies
	NA	not applicable or not available
Section H, item 4 (soundness of study conclusions or internal validity)		
	high	acceptable adequacy, completeness, and soundness of conclusions
	low	marginal adequacy, completeness, and soundness of conclusions based on primary reference
	NA	not applicable or not available
Section H, item 5 (defensibility)		

Template Section and Subsection	Ratings Used	Definitions
	high	method applicable to incident-based MRA of buildings and water systems
	low	method of uncertain usefulness for incident-based MRA of buildings and water systems
	UN	cannot be determined at present

SECTION 3: Microbial Risk Assessment Roadblocks and Recommended Solutions

Information relating to the conduct of microbial risk assessments is relatively incomplete and of highly variable quality. Critical roadblocks to the design of a preliminary biological risk assessment framework, such as data gaps or insufficient detail on models and methods, were encountered in all of the information sources selected for the compendium. Each of the compendium summaries includes an assessment describing how each of these roadblocks affected the outcome of that risk assessment, and provides a recommendation for circumventing the roadblocks where possible. (Some of the roadblocks may require extensive research.) Given the potential immediacy of a biothreat incident, it is recommended that the short-term circumventions be pursued. However, an approach to the long-term strategies needs to be planned as well. Several recommendations are made in the sections that follow.

In the studies reviewed, scientific roadblocks were commonly encountered by scientists conducting MRAs in the EA and DR areas. These were related primarily to incomplete understanding of the processes that influence exposure and delivery of doses, as well as of the progression from colonization or infection to manifestation of adverse effects or illness. Often risk assessors developed solutions that circumvented those roadblocks and permitted RC; these are also discussed. The subsections below discuss the critical roadblocks and gaps, and recommendations for circumventing or filling them, for each of the principal study areas. The major roadblocks encountered in EA and DR for incident-based risk assessment for biothreat agents in buildings and water distribution systems, as well as two RC roadblocks, are summarized in Table 3 (at the end of Section 3).

MRA methodologies developed by U.S. government agencies and international organizations usually involve multi-year plans, internal and external peer review, and public comment, and go through multiple revisions. The following extensively documented microbial risk assessments were under revision at the time of the search and thus were unavailable for inclusion in the compendium:

- USDA MRA: *E. coli* O157:H7 in ground beef, non-typhoid *Salmonella* in eggs and egg products, *Clostridium perfringens* in ready-to-eat meat and poultry products
- FDA MRA: *Vibrio parahemolyticus* in seafood
- WHO/FAO MRA: *Campylobacter* in poultry and *Vibrio* in seafood

In addition, information on the EPA Office of Water risk assessment for waterborne cryptosporidiosis was not reviewed.

3.1 Exposure Assessment Roadblocks

One roadblock in the EA area is the lack of knowledge regarding dosimetry and mechanisms controlling pathogenesis and virulence of inhalation hazards. This might be addressed by developing exposure models for airborne biothreat agents. Such models would benefit from the availability of several types of data, including the behavior of microbial agents in air under variable environmental conditions (e.g., air movement, humidity); the type of source (e.g., point source *vs*. area source); the size, density, and shape of the microbial agent released into air; and the rate of release of the agent into the environment.

Once the behavior and characteristics of the agent in the atmosphere are understood, established models of aerosol deposition and clearance in the human respiratory tract could be

employed to estimate the numbers of microorganisms retained within various parts of the body, including the regions of the respiratory tract (e.g., nasal, tracheobronchial, or alveolar). (The ability of some airborne biological agents to infect a host organism may vary with how many organisms are retained within a particular respiratory-tract region.) Once the number of organisms retained in the body after exposure can be measured or estimated, this information can be combined with the knowledge of the infectious properties of the individual agents to estimate risks of infection or disease.

A second roadblock that becomes clear from a review of the EA studies is that microbial risk assessors encountered an incomplete understanding of the processes that influence exposure and delivery of doses exceeding the "safe" level to the target tissue. Many food-safety risk assessments addressed this roadblock by developing elaborate conceptual "farm-to-fork" process models that describe hypothetical exposure scenarios defined by assumptions of times and temperatures of storage to predict pathogen numbers per serving at food consumption.

Many large, nationally representative datasets provide good-quality data for certain portions of these process models. Reliable, nationally representative data on human behaviors during food production, processing, distribution, preparation, and consumption are not available, however. In addition, the scientific bases for how physiological factors in the host influence exposures to biological agents by ingestion, dermal, or inhalation routes are incompletely understood, limiting reliable prediction of survival (for given exposures) to target tissue.

A third roadblock is the lack of data or theories to support the selection of biologically appropriate distributions or functions in early foodborne exposure assessment models. These early models did not present alternative model structures, systematically account for variability and uncertainty, or conduct sensitivity analyses for rating the importance of alternative interpretations of the data and the underlying model assumptions and structure.

A list of the major roadblocks for all three areas appears in Table 3, at the end of Section 3.

3.2 Dose-Response Roadblocks

Many risk assessors encountered a lack of quantitative data describing the DR relationship for the agent of concern. Often they used a surrogate measure, such as detection of an administered pathogen in feces after a large bolus dose, to approximate colonization or infection of the gastrointestinal tract and to establish a framework. Such an approximation can be appropriate, with full reporting of the time-course under which colonization is established (beyond the clearance of the dose). However, as noted in Table 3, most of the human clinical studies did not provide sufficient level of detail to establish equivalence to true infection.

In addition, both human and animal clinical datasets are typically sparse, with few dose groups, small numbers of individuals per group, and limited or no data at the low doses that are typical of properly prepared foods and properly treated water. Furthermore, mechanistic data with which to model the progression of adverse endpoints, such as diarrhea from colonization or infection, are lacking as well. In some cases, such a relationship is inconsistent with, and poorly predictive of, data for adverse endpoints. However, such a surrogate infection model is likely to be conservative, and, in the absence of more concrete data, may be of benefit to a risk assessor exploring biothreat possibilities.

One specific recommendation that can be made to circumvent DR roadblocks related to insufficient data builds on an approach employed in chemical risk assessment, the use of the "point of departure." This is a semi-quantitative method that could be adapted for biothreat agents from limited epidemiologic or clinical data. It uses the point of departure from an estimate of "safe" dose, such as no observed adverse effect level (NOAEL) or lowest observed adverse

effect level (LOAEL). The body of evidence for biological hazards such as anthrax supports threshold regions in animal clinical studies and human occupational studies below which adverse effects are unlikely. This solution is more scientifically defensible than current "zero tolerance" policies for exposure, which require cleanup to zero detection.

Among the DR templates summarized in the compendium, good-quality data exist for only a few of the organisms on the biothreat list, such as *Cryptosporidium*. (The same is true for the RC disease-transmission templates; *Yersinia* is one of the few examples.) While some data and modeling for EA could be generic – that is, appropriate for multiple biothreat agents – agent-specific dose-response relationships are likely to be necessary. There is considerable diversity in virulence mechanisms and the gene arrays controlling the expression of virulence, as well as in physiological measures of susceptibility in host-pathogen interactions, such as host immune status.

No direct, systematic method for measuring the relative pathogenicity and virulence for enteric pathogens under controlled laboratory conditions exists to date, so surrogates are frequently used. This approach may not be dependable, though. Consider, for instance, three "related" bacterial pathogens used in risk assessments for *E. coli* O157:H7. Two are other enteropathogenic *E. coli* strains, relatively weak pathogens that are fairly closely related, while the third is *Shigella dysenteriae*, a more distant relative that happens to have one virulence factor in common with the others, a Shiga toxin. *Shigella* invades host cells directly, while the enteropathogenic strains are non-invasive. The kinetics of disease progression for invasive and non-invasive pathogens is unlikely to be similar, yet a shigellosis model has been used by multiple risk assessment teams as a surrogate for the dose-response relationship for *E. coli* O157:H7.

3.4 Risk Characterization Roadblocks

The roadblocks discussed above for EA and DR also influence risk characterization. As shown in Table 3, however, a unique roadblock for the RC studies is the premise that qualitative or semi-quantitative microbial risk assessments are less useful to risk managers than quantitative assessments based on incomplete data and assumptions. This leads to reluctance to develop "safe" levels for biological hazards that could multiply under certain conditions. One solution to this roadblock is to adopt an established practice of chemical risk assessors: develop scientific documentation that will justify an existing approach (e.g., the hazard-quotient RC approach).

Many of the models included in the selected RC studies were somewhat hypothetical or theoretical, and largely unvalidated. However, biothreat incidents will also be unvalidated scenarios that must be dealt with on the basis of limited scientific evidence, intelligence information, scientific theory, and assumptions. A review of the studies in the compendium suggested that the use of certain types of data might be a solution to this problem. They are:

- data for related surrogate pathogens for which human clinical data are available
- data from epidemiologic investigations of outbreaks with the pathogen of interest
- data from animal clinical trials
- data from animal clinical trials adjusted by anchoring to epidemiologic surveillance data

The scientific defensibility of applying these solutions to methods for incident-based risk assessment will depend upon the body of evidence for the biothreat agents, the variability of pathogen and host, and the probability that enough of the agent can be delivered in plausible building and water distribution systems scenarios to cause illness.

MRA methods, in turn, could build upon principles and guidance developed in chemical risk assessment. Just as is true in toxicology, a dose of a biothreat agent (chemical) causes an

adverse effect (poisoning). Public perception of biological agents, however, is often that exposure equals illness or even death, independently of the dose.

Microbial risk assessors need a systematic, scientific body of evidence (like that now available in toxicology) to document more fully the dose-response relationships, or relative pathogenicity and virulence, for panels of biological agents at multiple doses, and particularly at low doses. Such a body of evidence would be helpful in increasing public awareness and encouraging open debate about acceptable levels of risk (>0) for pathogens.

3.4 Roadblock-Circumvention Matrix

Table 3 below summarizes the roadblocks and recommended method(s) of circumvention.

Table 3. Summary of Roadblocks and Recommended Circumventions

Roadblock	Recommended Circumvention
Exposure Assessment	
Incomplete understanding of the processes that influence exposure and delivery of doses	*Short term:* Consider development of waterborne scenarios, which may be more defensible than airborne and dermal scenarios. *Long term:* Extend airborne and dermal models for particulates and chemicals to biothreat agents.
Incomplete understanding of scientific bases for host physiological factors influencing exposures by ingestion, dermal, or inhalation routes for biological agents	*Short term:* Use the EPA Exposure Factors Handbook to identify values for calculating estimates of exposure. Exposure estimates should be correlated with the best known dose-response information for each organism or its validated surrogate. *Long term:* Extend body of knowledge from PBPK or compartment modeling of physiological, cellular, and sub-cellular events controlling exposure to target tissue.
Limited data or theories to support the selection of biologically appropriate distributions or functions in early foodborne exposure assessment models	Increase attention to weight-of-evidence approaches to develop cohesive explanation for body of evidence.
Limited consideration of alternative model structures or data interpretations for early foodborne models	Increase attention to weight-of-evidence approaches to develop cohesive explanation for body of evidence.
Limited systematic accounting for variability and uncertainty for early foodborne models	Seek greater transparency and more realistic interpretation of predictions in light of rigor of treatment of variability and uncertainty.
Limited capacity to conduct sensitivity analyses for rating the importance of alternative interpretations of the data and the underlying model assumptions and structure for early foodborne models	*Short term:* Build simpler models that are less cumbersome to modify, run, and interpret. *Long term:* Develop simple approximations that are rigorous and scientifically defensible.

Lack of knowledge on dosimetry and mechanisms controlling pathogenesis and virulence for biothreat agents by priority routes (airborne, waterborne, dermal, foodborne)	*Short term:* Obtain data for priority agents for inhalation and dermal routes, as well as waterborne; foodborne too if scenario becomes a priority. *Long term:* Partner with government and military laboratories to generate data and extend available models from other fields – e.g., toxicology, PBPK modeling.
Dose-Response	
Incomplete understanding of progression from colonization or infection to adverse effects or illness	*Short term:* Model adverse endpoints directly. *Long term:* Generate data to describe mechanisms of pathogenesis and virulence for priority biothreat agents.
Lack of quantitative data describing the DR relationship for the agent(s) of concern	*Short term:* Develop simple qualitative or semi-quantitative models for "safe" levels. *Long term:* Generate data to describe dose-response relationship more quantitatively.
Sparse quantitative data, particularly at low doses	*Short term:* Fit available data to alternative DR functional forms and extrapolate to low-dose region. *Long term:* Generate data to fully describe dose-response relationship, particularly in the low-dose region.
Risk Characterization	
Premise that qualitative or semi-quantitative MRAs are less useful to risk managers than quantitative assessments based on incomplete data and assumptions	Develop scientifically defensible qualitative and quantitative methods in a tiered approach based on availability of data and regulatory need.
Reluctance to develop "safe" levels for biological hazards that could multiply under certain conditions	*Short term:* Promote analytical-deliberative process in scientific and public meetings to engage community in dialogue about dose-response. *Long term:* Partner with risk managers in the government and military to develop scientific databases and decision support tools to respond to changing policy needs.

APPENDIX A: Criteria-Selected References and Reviews

A.1 Exposure Assessment Methods

A.1.1 Ingestion (Food)

Bemrah N., M. Sanaa , M.H. Cassin, et al. 1998. Quantitative risk assessment of human listeriosis from consumption of soft cheese made from raw milk. Prev. Vet. Med. 37(1-4): 129-145. 36

Brown, M.H., K.W. Davies, C.M.-P. Billon, C. Adair and P.J. McClure. 1998. Quantitative microbiological risk assessment: Principles applied to determining the comparative risk of Salmonellosis from chicken products. J. Food Protect. 61(11): 1446-1453. 38

Coleman, M.E., S. Sandberg and S. Anderson. 2003. Impact of microbial ecology of meat and poultry products on predictions from exposure assessment scenarios for refrigerated storage. Risk Anal. 23(1): 215-28. 40

Coleman, M.E., M.L. Tamplin, J.G. Phillips and B.S. Marmer. 2003. Influence of agitation, inoculum density, pH, and strain on the growth parameters of *Escherichia coli* O157:H7 - relevance of risk assessment. Int. J. Food Microbiol. 83: 147-160. 43

Davidson, V.J. and J. Ryks. 2003. Comparison of Monte Carlo and fuzzy math simulation methods for quantitative microbial risk assessment. J. Food Protect. 66(10): 1900-1910.46

Delignette-Muller, M.L. and L. Rosso. 2000. Biological variability and exposure assessment. Int. J. Food Microbiol. 58: 203-212. 48

Duffy, S. and D.W. Schaffner DW. 2001. Modeling the survival of *Escherichia coli* O157:H7 in apple cider using probability distribution functions for quantitative risk assessment. J. Food Protect. 64(5): 599-605. 50

FAO/WHO. 2002b. Risk assessments of *Salmonella* in eggs and broiler chickens. Food and Agriculture Organization/World Health Organization. http://www.who.int/foodsafety/publications/micro/salmonella/en/ 52

FAO/WHO. 2004. Risk assessment of *Listeria monocytogenes* in ready-to-eat foods. Food and Agriculture Organization/World Health Organization. http://www.who.int/foodsafety/publications/micro/mra_listeria/en/ 54

Farber, J.M., W.H. Ross and J. Harwig. 1996. Health risk assessment of *Listeria monocytogenes* in Canada. Int. J. Food Microbiol. 30(1-2): 145-156. 56

FDA/USDA. 2003. Quantitative assessment of relative risk to public health from foodborne *Listeria monocytogenes* among selected categories of ready-to-eat foods. http://www.foodsafety.gov/~dms/lmr2-toc.html 58

Hajmeer, M.N. and I.A. Basheer. 2003. A hybrid Bayesian-neural network approach for probabilistic modeling of bacterial growth/no-growth interface. Int. J. Food Microbiol. 82(3): 233-243. 61

Hald T., D. Vose, H.C. Wegener and T. Koupcev. 2004. A Bayesian approach to quantify the contribution of animal-food sources to human salmonellosis. Risk Anal. 24(1): 255-269. 63

Hope, B.K., A.R. Baker, E.D. Edel et al. 2002. An overview of the *Salmonella enteritidis* risk assessment for shell eggs and egg products. Risk Anal. 22(2): 203-218. 66

Zwietering, M.G. and S.J.C. van Gerwen. 2000. Sensitivity analysis in quantitative microbial risk assessment. Int. J. Food Microbiol. 58: 213-221. 106

A. Exposure Assessment Study Identification (Food)	Bemrah N., M. Sanaa , M.H. Cassin, et al. 1998. Quantitative risk assessment of human listeriosis from consumption of soft cheese made from raw milk. Prev. Vet. Med. 37(1- 4): 129-145.
B. Objectives and Type of Study	1. purpose: scientific; To quantify risk of exposure to *L. monocytogenes* from consumption of soft cheese made from raw milk from a public health perspective. 2. type: EA
C. Publication Attributes	1. sponsors/affiliations: Epidemiology and Animal Health Management Laboratory, Alfort Veterinary School, Maisons-Alfort, France 2. peer-review mechanism: peer-reviewed journal
D. Data and Study Design	1. type: data published on the different sources of milk contamination (environment and mastitis) and bacterial growth 2. source: published literature 3. extent of data: quantitative data of raw milk contamination and growth in cheese 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: to estimate the potential exposure to *L. monocytogenes* in a single serving 2. specific characteristics: Exposure characterized by the probability distribution of *L. monocytogenes* colony-forming units (CFU) in 31-gram servings of cheese (which represents 1/8 of a 250-gram cheese. A table summarizing the various exposure variables is provided along with their assumed distribution. Each one of the exposure variables is discussed and the range of values provided in the literature is provided. Variables include those associated with milk production, cheese processing, consumption, and dose response. 3. assumptions: made for number of farms, herd size, and milk volume per cow; triangular distributions used when exact distributions unknown. Poisson distribution used for organisms distribution in homogeneous liquid. 4. limitations: data retrieved were more than six years old and did not account for recent improvements in hygiene 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions: NA 2. authors' extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: indicated by the assumptions that had to be used in E3 2. proposed solutions: research needed for areas having no available data

H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	Provided a thorough exposure assessment for *L. monocytogenes* which could be used as a template for obtaining the types of data necessary for other pathogens in a similar foodborne exposure scenario.
K. Cross-References	NA

A. Exposure Assessment Study Identification (Food)	Brown, M.H., K.W. Davies, C.M.-P. Billon, C. Adair and P.J. McClure. 1998. Quantitative microbiological risk assessment: Principles applied to determining the comparative risk of Salmonellosis from chicken products. J. Food Protect. 61(11): 1446-1453.
B. Objectives and Type of Study	1. purpose: future regulatory interest; to use existing mathematical models as a Quantitative Risk Assessment (QRA) tool to provide transparent, model-based QRA to allow effective risk communication within food manufacturing business 2. type: EA
C. Publication Attributes	1. sponsors/affiliations: Unilever Research Laboratory 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: size of portion including weight and dimensions, incidence of infectious agent in poultry raw material, level and distribution of microorganisms in raw material 2. source: experimental data, published scientific literature, unpublished internal surveys 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low

E. Method/Model/Approach	1. general characteristics: estimate of risk of salmonellosis due to undercooked chicken consumption, obtained by integration with respect to time, microbial distribution, and extent of cooking 2. specific characteristics: expected risk calculated by integrating frequency of contamination, models describing heating effect, and dose response; lognormal distribution used to describe distribution of microorganisms in raw material; simple log-linear model used to represent fate of microbes during heat treatment 3. assumptions: for thermal inactivation, frozen product counts equaled that in raw material; microbes surviving factory cook used as challenge for home cooking; heat inactivation kinetics in frozen products not significantly different from published values; microbial survivors of heat treatment are infectious 4. limitations: study only considers heating effect on microbial numbers; heat transfer equation used one-dimensional solution based on shortest thermal path instead of three-dimensional solution 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions: risk of infection is very sensitive to “product and cooking attributes” 2. authors’ extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: effects of growth and recontamination not considered 2. proposed solutions: expand model to consider recontamination; extend heat transfer coefficient to a choice of several relevant to different products or processes; use more flexible heat transfer model to account for freezing, thawing, and several processing steps
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: low 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	Brown et al., 1998 in RC

A. Exposure Assessment Study Identification (Food)	Coleman, M.E., S. Sandberg and S. Anderson. 2003. Impact of microbial ecology of meat and poultry products on predictions from exposure assessment scenarios for refrigerated storage. Risk Anal. 23(1): 215-28.

B. Objectives and Type of Study	1. purpose: scientific, future regulatory interest 2. type: EA
C. Publication Attributes	1. sponsors/affiliations: USDA Food Safety and Inspection Service 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: experimental data for microbial growth (Pin and Barnayi 1998; Buchanan and Bagi 1997; ARS Pathogen Modeling Program; Buchanan and Klatwitter 1992); survey data for initial levels and frequency of positive broiler (FSIS, www.fsis.usda.gov/OPHS/baseline/contents.htm) and ground beef samples (FSIS, www.fsis.usda.gov/OA/topics/o157.htm#3) and refrigeration temperatures (Audits International 1999) 2. source: published studies and government datasets 3. extent of data: large datasets for bacterial growth curves in culture broth; large surveys for broiler and ground beef microbial characterization and for refrigeration temperatures 4. sampling plan: factorial design for growth studies under various temperature, pH, salt conditions; probability based sampling for broiler survey; broiler rinsate and ground beef samples analyzed for presence and level of pathogens including *E. coli* O157:H7, *Campylobacter*, *Listeria*, and non-typhoid *Salmonella* and level of total Aerobic Plate Count (APC); additional data generated for *Clostridium perfringens* and *Staphylococcus aureus* not used as model inputs 5. sample size: large number of samples for bacterial growth curves, e.g., 184 curves for *E. coli* O157:H7 model in ARS Pathogen Modeling Program; survey data included 1,297 broiler samples and 563 ground beef samples and 943 samples for refrigeration survey 6. performance characteristics: only simple statistics provided (e.g., means or geometric means, confidence limits on the mean) 7. relevance: high for *E. coli* O157:H7
E. Method/Model/Approach	1. general characteristics: 10,000 iteration Monte Carlo simulation using Latin hypercube sampling from the distributions specified below 2. specific characteristics: beta for probability of contamination; lognormal for initial density of indigenous biota and point estimates for maximal densities reported in surveys for initial densities of pathogens; triangular for refrigeration temperatures and times (point estimates used for maximal growth rates and maximal population densities) 3. assumptions: survey results representative of food supply; total Aerobic Plate Count (APC) representative of indigenous microbiota; pseudomonads plausible surrogates for growth of indigenous microbiota; growth kinetics in broth representative of unconstrained growth in meat and poultry products; growth of indigenous microbiota is self-constraining at 10^9 CFU/g and antagonistic to pathogens at 10^7 CFU/g; microbial populations are homogeneously distributed in meat and poultry products; best case scenario assumed proper refrigeration temperatures throughout production, distribution, and handling; times at selected temperatures expert opinions 4. limitations: unadjusted growth models represent optimal growth in the absence of competitive microbiota

	causing bias in overprediction of growth potential; sparse validation for growth constraints in non-sterile foods, particularly for low initial inoculum levels observed for pathogens under proper handling and storage conditions 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: low frequency of pathogen contamination and growth in broilers and ground beef with proper refrigeration; antagonism of pathogen growth by indigenous microbiota likely in refrigerated meat and poultry products; 2. extrapolations: pseudomonads used as surrogate for heterogeneous population of indigenous microbiota of meat and poultry to constrain maximal growth of pathogens under optimal experimental conditions in culture broth
G. Data Gaps and Proposed Solutions	1. identification of data gaps: distribution of pathogens in solid and liquid foods (random homogeneous or clustered?); time-temperature scenarios and frequencies for US meat and poultry; frequency of deviations from food handling guidance on temperature controls and storage times; 2. proposed solutions: see E.3. and F. above
H. Weight of Evidence	1. robustness of method: high 2. representativeness of data: high 3. generalizability or external validity: high 4. soundness of study conclusions or internal validity: high 5. defensibility: high for threat scenarios that support bacterial growth
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	1. useful for threat scenarios permitting bacterial growth, in biofilms in water distribution systems or for contamination of foods or food service facilities 2. growth may be unlikely in water distribution systems and buildings with adequate security measures
K. Cross-References	NA

A. Exposure Assessment Study Identification (Food)	Coleman, M.E., M.L. Tamplin, J.G. Phillips and B.S. Marmer. 2003. Influence of agitation, inoculum density, pH, and strain on the growth parameters of *Escherichia coli* O157:H7 - relevance of risk assessment. Int. J. Food Microbiol. 83: 147-160.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific, regulatory interest - Article focuses on uncertainty in extrapolation

	of kinetic models for growth generated in culture broth to food matrices. 2. type: EA
C. Publication Attributes	1. sponsors/affiliations: University of Maryland Eastern Shore, USDA Food Safety and Inspection Service and Agricultural Research Service, Eastern Regional Research Center 2. peer-review mechanism: scientific journal review
D. Data and Study Design	1. type: Current studies were designed to address four factors that may bias exposure assessment models for *Escherichia coli* O157:H7: temperature, initial density of the pathogen, agitation or aeration, and strain. 2. source: targeted research 3. extent of data: large datasets for bacterial growth in culture broth and microtiter plates; nine strains were used 4. sampling plan: factorial design 5. sample size: Study included a 2x2x3 factorial design to evaluate initial density, a 2x2 design was selected to evaluate effects of lower pH. Approximately 10 to 25 observations were made over the full range of the growth curve at each incubation temperature. Approximately six observations were obtained for the multi-strain experiments. 6. performance characteristics: NA 7. relevance: high
E. Method/Model/Approach	1. general characteristics: Study characteristics included a 2x2x3 factorial design with duplicate flasks used for each combination of initial density. A 2x2 design was selected to evaluate the effects of lower pH at 10C in the flask system. Two experimental designs were developed for the qualitative screening assays of growth/no-growth interface for the nine strains using a microtiter plate format. 2. specific characteristics: For the factorial design, 10 to 25 observations were obtained for each treatment over the full range of the growth curve at each incubation temperature. At least six observations per treatment were obtained for the multi-strain experiments. Growth/no growth was visually assessed in duplicate experiments. Kinetic data from the experiments were fit to simple linear regression and the Baranyi models. 3. assumptions: NA 4. limitations: NA 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: The growth/no-growth interface observed in microtiter plate assays was temperature dependent. At pH 5.5, near the lower limit of growth temperature for *E. coli* O157:H7, strain variability for the panel of strains isolated from beef, agitation, and initial density appeared as a relatively minor effect, compared to the significance of agitation and initial density treatments on kinetic parameters. 2. authors' extrapolations from the observed data to other populations or conditions: Factors that may contribute to shorter lag and higher growth rate and maximum population density (MPD) in vigorously agitated liquid media may be a greater availability of dissolved oxygen and the cells under shaken conditions are less likely to remain

	clustered in microcolonies. The current study design was sufficient to demonstrate statistical significance of the slope parameters for all four treatments at 10C. The results caution against simplifications of the complex community of competing bacterial species in foods without systematic study. The effects of agitation, initial density, pH, and strain were significant for growth kinetics near the boundaries of the growth/no-growth interface for *E. coli* O157:H7.
G. Data Gaps and Proposed Solutions	1. data gaps: Risk assessors have not fully incorporated the extensive body of evidence on microbial ecology of foods. 2. proposed solutions: Risk assessors should evaluate the uncertainty in predictions of growth kinetics at the 1- to- 2-day period recommended by FSIS for refrigerated storage in consumers' homes. Develop testable scenarios that depict potential deviations from proper handling to determine the probability and extent of growth in nonsterile ground beef that was temperature abused.
H. Weight of Evidence	1. robustness of method: high 2. representativeness of data: high 3. generalizability or external validity: high 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	Article provides a detailed account of some of the factors that contribute to the growth of the pathogen *E. coli* O157:H7 at less than optimal conditions.
K. Cross-References	NA

A. Exposure Assessment Study Identification (Food)	Davidson, V.J. and J. Ryks. 2003. Comparison of Monte Carlo and fuzzy math simulation methods for quantitative microbial risk assessment. J. Food Protect. 66(10): 1900-1910.
B. Objectives and Type of Study	1. purpose noted by study authors: evaluate and compare the use of fuzzy values and probability distributions to represent variability and uncertainty in risk assessment 2. type: EA
C. Publication Attributes	1. sponsors/affiliations: Ontario Ministry of Agriculture and Food; University of Guelph, Canada. 2. peer-review mechanism: scientific journal review

D. Data and Study Design	1. type: published and unpublished data on levels of *Campylobacter jejuni* in poultry at various stages of processing 2. source: Berrang and Dickens, 2000; Oosterom et al., 1983; Izat et al., 1988; Abu-Ruwaida et al., 1994; Cason et al., 1997; Line (unpublished data) 3. extent of data: extensive data on changes in levels of *Campylobacter jejuni* on chickens due to processing at five stages of poultry processing 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: high
E. Method/Model/Approach	1. general characteristics: comparison between the use of fuzzy simulation (i.e., fuzzy values and interval arithmetic) and Monte Carlo simulation (i.e., probability distributions and Latin Hypercube sampling) to model variability and uncertainty in exposure assessment 2. specific characteristics: Monte Carlo simulation was performed with @Risk using 10,000 iterations and Latin Hypercube sampling; fuzzy multiplication of three or more terms used the approximation method of Giachetti and Young (1997); exposure estimates were modeled in each of the 5 steps included in the poultry preparation process described by Fazil et al. (1999) - soft scald, defeathering, eviscaration, washing and chill with chlorinated water 3. assumptions: distributions for variability and uncertainty could be represented with triangular membership functions (fuzzy approach) and triangular probability distributions (Monte Carlo approach); cross-contamination could occur during defeathering and evisceration processes 4. limitations: correlations between probability distributions were not considered in the Monte Carlo simulation approach, which may have increased the probability of extreme values, and the skew in the risk distributions, if the data indicated there was correlation among the extreme values of the input distributions 5. relevance: high
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: estimates of the mean concentration of *C. jejuni* at each processing step were similar between the two simulation approaches, and were generally consistent with literature values (authors do not cite the sources of the literature values that are referred to); the ranges of simulated values produced with the fuzzy simulation approach were greater than the range produced with the Monte Carlo approach 2. extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: high

	2. representativeness of data: high 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility: high
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	The paper describes in general terms how and when fuzzy simulation may be appropriate (possibly for incident-based microbial risk assessment of buildings and water systems) but does not offer a specific model or data that are directly applicable; the paper provides references to data on the concentration of *C. jejuni* that may be useful; not clear from the paper if uncertainty in parameter estimates was considered in the exposure assessment (despite the stated objective of the research)
K. Cross-References	Berrang and Dickens, 2000; Fazil, et al. 1999; Giachetti and Young, 1997; McNab, 1998

A. Exposure Assessment Study Identification (Food)	Delignette-Muller, M.L. and L. Rosso. 2000. Biological variability and exposure assessment. Int. J. Food Microbiol. 58: 203-212.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific; to assess the effect of intra-species variability and uncertainty in microbial growth parameters on the predicted final microbial density 2. type: EA
C. Publication Attributes	1. sponsors/affiliations: Laboratory of Microbial Parasitic Ecology, France; Groupe DANONE, France 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: experimental data for microbial growth parameters for *Bacillus cereus*. 2. source: published literature; expert opinion 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: The study examines the results of varying the growth parameters and shelf-life

	conditions of *Bacillus cereus* in pasturized milk. 2. specific characteristics: distributions for variability or uncertainty for growth parameters, initial and maximum level of contamination, and storage temperatures/duration were based on data from literature and expert opinion. Simple logistic or Perl-Verlhurst model for primary growth (Baranyi and Roberts, 1994); square root type models used to describe temperature effects, gamma model (Zweitering et al., 1996) and the CTMI model (Rosso et al., 1993); 10,000 simulations using Latin Hypercube sampling. 3. assumptions: storage and transport scenarios were representative of actual conditions 4. limitations: temperature during transport from producer to purchase not considered; lag time for microbial growth was not considered 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: intra-species variability on microbial growth parameters for *B. cereus* may have great impact on accuracy of exposure assessment. 2. extrapolations: may also see similar results for *Listeria monocytogenes*
G. Data Gaps and Proposed Solutions	1. data gaps: data for optimal and maximal growth temperature, and maximal density of microorganisms were not adequate to fit statistical distribution shelf-life data (assumed BetaPERT distributions for these model parameters) 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: low 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	may be useful for contamination of storage facilities
K. Cross-References	NA

A. Exposure Assessment Study Identification (Food)	Duffy, S. and D.W. Schaffner DW. 2001. Modeling the survival of *Escherichia coli* O157:H7 in apple cider using probability distribution functions for quantitative risk assessment. J. Food Protect. 64(5): 599-605.

B. Objectives and Type of Study	1. purpose noted by study authors: scientific, future regulatory interest 2. type: EA
C. Publication Attributes	1. sponsors/affiliations: New Jersey Agricultural Station 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: experimental data for *E. coli* O157:H7 growth under different conditions of storage temperature and preservative use/type 2. source: published studies (Dingman, 1999, 2000; Garfand-Miller & Kaspar, 1994; Leyer et al., 1995; Roering et al., 1999; Ryo & Beuchat, 1998; Semanchek & Golden, 1996; Zhao et al., 1993) 3. extent of data: adequate experimental studies from 8 separate articles examining growth and decline of *E. coli* in apple cider storage conditions primarily varying temperature and preservative use/type across 9 different strains of *E. coli* O157:H7 4. sampling plan: studies appear to be single-factor designs (one independent variable each) 5. sample size: NA 6. performance characteristics: considerable variation in study protocols (inconsistent parameters include inoculum size, volume of cider, apple cultivar, bacterial strain, and enumeration media/frequency) and study results; statistical methods are NA 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: 1,000 iteration Monte Carlo simulations sampling from distribution functions generated for each temperature and preservative condition as stated below 2. specific characteristics: logistic for cider held under ideal refrigeration and refrigeration abuse, logistic and uniform for cider held at room temperature, beta for cider treated with sodium benzoate, normal for cider treated with potassium sorbate, and gamma for cider treated with both sodium benzoate and potassium sorbate 3. assumptions: first-order kinetics for extrapolated change in *E. coli* concentration/day if enumeration was completed less frequently than once per day in the studies, an inoculum size of 5 log CFU/mL is a representative initial concentration of *E. coli* for simulations, competition from indigenous microbiota in cider was representative in studies, handling of cider before testing was consistent among studies and indicative of farm-to-fork handling 4. limitations: published data points represent averages from the original studies so the potential range of the original data is lost, no available technique to differentially weight raw data studies based on adherence to cider mill-like experimental conditions, and highly variable study results were incorporated into the probability distribution function (PDF) with this variation likely attributed to factors including: widely varying incubation volumes of cider (up to 100-fold difference the stated lowest and highest volume), different apple cultivars and enumeration media used (selective vs. recovery), and different strains of tested *E. coli* 5. relevance: medium
F. Study Conclusions and Extended	1. conclusions supported by the data: *E. coli* O157:H7 simulated concentrations in apple cider showed a general

Applications	decline with time at any of the modeled temperature and preservative conditions, although variation in growth rate increased with increasing temperature 2. extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: conflicting published results, study method/results non-generalized 2. proposed solutions: standardized guidelines for conducting studies so results can be generalized
H. Weight of Evidence	1. robustness of method: high 2. representativeness of data: high 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility: high
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	1. useful for threat scenarios involving *E. coli* O157:H7 contamination of consumable liquids similar in pH (~3-4) and chemical content to apple cider 2. other comments by reviewer: growth might be unlikely in processing/distribution/consumption buildings with adequate security, and authors acknowledges limitations of available data because of non-standard methods
K. Cross-References	NA

A. Exposure Assessment Study Identification (Food)	FAO/WHO. 2002b. Risk assessments of *Salmonella* in eggs and broiler chickens. Food and Agriculture Organization/World Health Organization. http://www.who.int/foodsafety/publications/micro/salmonella/en/
B. Objectives and Type of Study	1. purpose: scientific and future regulatory interest; compile currently available information relevant to risk assessment of *Salmonella* in eggs and broiler chickens; identify data gaps; develop example risk assessment models; consider efficacy of some risk management interventions 2. type: EA
C. Publication Attributes	1. sponsors/affiliations: FAO/WHO 2. peer-review mechanism: Technical Report initiated in 1999 and reviewed several times during preparation and after completion through consultations and by an extensive list of selected reviewers and members of the public during a public comment period
D. Data and Study Design	1. type: prevalence of the pathogen

	2. source: international data collected during this risk assessment and published studies 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: Monte Carlo simulation model of hypothetical exposures to contaminated servings of eggs and broilers modeled based on data and assumptions, including US model under revision 2. specific characteristics: “generic” risk assessment model “deliberately configured and parameterized NOT to represent any one country; scenarios defined for baseline risk and undercooking for broilers 3. assumptions: contamination of hens and eggs occurs at constant frequency independent of host, bacterial strain, and environmental, seasonal, regional, and demographic factors; flocks of hens and eggs are homogeneous; contamination is random and independent of hen/egg age and other host, bacterial, or environmental factors 4. limitations: influential parameters based on expert opinion or assumption unvalidated 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions: assumptions of storage times and temperatures are influential in modeling counts per serving 2. authors’ extrapolations: the general framework and analysis may be adapted to a country or region with development and inclusion of country-specific data for model inputs
G. Data Gaps and Proposed Solutions	1. data gaps: prevalence and levels of the pathogen from representative national surveys; preparation and consumption patterns among consumers, including times and temperatures of storage; validation of predictive microbiology models for growth and survival; biology of host-pathogen interaction for hens (and humans) 2. proposed solutions: conduct targeted research; elicit expert opinion
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: low 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	generic model based on pooled data from multiple sources and countries of origin and assumptions may not support rigorous science-based modeling; 2004 update of US work cited by authors in draft form (USDA/FSIS 1998) is more relevant for compendium review upon release anticipated in October
J. Reviewer Comments	NA

K. Cross-References	NA

A. Exposure Assessment Study Identification (Food)	FAO/WHO. 2004. Risk assessment of *Listeria monocytogenes* in ready-to-eat foods. Food and Agriculture Organization/World Health Organization. http://www.who.int/foodsafety/publications/micro/mra_listeria/en/
B. Objectives and Type of Study	1. purpose: scientific and future regulatory interest; undertaken at request of the Codex Committee on Food Hygiene for scientific advice as a basis for future development of guidelines. 2. type: EA
C. Publication Attributes	1. sponsors/affiliations: FAO/WHO 2. peer-review mechanism: Technical Report reviewed several times during preparation and after completion through consultations and by an extensive list of selected reviewers and members of the public during a public comment period
D. Data and Study Design	1. type: prevalence data, limited concentration data for European commodities, limited data for US and Canadian consumption, microbial ecology in food 2. source: studies derived for other purposes that have been published in scientific literature, reports from regulatory agencies, consumption surveys, outbreak investigations reports, and industry files. 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: four hypothetical EA models for *L. monocytogenes* in pasteurized milk, ice cream, fermented meats, and cold-smoked fish; predictive modeling for growth, survival and inactivation of *L. monocytogenes* in laboratory broth media and some foods. 2. specific characteristics: hypothetical scenarios developed using semi-quantitative and quantitative methods; pooling data from multiple sources with and without weighting; growth modeled from retail to consumption using models with positive bias, such that growth may be overestimated; 3. assumptions: serving size and frequency of consumption by sub-population; distribution of the pathogen in foods 4. limitations: sampling methodology and test protocols not considered before pooling data from multiple sources;

	consumption based on US and Canadian data; enumeration data based on European studies; contamination data often not "recent, systematic, quantitative, or representative for different countries" 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions: outputs included distributions for the frequency of contaminated servings and the number of servings per year by size of serving for four hypothetical models 2. authors' extrapolations: studies assumed representative of multiple countries, commodities
G. Data Gaps and Proposed Solutions	1. data gaps: specific data pertaining to consumption, prevalence, concentration 2. proposed solutions: estimates based on scientific knowledge and predictive microbiology models
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: low 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	provides four hypothetical examples for different food products
K. Cross-References	same study in DR, RC; FDA/USDA, 2003 in EA, DR, RC

A. Exposure Assessment Study Identification (Food)	Farber, J.M., W.H. Ross and J. Harwig. 1996. Health risk assessment of *Listeria monocytogenes* in Canada. Int. J. Food Microbiol. 30(1-2): 145-156.
B. Objectives and Type of Study	1. purpose: scientific, regulatory; Major steps used in the formulation of a health risk management for *L. monocytogenes* in foods are discussed. 2. type: EA
C. Publication Attributes	1. sponsors/affiliations: Health Canada, Food Directorate 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: experimental data for microbial growth for meats and dairy products; growth kinetic models employed where possible

	2. source: data from Agri-Food and Agriculture Canada; Disappearance data for cheese from Statistics Canada 3. extent of data: Some data for bacterial growth, predictive modeling 4. sampling plan: model design for growth under two temperature conditions 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: growth kinetic model for two temperatures (4 deg C and 8 deg C) 2. specific characteristics: growth model indicates that level of cells increase from 1 cell to about 10 E5 in just under 40 days at 4 deg C, while at 8 deg C, the same levels can be achieved in about 15 days. 3. assumptions: none reported 4. limitations: none reported 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: temperature abuse is partly responsible for the wide range of levels of *L. monocytogenes* observed in food at the retail level. 2. authors' extrapolations from the observed data to other populations or conditions: None reported
G. Data Gaps and Proposed Solutions	1. data gaps: frequencies of *L. monocytogenes* levels in other foods; more data points and general relevance to public threat of listeriosis 2. proposed solutions: gather more data for enumeration and growth kinetic models at various temperatures and various food matrices.
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: low 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	Useful for predicting growth curves of pure cultures of *L. monocytogenes* at 4 and 8 deg C in some matrices.
K. Cross-References	Farber J.M. et al, 1995 in DR, RC

A. Exposure Assessment Study Identification (Food)	FDA/USDA. 2003. Quantitative assessment of relative risk to public health from foodborne *Listeria monocytogenes* among selected categories of ready-to-eat foods. http://www.foodsafety.gov/~dms/lmr2-toc.html
B. Objectives and Type of Study	1. purpose: future regulatory interest; to estimate exposure in 23 ready-to-eat food categories from presence and levels of contamination, growth or decline during storage, and consumption amounts and frequency per year for three US populations of concern 2. type: EA
C. Publication Attributes	1. sponsors/affiliations: US Department of Health and Human Service, Food and Drug Administration's Center for Food Safety and Applied Nutrition (DHHS/FDA/CFSAN) in collaboration with US Department of Agriculture's Food Safety and Inspection Service (USDA/FSIS). 2. peer-review mechanism: Two reviews of previous drafts of the model and its underlying assumptions conducted by the National Advisory Committee on Microbiological Criteria for Foods; draft risk assessment also made available for public comment (6-month period)
D. Data and Study Design	1. type: numerous data sets including published scientific literature, food intake surveys, health statistics, unpublished food product surveys acquired from state and federal public health officials and trade associations and surveys specifically designed to augment the data available for the risk assessment. 2. source: published data and government and industry sources 3. extent of data: Numerous published and government epidemiological reports, two large food consumption surveys, surveys for refrigeration storage times for frankfurters, and for the temperature of home refrigerators, microbial growth data in culture broth/foods. 4. sampling plan: NA 5. sample size: large for many variables in the model; sparse for quantitation of the pathogen when present in foods 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: estimate levels and frequency of exposure for all 23 food categories at consumption, including potential *Listeria monocytogenes* growth and inactivation due to cooking or reheating prior to consumption. 2. specific characteristics: data available for foods representing the 23 food categories analyzed qualitatively and quantitatively to provide an overall estimate of number of servings containing various levels of the pathogen; relative rankings of likelihood of consuming a potentially contaminated serving computed; log normal distributions used for levels of contamination. 3. assumptions: data from US and international outbreaks equally valid; results from a large number of a one or two day survey interviews representative of annual consumption patterns; data for individual foods are representative of the food categories as whole, ignoring potential seasonal, compositional, geographic and other

	factors. 4. limitations: the amounts and exact types of foods consumed often not directly measured; for example, sandwich consumption modeled using proportion of the food of interest in a standard sandwich recipe; milk servings not determined nor the state of the milk (raw or pasteurized). No demographic data was collected with the food consumption data. Quantitative enumeration data for naturally contaminated foods are sparse. Data were weighted for geographic and temporal relevance. 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions: 2. authors' extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: no systematic quantitative surveys of US food supply exists for this pathogen; strain variability in foods not well characterized, particularly regarding the fraction of *Listeria* spp. in foods expressing virulence factors; ability to compare across all 23 food categories problematic for some poorly represented food categories; growth models largely unvalidated 2. proposed solutions: conduct systematic surveys and targeted research
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: low 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	Interesting study begun in 1999 and completed after multiple rounds of peer review and public comment in 2003; extensive and useful discussion of rationale for extrapolations and assumptions; large interest nationally and internationally in pathogen, largely due to ubiquitous distribution, ecological niche and physiological advantage of growth under refrigeration conditions; approach sensitive to the nuances of consumption and microbial growth as they affect the final exposure; general approach for relative ranking well considered, potential for indirect application to incident based risk assessment for biothreat agents
K. Cross-References	same study in DR, RC

A. Exposure Assessment Study Identification (Food)	Hajmeer, M.N. and I.A. Basheer. 2003. A hybrid Bayesian-neural network approach for probabilistic modeling of bacterial growth/no-growth interface. Int. J. Food Microbiol. 82(3): 233-243.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific 2. type: EA
C. Publication Attributes	1. sponsors/affiliations: University of California at Davis, California Department of Transportation 2. peer-review mechanism: scientific journal review
D. Data and Study Design	1. type: published data on *Escherichia coli* R31 growth in laboratory media 2. source: Salter et al., 2000 3. extent of data: n = 179 outcomes for growth/no growth related to explanatory variables (temperature, water activity) 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: combination of artificial neural network and Bayesian statistics were used to predict growth or no growth of *E. coli* given temperature and water activity as predictors 2. specific characteristics: artificial neural network and Parzen's probability distribution function estimator were used to calculate likelihood functions for growth/no growth; prior probabilities for growth/no growth were estimated directly from data as the proportion of observed growth/no growth divided by sample size; posterior probabilities were calculated using Bayes' theorem 3. assumptions: NA 4. limitations: approach was based on data from one study; very limited validation of approach 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: approach described performed better than nonlinear logistic regression and linear logistic regression for the given data and the selected performance criteria - fraction of predictions that were correct and false alarm rate (predicted growth when no growth was observed) 2. extrapolations: authors suggest the model could be added to a risk assessment model, and could be modified for real time analysis (e.g., using monitoring data for operating parameters of a process), approach may be useful to predict probability of growth of *E. coli* O157:H7 in food
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: low

	2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	NA

A. Exposure Assessment Study Identification (Food)	Hald T., D. Vose, H.C. Wegener and T. Koupcev. 2004. A Bayesian approach to quantify the contribution of animal-food sources to human salmonellosis. Risk Anal. 24(1): 255-269.
B. Objectives and Type of Study	1. purpose noted by study authors: regulatory 2. type: EA
C. Publication Attributes	1. sponsors/affiliations: Danish Institute of Food and Veterinary Research 2. peer-review mechanism: scientific journal review
D. Data and Study Design	1. type: Reported cases of human salmonellosis by sero and phage-type, prevalence of *Salmonella* sero- and phage-types in livestock and poultry flocks, and amount of meat and poultry available for consumption 2. source: Reported cases of human salmonellosis by sero and phage-type, including information on how many cases were preceded by traveling abroad or were determined to be part of an outbreak (Statens Serum Institute), prevalence of *Salmonella* sero- and phage-types in meat and poultry flocks (Danish Veterinary and Food Administration and Danish Institute of Food and Veterinary Research), and amount of meat and poultry available for consumption (Danish Veterinary and Food Administration and Danish Institute of Food and Veterinary Research) 3. extent of data: Data for Denmark in 1999. 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low

E. Method/Model/Approach	1. general characteristics: model developed to quantify the contribution of each major animal-food source to reported human salmonellosis cases in Denmark 2. specific characteristics: Bayesian stochastic model estimating the contribution of each major animal-food source to reported human salmonellosis cases 3. assumptions: A number of assumptions about the distribution of phage types within sero-types are made. Phage type distributions are assumed to be different for travelers and non-travelers. They are estimated based on phage-typed salmonellosis cases. Assumptions about the numbers of non-phage-typed cases that belong to outbreaks are also made. The probability that a Salmonellosis case traveled prior to infection is different for each phage-type. This quantity is estimated based on the Salmonellosis cases for which travel behavior was reported. These assumptions are made to account for incomplete reporting on human Salmonellosis cases. The basic model assumes that the expected number of human Salmonellosis cases by food source and phage- and sero- type is proportional to 1) the amount of an animal source food available for consumption, 2) the prevalence of that phage- and sero-type in the food source, 3) bacteria dependent factors for sero- and phage-type, and 4) food source dependent factors. Bacteria and food source factors are assumed a priori to have uniform distributions. Bacteria factors are assumed to be the same for all phage-types within a sero-type. The lower endpoint of the uniform distributions were all set to zero. The upper endpoints were determined by trial and error to be sufficiently wide such that the upper tails of marginal posterior distributions of these quantities were not arbitrarily cut-off. 4. limitations: This type of model can result in highly multi-modal posterior values if there are not some *Salmonella* sero- and phage-types that occur almost exclusively in only one animal food source, i.e., it could appear that several vastly different attributions of Salmonellosis cases to food sources are highly likely. This method requires intensive monitoring of human Salmonellosis cases and the presences of *Salmonella* bacteria in animal food sources. Phage typing is not performed on all reported cases of human Salmonellosis, nor is information on traveling prior to infection. 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: The quantitative statements (with associated uncertainty) produced by the model developed are helpful to policy makers in assessing the relative risk from various food sources, which can be used to direct national and international control programs aimed at reducing human Salmonellosis cases. 2. authors' extrapolations: Being able to detect statistically significant changes over time in the animal-food source of human Salmonellosis cases would assist policy makers in assessing the effectiveness of changes to control programs.
G. Data Gaps and Proposed Solutions	1. data gaps: Some of the uncertainty in the results is due to incomplete reporting of phage-type and prior travel behavior of salmonellosis cases. 2. proposed solutions: The authors do not specifically propose a solution, as intensive data collection was required to get the level of detailed data used in this study.
H. Weight of Evidence	1. robustness of method: low

	2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	NA

A. Exposure Assessment Study Identification (Food)	Hope, B.K., A.R. Baker, E.D. Edel et al. 2002. An overview of the *Salmonella enteritidis* risk assessment for shell eggs and egg products. Risk Anal. 22(2): 203-218.
B. Objectives and Type of Study	1. purpose noted by study authors: regulatory, future regulatory interest; to establish baseline risk of foodborne illness from *Salmonella enteritidis* (SE), to identify and evaluate potential risk mitigation strategies, to identify data gaps related to future research efforts 2. type: EA
C. Publication Attributes	1. sponsors/affiliations: USDA, Food Safety and Inspection Service 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: data on ecology of SE in layer hens, shell eggs, human behavior in the US; data on when and how rapidly SE grows in eggs; data on SE reduction from pasteurization of egg products 2. source: published studies and government datasets 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: model built of 5 separate modules in Excel spreadsheet to generate baseline results 2. specific characteristics: Monte Carlo simulation performed with @Risk comprised 1,000 iterations; each iteration performed calculations with randomly selected values from each distribution within model using Latin

	Hypercube sampling 3. assumptions: prevalence in spent hens representative of commercial hens; no growth assumed for egg white 4. limitations: data limited or non-existent for many variables so distributions generally based on expert opinion; contamination from obvious sources (food handlers, restaurant environment, etc.) not included; model does not yet separate uncertainty from inherent variability of the system 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: baseline model estimates average production of 2.3 million SE-contaminated shell eggs/year of the estimated 69 billion produced/year; number of SE bacteria/egg ranges from 1-400, most containing <40; each SE-contaminated egg could contribute to average of 4.4 servings 2. extrapolation: NA
G. Data Gaps and Proposed Solutions	1. data gaps: epidemiology of SE on farms, bacteriology of SE in eggs, human behavior in food handling and preparation, times and temperatures of egg storage 2. proposed solutions: more research in these areas is needed
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: low 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	summary of draft risk assessment (1998) updated and expanded in 2003; revision unavailable for compendium review as USDA is addressing peer review comments
K. Cross-References	same study in RC

A. Exposure Assessment Study Identification (Food)	Lindqvist, R. and A. Westoo. 2000. Quantitative risk assessment for *Listeria monocytogenes* in smoked or gravad salmon and rainbow trout in Sweden. Int. J. Food Microbiol. 58(3): 181-196.
B. Objectives and Type of Study	1. purpose noted by study authors: Scientific; To develop a quantitative risk assessment model in which the exposure and risk of acquiring listeriosis from consumption of package smoked or gravad salmon and rainbow

	trout were estimated. 2. type: EA
C. Publication Attributes	1. sponsors/affiliations: National Food Administration, Uppsala, Sweden 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: Prevalence data and concentration data for *L. monocytogenes* in packaged smoked or gravad salmon/rainbow trout based on surveys. Consumption(i.e., serving size) data for cold cuts and salmon. 2. source: Published studies for prevalence: Liva-Lab Stockholm (1993); Rohl (1996); Rohl (1995); SLV (1995); Loncarevic et al. (1996) and Detmer and Blomgren (1995). Published studies for concentration: SLV (1995) and Loncarevic et al. (1996). Consumption data from Nordisk Ministerrad Kobenhavn (1998) and SLV (1988). 3. extent of data: Prevalence and concentration data from 6 surveys. Based on these surveys, prevalence rates, ranging between 0.039 to 0.229 were determined. For concentration data, two surveys with different detection limits of 10 and 100 were used. The level in nondetects were assumed to be 1 and 10 cfu g^{-1}, respectively. Concentrations ranged from <10 to 132,000; 1.5 % of positive samples were $>10^4$ cfu g^{-1}. Consumption data ranged from 50 g to 175 g based on servings for cold cut meats and specific salmon products. 4. sampling plan: not provided. 5. sample size: For the prevalence data, prevalence rates from the six surveys based on: 2 positives/51 samples; 3 positives/32 samples; 3 positives/29 samples; 17 positives/103 samples; 16 positives/94 samples; 8 positives/35 samples. Sample size for concentration data: a total of 33 samples were positive out of 197 samples (all studies combined). Sample size for serving size not provided. 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: Various distributions were assumed for the data. 2. specific characteristics: A cumulative distribution assuming a minimum and maximum prevalence of 1 and 25% was derived and used for the study; for concentration, the data were described by a cumulative distribution assuming minimum and maximum level of 1 and 10^6 cfu g^{-1}, respectively. For serving size, the distribution for serving sizes was described by a modified triangular distribution based on parameters for minimum, maximum, and most likely serving sizes and by estimates of the percentages of servings below the minimum and maximum serving sizes. 3. assumptions: Concentrations of nondetects assumed to be 1 and 10 cfu g^{-1}. Assumed packaged salmon and rainbow trout as one hazard whether gravad, cold- or hot-smoked. Assumed all food would be stored at recommended temperature after purchase; however, proper storage conditions depend on consumer. 4. limitations: Concentration data limited by detection limits. 5. relevance: low
F. Study Conclusions and Extended	1. conclusions supported by the data: No conclusions warranted. Data served as input to the model.

Applications	2. authors' extrapolations from the observed data to other populations or conditions: None provided.
G. Data Gaps and Proposed Solutions	1. data gaps: prevalence and concentration in specified fish products; consumption data; growth data; data on times and temperatures of storage prior to consumption 2. proposed solutions: gather more data from national surveys
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: low 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	same study in DR, RC

A. Exposure Assessment Study Identification (Food)	Marks, H. and M. Coleman. 1998. Estimating distributions of numbers of organisms in food products. J. Food Protect. 61(11): 1535-1540.
B. Objectives and Type of Study	1. purpose: Future regulatory. Methods review for sampling and measurement error (fitting distributions of organisms in food). Use in exposure models estimating distribution of organisms in food for microbial risk assessments 2. type: EA
C. Publication Attributes	1. sponsors/affiliations: Prepared for the session Quantitative Microbial Risk Assessment sponsored by ILSI-N.A and the National Food Producers Association, 84th session. Acknowledged US Department of Agriculture (USDA), Food Safety Inspection Service (FSIS) and National Agricultural Library. 2. peer-review mechanism: scientific journal review
D. Data and Study Design	1. type: Differential equations presented to demonstrate the relationship between "true" values and observed or measured values (Burmaster and Anserson, 1994; CDC, 1993; Cohrssen and Covello, 1989; Coleman and Marks, 1998) ; microbial load in raw ground meat (USDA, 1996 refs for beef, chicken, and turkey); infectious dose of *Clostridium perfringens* (Labbe, 1989)

	2. source: Published studies, Government databases 3. extent of data: Example 1 examines the regulatory objective to assure safety of cooked, ready-to-eat meats produced with process deviations from good manufacturing practices. *C. perfringens* is used as the model food pathogen for determining relative growth. Example 2: Discusses measurement error for *Salmonella* concentrations determined via MPN for ground beef and poultry. 4. sampling plan: Example 1:random from a truncated subset of USDA data, from the gamma distribution 5. sample size: Example 1: large number of samples (452 plate counts) 6. performance characteristics: NA 7. relevance: high
E. Method/Model/Approach	1. general characteristics: Example 1: Method of moments (MOM) and maximum likelihood estimation MLE) used to fit the gamma population distribution. Example 2: Binomial distribution 2. specific characteristics: Example 1: Poisson measurement distribution (direct plate counts); gamma distribution (population distribution); Example 2: Differential equations used to express possibility of a positive sample and probability of a negative sample for a perfect test. BestFit software used for analysis. Kolmogrov-Smirnov test used as a criteria of selection to select the log normal distribution. 3. assumptions: Example 1: The initial density before cooling is low and gas forming anaerobes (GFA) serve as an appropriate indicator for *C. perfringens*. 4. limitations: Sample descriptions limited for Example 2. 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions: plausible exposure assessment for pathogens in food requires accounting for measurement variability of the test instrument and use of data analysis to estimate the underlying population distributions from observed or measured distributions 2. authors' extrapolations: Concentration of ingested pathogens might be used to predict when the system is working correctly under HACCP plans or standard operating procedures, as long as measurement and sampling error is accounted for. Apply the methods discussed to outbreak data in dose reconstruction modeling.
G. Data Gaps and Proposed Solutions	1. data gaps: Example 1: Initial density of *C. perfringens* spores and negative cells before cooling is unknown. The percentage of spores and vegetative cells in the total count, the percentage of spores that germinate after cooking, and distribution in samples is unknown 2. proposed solutions: Example 1:Develop a series of conservative assumptions which require validation (temporary solution)
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: high 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high

	5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	Mentions a companion paper (Coleman and Marks, 1998)

A. Exposure Assessment Study Identification (Food)	Marks, H.M., M.E. Coleman, C.-T. J. Lin and T. Roberts. 1998. Topics in microbial risk assessment: Dynamic flow tree process. Risk Anal. 18(3): 309-328.
B. Objectives and Type of Study	1. purpose: scientific, future regulatory interest; a systematic approach to risk assessment, employing data analysis for developing parsimonious models and accounts for variability and uncertainty of model inputs 2. type: EA
C. Publication Attributes	1. sponsors/affiliations: USDA Food Safety and Inspection Service 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: experimental data for growth and decline of pathogen (*E. coli*); survey data for consumption data and prevalence of pathogens in ground beef; outbreak investigation data for initial densities of pathogen 2. source: published studies and government datasets 3. extent of data: large databases for consumption and prevalence in ground beef; adequate experimental studies for growth and decline of pathogen; sparse data for initial densities of pathogen in ground beef; no data for dose-response of pathogen of interest in humans and inadequate dataset for pathogen of interest in animals (rabbits); no data on frequency for scenarios of time/temperature incubation throughout production, distribution, and food handling 4. sampling plan: factorial design for bacterial growth studies; 3-day food diary for CSFII; random and targeted sampling for FSIS prevalence survey 5. sample size: 12,000 observations for consumption in CSFII database (USDA Continuing Survey of Food Intake by Individuals, 1989, 1991); 184 growth curves for pathogen in culture media (ARS Pathogen Modeling Program); 38 ground beef patties for cooking study (Juneja et al., 1997); 9,821 ground beef samples in FSIS database for prevalence (FSIS, www.fsis.usda.gov/OA/topics/o157.htm#3); 6 ground beef samples for initial density (Johnson et al., 1995; Doyle personal communication, 1996) 6. performance characteristics: limited statistical results (mean or geometric mean and confidence limits for prevalence in ground beef; Most Probable Number or MPN assuming perfect method for quantitation of pathogen

	in ground beef 7. relevance: high
E. Method/Model/Approach	1. general characteristics: various statistical procedures, including analysis of variance and seemingly unrelated regression (SUR) with variance/covariance matrices to address variability and uncertainty; model for simple stochastic birth process for growth of pathogen before and after cooking; discrete modeling of scenarios of exposure for consumers of rare, medium, and well-done hamburgers for baseline, temperature abuse, and intervention models; Monte Carlo simulation using distributions below 2. specific characteristics: Burr Type XII for consumption of ground beef; beta for prevalence in ground beef; log/t-(7df) for initial density of pathogen in ground beef; multivariate normal for expected relative growth of pathogen in ground beef; normal for expected relative decline of pathogen in ground beef; negative binomial for likelihood of growth 3. assumptions: available data for exposure assessment sufficiently representative for healthy adult consumers of 114-gram hamburger meals prepared outside the home to rare, medium, or well-done states; available data insufficient to define explicitly farm-to-fork exposure assessment (growth and decline) for population of US consumers 4. limitations: measurement error not accounted for, and therefore, the percent occurrence could be understated and the magnitude and percentage of high densities could be overstated, resulting in biasing estimated risk 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: magnitude of differences in annual estimates of illness strongly influenced by limitations of the data as evidenced by large differences between mean and median estimates; threshold of only three pathogen cells surviving cooking associated with 1,000-fold lower annual illness rate than non-threshold model for consumers of hamburgers cooked at recommended temperature 2. authors' extrapolations: the approach can be extended to the most general situation describing birth and death together, and dropping the assumption of the lack of time dependence of the probabilities of birth or death within an increment of time
G. Data Gaps and Proposed Solutions	1. identification of data gaps: verification of binomial distribution for pathogen survival of cooking; test of independence of survival, infectivity, and initial density per serving; continuous modeling of growth and decline using thermal heat transfer equations; validation of predictive microbiology models in ground beef 2. proposed solutions: research in low exposure to foods that use thermal cooking step; better data needed for pathogen occurrence and density
H. Weight of Evidence	1. robustness of method: high 2. representativeness of data: high 3. generalizability or external validity: high 4. soundness of study conclusions or internal validity: high 5. defensibility: low

I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	Useful for two bacterial threat agents as potential contaminants of food for building scenarios
K. Cross-References	same study in DR and RC; Cassins et al., 1998

A. Exposure Assessment Study Identification (Food)	Mattick, K.L., F. Jorgensen, J.D. Legan, et al. 2000. Survival and filamentation of *Salmonella enterica* serovar *enteritidis* PT4 and *Salmonella enterica* serovar *typhimurium* DT104 at low water activity. Appl. Environ. Microbiol. 66: 1274-1279.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific 2. type: EA
C. Publication Attributes	1. sponsors/affiliations: the Food Microbiology Research Unit and the Environmental Microbiology Research Group of the University of Exeter, United Kingdom, and Nabisco, Incorporated, New Jersey 2. peer-review mechanism: peer reviewed journal
D. Data and Study Design	1. type: data generated by authors to study the effects of water activity of the survival of *Salmonella* strains in foods at different water activities. 2. source: laboratory data 3. extent of data: NA 4. sampling plan: NA 5. sample size: Number of treatments: temperature: 2 (21°C and 37°C), water activity: 6 (0.86 to 0.95 a_w), bacterial species: 2, growth phases: 2, medium types: 2 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: the study evaluated the survival of *Salmonella* in different materials at different water activities. 2. specific characteristics: the authors addressed different humectant's effects on *Salmonella* survival, and demonstrated long term survival under reduced available water conditions. The study also demonstrated a physiological change in growth conditions under reduced available water, wherein the cells grew more filamentously when under drier conditions. These conditions could result, upon hydration, in septation, followed by an apparent increase in cell numbers.

	3. assumptions: NA 4. limitations: this study applies to growth conditions in the presence of materials that lower the abundance of free water to the cells. These conditions are not expected to occur in drinking water or other conditions related to human exposure other than food. 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: Survival of *Salmonella* species at low aw conditions (aw=0.92 to 0.98) can result in filamentous growth. Owing to the ability of these cells to later divide (form septa) and form relatively high populations quickly, this presents a potential health risk that needs to be further investigated in food related industry. 2. extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: high 2. representativeness of data: low 3. generalizability or external validity: high 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	NA

A. Exposure Assessment Study Identification (Food)	Nauta, M.J., E.G. Evers, K. Takumi and A.H. Havelaar. 2001. Risk assessment of Shiga-toxin producing *Escherichia coli* O157 in steak tartare in the Netherlands. RIVM report 257851003. http://www.rivm.nl/bibliotheek/rapporten/257851003.html
B. Objectives and Type of Study	1. purpose: scientific; future regulatory interest 2. type: EA
C. Publication Attributes	1. sponsors/affiliations: Directory Board of RIVM, Netherlands

	2. peer-review mechanism: NA
D. Data and Study Design	1. type: data from literature 2. source: published and unpublished studies; expert opinion from a workshop conducted on 30 Jan 2001 at RIVM Bilthoven 3. extent of data: extensive sets of data from multiple sources on prevalence and concentration of Shiga-toxin producing *E. coli* O157 in cattle at the farm, slaughterhouse, and retail, food consumption in the Netherlands, and food handling processes 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: high
E. Method/Model/Approach	1. general characteristics: Modular Process Risk Model (MPRM) in which transmission of the microorganism along a food pathway is modeled by describing the changes in prevalence and number of microorganisms per unit through consecutive modules simulating food handling (mixing, partitioning, removal, cross-contamination) and microbial (growth, inactivation) processes 2. specific characteristics: model designed to estimate exposure to Shiga-toxin producing *Escherichia coli* O157 in steak tartare in the Netherlands; the food pathway is modeled as a series of 9 steps starting with animals at the farm and ending with consumption of steak tartare; although they occur throughout the entire pathway, growth and inactivation are modeled only at three stages along the food pathway - during the time between carcass halving and carcass trimming, during storage after tartare production, and during preparation of tartare patties - due to lack of critical information (e.g., process time, temperature) for other stages of the pathway; model parameters were estimated for two different types of slaughterhouses, two different types of butchers, three different patty preparation styles (raw, medium, well done), and three different age classes of consumers; model parameters estimated as distributions rather than point estimates to the extent possible; Monte Carlo simulations (up to 50,000 iterations each) were run for the various exposure scenarios to derive distributions of expected exposures 3. assumptions: animals, feces and contamination are all independent, i.e. the presence of a Shiga-toxin *E. coli* O157-contaminated animal does not affect the probability of contamination of another one; the probability of finding Shiga-toxin *E. coli* O157 on meat destined for tartare is equal to the probability of finding it at a random place on the carcass 4. limitations: unrealistic assumptions in some cases; data not always available for cattle in the Netherlands, so extrapolations based on US studies were made to Dutch population in some cases; estimates are highly uncertain as a consequence of lack of adequate data for many parts of the food pathway 5. relevance: high
F. Study Conclusions and Extended Applications	1. conclusions: reasonable estimates of exposure to Shiga-toxin *E. coli O157* in steak tartare under different exposure scenarios

	2. authors' extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: high 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	same study in DR and RC

A. Exposure Assessment Study Identification (Food)	Nauta, M.J., S. Litman, G.C. Barker and F. Carlin. 2003. A retail and consumer phase model for exposure assessment of *Bacillus cereus*. Int. J. Food Microbiol. 83(2): 205-218.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific, future regulatory interest - To illustrate how the consumer part of the food pathway may be modeled for an exposure assessment, to compare the exposure to psychrotrophic and mesophilic strains of *B. cereus*, to show impact of post-industrial storage conditions on exposure, and to indicate what type of data and additional research are needed for a quantitative microbiological risk assessment that includes the consumer phase of the food pathway. 2. type: EA
C. Publication Attributes	1. sponsors/affiliations: Commission of the European Communities, Agriculture and Fisheries (FAIR) specific RTD program. 2. peer-review mechanism: scientific review journal
D. Data and Study Design	1. type: describes a model of *B. cereus* in the retail and consumer phase of the food pathway of a specific vegetable "refrigerated processed food of extended durability"(REPFEDs). 2. source: published studies, some government datasets are referenced 3. extent of data: distribution of mean temperatures, temperature profiles, exposure assessments

	4. sampling plan: factorial design - packages of vegetable puree 5. sample size: 600 packages 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: The model combines the food pathway characteristics with the basic models for partitioning and growth. Two different strains were compared - psychrotrophic and a mesophilic strains at five different temperatures. A batch of 600 packages were evaluated. 2. specific characteristics: Set up using the modular process risk model methodology; a stochastic model using Monte Carlo simulations; exponential distribution and Gamma distribution was applied to the food pathway assessment; Binomial distribution 3. assumptions: The storage time is implemented as 80% sold until 7 days before the use-by-date and the rest sold in the last week before the use-by-date, both with a uniform distribution. Storage temperature was a uniform 4C, during transport 10C to 25C. That transport time is Gamma distributed. Exponential distribution is assumed to describe the distribution of times that the products are kept in the refrigerator. It is assumed that consumer behavior regarding storage time is influenced by the use-by-date on the package. Growth in the model food was as similar as nutrient broth. The packages contain spores only and no vegetative cells are present. Spore germination is assumed to take place when the minimum growth temperature as defined for the lag phase is exceeded. It is assumed that a batch is contaminated with one *B. cereus* strain only. 4. limitations: Growth data from a psychrotrophic and a mesophilic strain in nutrient broth at a few constant temperatures was applied to predict growth in real food, at varying temperatures, for a variety of strains. 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: The level of *B. cereus* at the end of industrial processing is a poor Predictor for health risks. The assessment shows that a constant domestic temperature of 4C may not be sufficient to prevent *B. cereus* to grow to a critical level. The *B. cereus* level at the end of industrial processing is a bad predictor for the high levels at the moment the package is taken from the refrigerator by the consumer.
G. Data Gaps and Proposed Solutions	1. data gaps: Refer to the list of assumptions (section E. 3). 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA

J. Reviewer Comments	NA
K. Cross-References	NA

A. Exposure Assessment Study Identification (Food)	Notermans, S., J. Dufrenne, P. Teunis, et al. 1997. A risk assessment study of *Bacillus cereus* present in pasturized milk. Food Microbiology 14: 143-151.
B. Objectives and Type of Study	1. purpose: scientific, future regulatory - risk assessment of *Bacillus cereus* present in pasturized milk. 2. type: EA
C. Publication Attributes	1. sponsors/affiliations: National Institute of Public Health and the Environment 2. peer-review mechanism: scientific journal review
D. Data and Study Design	1. type: Human exposure, storage tests and survey on the storage conditions of pasturized milk in the household in the Netherlands. 2. source: Regional Inspectorate for Health Protection in Leeuwarden datasets and published journals 3. extent of data: Every two weeks, from March 1995 until February 1996, two packages of freshly pasturized milk were obtained from six different milk-processing plants in The Netherlands. 4. sampling plan: information regarding the storage conditions (time and temperature) of pasturized milk was obtained from households to establish the probability of exposure to contaminated milk (n=25); pooled samples of milk (n=38) stored under controlled conditions analyzed by MPN. 5. sample size: 38 mixed samples, six to seven samples from each processing plant, were used in the storage tests; 125 refrigerators surveyed 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: deterministic model for likelihood of milk containing $>10^5$ pathogens/mL 2. specific characteristics: Initial counts were multiplied by fraction containing $>10^5$ MPN/mL and the probability for growth under given storage conditions 3. assumptions: In the calculations, storage times and temperature were considered to be independent. 4. limitations: NA 5. relevance: medium
F. Study Conclusions and Extended	1. conclusions supported by the data: The study revealed that day-old pasteurized milk contained about 10 *B.*

Applications	*cereus* organisms per 100mL and that all 38 samples of each of the two 11 packages contained *B. cereus*. At each of the incubation temperatures, the number of *B. cereus* increased during the storage period. At the time of consumption approximately 7% of the portions of pasteurized milk consumed contained >10^5 cfu *B. cereus* mL^{-1}. 2. authors' extrapolations from the observed data to other populations or conditions: *B. cereus* present in milk may cause harm to the consumer. In the calculations, storage times and storage temperatures were considered to be independent, which is not true. Results obtained revealed that although *B. cereus* can cause foodborne illness, no clear results are available to estimate a does-response relationship. Safety criteria have been set; these vary from 10^4-$10^5 g^{-1}$ of a food product. Calculations demonstrate that 11% of the portions of milk consumed in The Netherlands contains >10^4 *B. cereus* mL^{-1}, while 7% of the portions contain >10^5 mL^{-1}. The expiry date of pasteurized milk produced in the Netherlands can be set at 7 days based on a storage temperature of 7 °C.
G. Data Gaps and Proposed Solutions	1. data gaps: dose-response relationships 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: low 5. defensibility: low
I. Criteria for Exclusion from Compendium	None
J. Reviewer Comments	Authors noted lack of coherence of various sources of dose-response data (Landeveld et al. 1996; Dack et al. 1954; Kramer and Gilbert 1989; Hague 1995; Nikodemusz 1967). Considering a risk management criteria of 10^5/mL, the authors estimate that 7% of servings in The Netherlands might exceed the criterion. No formal risk characterization was conducted.
K. Cross-References	NA

A. Exposure Assessment Study Identification (Food)	Notermans, S., J. Dufrenne, P. Teunis and T. Chackraborty. 1998. Studies on the risk assessment of *Listeria monocytogenes*. J. Food Protect. 61(2): 244-248.
B. Objectives and Type of Study	1. purpose: noted by study authors: scientific and future regulatory interest 2. type: EA

C. Publication Attributes	1. sponsors/affiliations: Nutrition and Food Research Institute, The Netherlands 2. peer-review mechanism: scientific journal review
D. Data and Study Design	1. type: Data establishing the human exposure rate, testing the virulence of *Listeria* strains, anddeterminations of infective dose and lethal dose for mice. 2. source: published studies (Teufel and Bendzulla) 3. extent of data: Estimations of the human exposure rate using test results from food products, 22 strains of *Listeria* were tested for virulence on groups of 4 mice, groups of 10 mice were used for testing the infective and lethal dose. 4. sampling plan: factorial design 5. sample size: Test results for 7,063 food products used for exposure 6. performance characteristics: Dose-response curves and exponential dose-response relations were fitted by maximum likelihood estimations. 7. relevance: low
E. Method/Model/Approach	1. general characteristics: deterministic model for frequency of exposures to pathogen at 4 levels in 4 food products in The Netherlands 2. specific characteristics: levels of pathogen in 4 food products multiplied by frequency of consumption at 4 levels 3. assumptions: portions of 100g of the product were consumed. 4. limitations: NA 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: average yearly exposure to 3 $\log_{10}$, 5 $\log_{10}$, and >6 $\log_{10}$ amount of *L. monocytogenes* occurs 19.3, 3.8, and 0.8 times, respectively
G. Data Gaps and Proposed Solutions	NA
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: low 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA

K. Cross-References	NA

A. Exposure Assessment Study Identification (Food)	Panisello, P.J. and P.C. Quantick. 1998. Application of food MicroModel predictive software in the development of Hazard Analysis Critical Control Point (HACCP) systems. Food Microbiol. 15(4): 425-439.
B. Objectives and Type of Study	1. purpose: scientific and future regulatory interest; This paper describes the role of Food Micromodel (FMM) as a supporting instrument in the Hazard Analysis Critical Control Point (HACCP), using paté as an example. 2. type: EA
C. Publication Attributes	1. sponsors/affiliations: Food Research Centre (FRC) at Lincoln University 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: microbial surveys on the quality of paté and other related products; extensive predictive microbiology studies described by microbial growth curves in (FMM) included *Salmonella spp., A. hydrophila, L. monocytogenes, Y. enterocolitica, C. botulinum, S. aureus, E. coli,* and *C. jejuni*. 2. source: literature sources, including communicable disease reports published by the Public Health Laboratory Service; growth data generated through FRC 3. extent of data: NA. 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: some high
E. Method/Model/Approach	1. general characteristics: used FMM software (version 2.52) to predict no growth or growth rates, lag phases, and log colony-forming units obtained after 7 days across pH levels for each of the 8 pathogens at constant temperature in refrigeration range 2. specific characteristics: Four zones classified based on growth/no growth as related to pH level: 1) safe zone - no growth predicted; 2) caution zone - growth recorded, but lag phase exceeds the shelf life of product; 3) danger zone - growth recorded, but the lag phase does not exceed shelf life of the product; and 4) critical zone - bacteria grow at maximum rate. 3. assumptions: NA 4. limitations: NA 5. relevance: low

F. Study Conclusions and Extended Applications	1. conclusions: likelihood of growth was predicted for pH zones for paté using FMM software for 8 pathogens 2. authors' extrapolations: FMM supporting tool based on predictive microbiology for food safety research, industry practices, and decision making
G. Data Gaps and Proposed Solutions	NA
H. Weight of Evidence	1. robustness of method: high 2. representativeness of data: some high 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	This study primarily reported growth under limited conditions without modeling of likely fate and transport to consumption or adverse effects.
J. Reviewer Comments	NA
K. Cross-References	NA

A. Exposure Assessment Study Identification (Food)	Pouillot, R., I. Albert, M. Cornu, et al. 2003. Estimation of uncertainty and variability in bacterial growth using Bayesian inference application to *Listeria monocytogenes*. Int. J. Food Microbiol. 81(2): 87-104.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific; describe a method for estimating the parameters of microbial growth models that evaluates variability and uncertainty separately 2. type: EA
C. Publication Attributes	1. sponsors/affiliations: Agence Francaise de Securite des Alimenis; Institut National de la Recherche Agronomique; CNRS-INSERM-MiRe 2. peer-review mechanism: scientific journal review
D. Data and Study Design	1. type: data obtained from literature, not specific as to type of study design 2. source: published studies (12 sources) 3. extent of data: growth curve data obtained from 12 studies 4. sampling plan: NA

	5. sample size: total of 124 growth curves for 22 strains of *L. monocytogenes* (although authors indicate that the same strains were treated as different strains if the growth curves were obtained from different papers) 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: predictive microbiology using Bayesian approach and Markov Chain Monte Carlo (MCMC) method to calculate posterior distributions for the logarithm of the concentration of *L. monocytogenes*, and the following model parameters: the logarithm of the maximum achievable concentration of *L. monocytogenes*, lag time parameter (K), optimal growth rate, minimum temperature at which growth occurred (T_{min}), maximum temperature at which growth occurred (T_{max}), and optimal growth temperature (T_{opt}) 2. specific characteristics: estimates for the means of (normal) prior distributions were taken from Augustin and Carlier, 2000 (Mathematical modeling of the growth rate and lag time for *Listeria monocytogenes.* International Journal of Food Microbiology 57: 169-181.), which were based on regression analysis of data obtained from literature review of all published growth curves for *L. monocytogenes*; values for the standard deviations of these distributions were selected based on expert judgment (Smith et al., 1995. Bayesian approaches to random-effects meta-analysis: a comparative study. Statistics in Medicine 14, 2685-2699.), such that the prior distributions varied within a wide range of values; parameter values for the prior distributions for the standard deviation of model errors were assigned according to Spiegelhalter et al. (1996); following an 'adaption phase' of 50,000 iterations, convergence of the MCMC algorithm was determined by visual inspection and Gelman and Rubin convergence statistics for three independent MCMC chains; inferences were based on the 20,000 iterations that followed the adaption phase for each of the three chains (i.e., inference was based on 60,000 model iterations, or outputs); parametric distributions were fitted to the MCMC output using maximum likelihood to estimate the parameters, and the Anderson-Darling statistic to select the best distribution 3. assumptions: growth kinetics are same in skimmed and whole milk; temperature is the only parameter that influences growth; lag time is proportional to generation time; maximum achievable concentration of microbes is constant for a given culture medium; optimal growth rate is constant for a given strain and medium; variability in the stochastic model parameters are modeled with normal distributions; uncertainty in the means of the distributions modeling variability are assumed to follow normal distributions, while uncertainty in the standard deviations of the distributions modeling variability are assumed to follow gamma distributions 4. limitations: because the authors considered growth curves for the same strain of *L. monocytogenes* from different laboratories as different strains, the laboratory, physiological and strain effects are confounded in this study; within-strain variability is not considered for the optimal growth rate, T_{min}, T_{opt} and T_{max} growth rate temperatures; sensitivity analysis for model inputs was not performed; model uncertainty was not evaluated 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: inter-strain variability for T_{min} and K is high; posterior mean for K is much lower than prior estimates from literature (authors suggest this finding is preliminary) 2. extrapolations: posterior distributions for microbial growth that are developed using the approach proposed by the authors could be used in microbial risk assessment to model variability and uncertainty (separately) in a

	'second-order' or '2-D' Monte-Carlo simulation approach
G. Data Gaps and Proposed Solutions	1. data gaps: data for estimating strain variability 2. proposed solutions: generate targeted data
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	as described in the paper, the method could be prohibitively data intensive, requiring distributions for many parameters; a well-designed sensitivity analysis could indicate some parameters that do not have a significant effect on the output distributions, which could then lead to a simplified, and more feasible model with respect to data needs; sensitivity analysis could also be used to prioritize research needs
K. Cross-References	Marks et al., 1998

A. Exposure Assessment Study Identification (Food)	Reinders, R.D., R. De Jonge and E.G. Evers. 2003. A statistical method to determine whether micro-organisms are randomly distributed in a food matrix, applied to coliforms and *Escherichia coli* O157 in minced beef. Food Microbiol. 20(3): 297-303.
B. Objectives and Type of Study	1. purpose noted by study authors: development of new scientific methodology, with possible future regulatory application 2. type: EA
C. Publication Attributes	1. sponsors/affiliations: National Institute for Public Health and the Environment, Netherlands; Utrecht University, Netherlands 2. peer-review mechanism: scientific journal review
D. Data and Study Design	1. type: experimental data for endogenous coliforms and *E. coli* O157 2. source: this study 3. extent of data: measured endogenous coliforms before and after grinding and spiked *E. coli* O157 after

	grinding once or twice 4. sampling plan: NA 5. sample size: coliforms: n=25 and 75 before and after grinding, respectively; *E. coli*, n=50 (after grinding) for two levels of clustering, for a total of n=100 observations 6. performance characteristics: NA; authors report that preliminary work indicates experimental error is minimal (Reinders et al. 2002. Variations in the numbers of Shiga toxin-producing *E. coli* O157 in minced beef. Report No. 149106.009, National Institute for Public Health and Environment, Bilthoven, The Netherlands.) 7. relevance: high
E. Method/Model/Approach	1. general characteristics: a Poisson model with mean varying according to a gamma distribution is proposed to describe the distribution of coliforms and *E. coli* O157 in beef, before and after grinding 2. specific characteristics: parameter estimation by maximum likelihood; goodness-of-fit of fitted distribution to EDF was determined by the Kolmogorov-Smirnov statistic; likelihood-ratio tests were used to compare the fit of Poisson and Poisson(Gamma) distributions to the data (H_0: Poisson mean is constant; H_1: Poisson mean is Gamma distributed), and to test the null hypothesis that the microorganisms were not clustered in space (i.e., the Poisson mean was constant) 3. assumptions: experimental error was a negligible part of total observed variability in micro-organism counts 4. limitations: experiments were carried out in laboratory scale grinders - the extent to which contaminated food from local sources are distributed throughout the food material may vary between grinder designs 5. relevance: high
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: local contamination of beef with coliforms and *E. coli* can be effectively disseminated by grinding; clustering of coliforms and *E. coli* in beef can be detected by comparing a Poisson distribution with constant mean to a Poisson distribution with Gamma mean, using a likelihood ratio test; the distribution of coliforms and *E. coli* in beef can be adequately described by a Poisson distribution with constant mean when clustering is not present, and with a Poisson with Gamma mean, or a lognormal distribution, when clustering is present; an advantage of the Poisson(Gamma) distribution is that it describes the extent of clustering, whereas the lognormal model cannot 2. extrapolations: the described approach could be used in the microbial risk assessment of a food chain when the distribution of micro-organisms are important (authors cite Nauta et al. 2001. http://www.rivm.nl as an example)
G. Data Gaps and Proposed Solutions	1. data gaps: effect of grinder on dissemination rate; proportion of total variance attributable to experimental error should be checked for laboratory method/food matrix combinations 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: high

	3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility: high
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	expect food contamination scenarios require non-homogenous assumptions about distributions, means insufficient, particularly for growth scenarios where effects of clustering more influential
K. Cross-References	Reinders et al., 2002; Reinders et al., 2002; Nauta et al., 2001

A. Exposure Assessment Study Identification (Food)	Ross, T., P. Dalgaard and S. Tienungoon. 2000. Predictive modeling of the growth and survival of *Listeria* in fishery products. Int. J. Food Microbiol. 62(3): 231-245.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific; Identification of experimental procedures and predictive models that precisely identify the growth and survival of *Listeria* in fishery products. 2. type: EA
C. Publication Attributes	1. sponsors/affiliations: University of Tasmania, Australia; Danish Institute for Fisheries Research; Ministry of Public Health, Bancock, Thailand 2. peer-review mechanism: full scientific peer review
D. Data and Study Design	1. type: experimental data for microbial growth and survival under various conditions 2. source: published literature studies 3. extent of data: large data sets 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: Sources of data and models relevant to assessment of the human health risk of *L. monocytogenes* in seafoods are identified. 2. specific characteristics: The integration of models for microbial growth, growth limits or inactivation into models that can predict increases or decreases in microbial populations are considered. The specific conditions, e.g.

	temperature, pH, water activity, atmosphere, smoke components, interaction of abiotic factors are identified from experimental data and integrated into a predictive modeling equation. 3. assumptions: times and temperatures of storage 4. limitations: NA 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: The integration of models for microbial growth, growth limits or inactivation into models that can predict both increases or decreases in microbial populations over time will also improve the utility of predictive models for exposure assessment. 2. authors' extrapolations from the observed data to other populations or conditions: None reported
G. Data Gaps and Proposed Solutions	NA
H. Weight of Evidence	1. robustness of method: high 2. representativeness of data: low 3. generalizability or external validity: high 4. soundness of study conclusions or internal validity: high 5. defensibility: high
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	Lag times are less reliably predicted than generation times. Modeling and experimental results are not indicative of the growth of other organisms on the product (called Jameson effect), and the effect of such growth on the organism of concern. The softwares currently available do not consider the effect of factors which may contribute to the Jameson effect.
K. Cross-References	NA

A. Exposure Assessment Study Identification (Food)	Sanaa, M., L. Coroller and O. Cerf. 2004. Risk assessment of listeriosis linked to the consumption of two soft cheeses made from raw milk: Camembert of Normandy and Brie of Meaux. Risk Anal. 24(2): 389-399.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific, future regulatory; to report an improved and more contemporary risk assessment based on data collected in the years 2000-2001.

	2. type: EA
C. Publication Attributes	1. sponsors/affiliations: CNIEL, French National Interprofessional Centre of the Dairy Economy 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: data for organism growth in milk (Augustin, 2000), experimental data for organism growth in soft cheese (Back, *et al.* 1993; Maisnier-Patin, *et al.* 1992; Ryser and Marth, 1987) 2. source: published studies 3. extent of data: NA 4. sampling plan: NA 5. sample size: milk collections from 347 farms for Camembert production and 79 farms for Brie production (total volume collected represents twice the volume needed for production); organism testing performed on 50 mL samples from tanker trucks and 25 mL samples from farm bulk tanks 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: 100,000 iteration Monte Carlo simulation using SAS system for Windows V8 and @ Risk 2. specific characteristics: beta function to model intra-month variability in *L. monocytogenes* concentration of raw milk, triangular for number of bulk tanks collected per day - used in Poisson distribution to calculate *L. monocytogenes* concentration in tanker milk, normal distribution for volume variability in bulk tanks, growth simulated with modified logistic model, effect of temperature-pH on exponential growth rate calculated using cardinal model, dose-response relationship by Poisson distribution of number of expected listeriosis cases per 10e8 servings. 3. assumptions: cell progeny do not spread within the solid cheese matrix as they would in liquid broth, basic hygiene rules are followed along the whole chain. 4. limitations: lack of robustness in some data created data gaps in the analysis 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: 99% of iterations yielded serving with less than 100 cfu/serving (3.7 cfu/g), and 0.03-0.22% fo serving yielded >1,00 cfu 2. extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: model does not consider organism inactivation by competition for nutrients, bacteriocins, etc.; does not account for water activity influence; does not take into account withdrawal of *L. monocytogenes* positive lots of cheese before release; does not take into account possible contamination or cross-contamination during cheese production and distribution; validity of distribution used for growth delay in raw milk cheese not confirmed. 2. proposed solutions: improve model such that microbial inhibitor interactions, water activity influence, and positive lot withdrawal are accounted for; generate more data to confirm validity of growth delay distribution.

H. Weight of Evidence	1. robustness of method: high 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	same study in RC

A. Exposure Assessment Study Identification (Food)	Strachan N.J., G.M. Dunn and I.D. Ogden. 2002. Quantitative risk assessment of human infection from *Escherichia coli* O157 associated with recreational use of animal pasture. Int. J. Food Microbiol. 75: 39-51.
B. Objectives and Type of Study	1. purpose: Scientific/Regulatory; use risk assessment to determine the probability of *E. coli* O157:H7 infection following visiting an area grazed by infected livestock 2. type of study: EA
C. Publication Attributes	1. sponsors/affiliations: Department of Plant and Soil Science, School of Physics, and Applied Food Microbiology Group (University of Aberdeen) 2. peer-review mechanism: peer-reviewed journal
D. Data and Study Design	1. type: data from published studies 2. source: Zhao et al. (1995), Shere et al. (1998), and others3. extent of data: EA data included prevalence (% of cattle infected), concentration of *E. coli* in cattle feces, and fate of *E. coli* in the pasture (build-up and decay). 4. sampling plan: NA 5. sample size: NA. 6. performance characteristics: NA 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: this study used a Monte Carlo method to try to develop a means to estimate the exposure 2. specific characteristics: Model variables included the probability of infection based on the percentage of

	infected cattle, the number of organisms shed in the feces, the length of time the cattle grazed on the field, the length of time that the cattle had been removed from the field prior to being visited, and the length of stay of the visitors. Additional model parameters included the amounts of soil ingested, bulk soil density, and number of people visiting the field. 3. assumptions: NA 4. limitations: one set of data used, and these data were not considered fully representative. 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: Monte Carlo analysis suggests that a 3 week period of non-livestock use occur in any pasture that is expected to be visited by the general population. Removal of feces from the field may also reduce the likelihood of exposures. 2. extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: All results are based on data for 31 cattle. Results are also based on experiments done on cattle in the US, whereas shedding of *E. coli* O157 by cattle in the United Kingdom and in Scotland were shown to be different (higher) than these observations. 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: high 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	Only 31 test animals were used as the basis of the modeling approach executed, and the data were from cattle raised in the United States, not the United Kingdom. The authors noted significant differences have been observed in the microbial loadings of the two countries. The parameters of the modeling were only described briefly, and no explicit model statements were provided. No goodness-of-fit types of analyses were conducted to evaluate this model's strengths against others. No transport processes were mentioned, and fate data and predictions were simplistic
J. Reviewer Comments	in appropriate method for incidence based risk assessment for buildings or water systems
K. Cross-References	NA

A. Exposure Assessment Study Identification (Food)	USDA/FSIS. 2003. Risk assessment for *Listeria monocytogenes* in deli meats. US Department of Agriculture/Food Safety and Inspection Service. www.fsis.usda.gov/OPPDE/rdad/FRPubs/97-013F/ListeriaReport.pdf
B. Objectives and Type of Study	1. purpose: regulatory; to evaluate hypothetical mitigations for contaminated ready-to-eat (RTE) meat 2. type: EA
C. Publication Attributes	1. sponsors/affiliations: USDA, FSIS 2. peer-review mechanism: report mentioned public comment period, but no peer review process
D. Data and Study Design	1. type: retail survey data from National Food Processors Association; experimental results from studies on duration of contamination event, transfer of organisms from food contact surface (FCS) to food, conversion of FCS *Listeria* spp. concentrations to food surface *L. monocytogenes* concentrations 2. source: published scientific studies, government survey, government datasets 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: Monte Carlo simulation in-plant dynamics linked to FDA/USDA retail-to-table exposure assessment 2. specific characteristics: theoretical mass balance approach for in-plant model 3. assumptions: *Listeria* spp. are evenly distributed across FCSs, and *L. monocytogenes* are evenly distributed within a lot of product; foods encompassed by the food categories account for all cases of foodborne listeriosis; a *Listeria* reservoir exists in the plant and is capable of contaminating FCSs. 4. limitations: model only considers FCS as source of contamination in product; only a generic FCS is modeled; variability across FCS or within a lot is not accounted for in model 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions: proposed minimal frequency of testing and sanitation of FCSs estimated to result in a small reduction in *L. monocytogenes* on deli meats at retail 2. authors' extrapolations: model may also be extended to frankfurters
G. Data Gaps and Proposed Solutions	1. data gaps: amount of *Listeria* spp. on FCS during contamination event; ratio of concentrations of *L. monocytogenes* to *Listeria* spp.; enumeration data for positives to verify theoretical in-plant dynamics 2. proposed solutions: generate data for model calibration and validation
H. Weight of Evidence	1. robustness of method: NA

	2. representativeness of data: low 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	data used to calibrate model unavailable for independent model validation
K. Cross-References	same study in RC; FDA/USDA, 2003

A. Exposure Assessment Study Identification (Food)	van Gerwen, S.J.C. and Zwietering, M.H. 1998. Growth and inactivation models to be used in quantitative risk assessments. J. Food Protect. 61: 1541-1549.
B. Objectives and Type of Study	1. purpose: noted by study authors: scientific; A discussion of the growth and inactivation models that can be used in a step wise procedure for quantitative risk assessment is presented. 2. type: EA
C. Publication Attributes	1. sponsors/affiliations: Wageningen Agricultural University, Dept of Food Technology and Nutritional Sciences, The Netherlands 2. peer-review mechanism: Full scientific peer review
D. Data and Study Design	1. type: experimental data and several modeling studies for growth and inactivation of *B. cereus* in potatoes 2. source: published data 3. extent of data: large data sets for bacterial growth 4. sampling plan: factorial design for growth studies under various process steps, temperature and using various models 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: Several primary and secondary growth and inactivation models presented for quantitative risk assessment for growth and inactivation of *B. cereus* in vacuum packed cooked potatoes 2. specific characteristics: Growth mostly occurred in the last stage of production process, i.e. storage and during

	cooling after pasteurization. Lag exponential models used to predict growth of *B. cereus*. Specific growth rates and lag time were estimated by the gamma and polynomial models 3. assumptions: simple primary and secondary growth models are just as accurate as more complex ones 4. limitations: only primary and secondary growth models applied 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: growth and inactivation models can be used in a step-wise procedure for quantitative risk assessment 2. authors' extrapolations: NA
G. Data Gaps and Proposed Solutions	NA
H. Weight of Evidence	1. robustness of method: high 2. representativeness of data: low 3. generalizability or external validity: high 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	NA

A. Exposure Assessment Study Identification (Food)	Van Impe, J.F., B.M. Nicolai, M. Schellekens, et al. 1995. Predictive microbiology in a dynamic environment: a system theory approach. Int. J. Food Microbiol. 25(3): 227-249.
B. Objectives and Type of Study	1. purpose noted by study authors: to introduce system theory approach in predictive microbiology 2. type: EA
C. Publication Attributes	1. sponsors/affiliations: Food Linked Agro-Industrial Research project of the European Commission; Katholieke Universiteit, Belgium; Universiteisrestaurants ALMA, Belgium 2. peer-review mechanism: scientific journal review

D. Data and Study Design	1. type: literature data for *Brochothrix thermosphacta* and *Laxtobacillus plantarum* 2. source: published studies (Nicolai et al., 1995; Zwietering et al., 1991; Van Impe et al., 1995) 3. extent of data: details for *Brochothirx thermosphacta* provided in Nicolai et al., 1995 (authors indicate a large set of growth curves at constant and fluctuating temperatures, and survivor curves at constant temperatures were used to validate the model, as described in Nicolai et al., 1995); details for *Laxtobacillus plantarum* are reported in Van Impe et al. (1995; under preparation at the time that the subject paper was published) 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: development of a dynamic model for bacterial growth that simulates the growth-death cycle of bacteria in chilled prepared food 2. specific characteristics: modified Gompertz equation is used to model growth rate (Zwietering, et al., 1990); the growth-temperature relationship was modeled using a modified version of Ratkowsky's model (Ratkowsky et al., 1982, 1983; Zwietering et al., 1991); asymptote (of the growth curve)-temperature model is an exponential function of the difference between the temperature and the maximum temperature at which growth is observed, and two parameters (authors do not provide a rationale for this model); the lag time-temperature relationship is modeled with a hyperbolic equation suggested by Zwietering et al. (1990); the preceding equations, which are appropriate for predicting bacterial growth rate at constant temperature, were combined mathematically, and then differentiated with respect to time and subsequently modified to allow modeling inactivation by allowing temperatures outside the range of bacterial growth (i.e., outside [T_{min}, T_{max}]); the transition zone between growth and inactivation is modeled with a modified version of the Arrhenius-type model proposed by Bigelow (1921); the dynamic model is capable of modeling unlimited cycles of lag time - growth - transition zone - inactivation- lag time - growth, etc., as a function of temperature; parameter estimation is described as a two-step process: first step - maximum specific growth rate, lag time, asymptote of the growth curve (A), and other parameters, are estimated from data on growth rates for a given micro-organism at different levels (but constant) temperatures; second step - data from experiments that are carried out at varying temperature are used to refine the estimates of the parameter estimates made in step 1 3. assumptions: growth rate is a function of temperature only; asymptote of the bacterial growth curve is not a function of temperature 4. limitations: further model development may be required to simulate deviations of the temperature inactivation rate constant from the Arrhenius-type model that have been observed for some micro-organisms under some environmental conditions (Tomlins and Ordal, 1976; Gould, 1989); further model validation is warranted under time varying temperature conditions 5. relevance: low
F. Study Conclusions and Extended	1. conclusions supported by the data: the dynamic model predicts population growth/decline patterns as a

Applications	function of temperature that are consistent with expected results; predictions produced with the dynamic model at constant temperature agree with the constant temperature modified Gompertz model (Zwietering et al., 1990, 1991); the model output agreed very well with experimental data for *Brochothrix thermosphacta* and *Laxtobacillus plantarum* 2. extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: high 2. representativeness of data: low 3. generalizability or external validity: high 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	NA

A. Exposure Assessment Study Identification (Food)	Whiting, R.C. and R.L. Buchanan. 1997. Development of a quantitative risk assessment model for *Salmonella enteritidis* in pasteurized liquid eggs. Int. J. Food Microbiol. 36: 111-125.
B. Objectives and Type of Study	1. purpose: scientific and future regulatory interest; construct viable risk assessment model incorporating dose response and food microbiology to quantitatively assess hazards associated with a food process. 2. type: EA
C. Publication Attributes	1. sponsors/affiliations: US Department of Agriculture 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: experimental data for microbial growth in contaminated flocks and eggs; growth modeling applied to thermal processing and storage; abuse of storage temperatures by consumer and probability of infection. 2. source: published studies and epidemiological surveys 3. extent of data: extensive survey of experimental studies on pathogen presence in contaminated flocks and

	eggs, experimental studies for growth, survival, and thermal death of pathogen; incorporated data on frequency for scenarios of time/temperature incubation throughout production, distribution and consumer handling. 4. sampling plan: NA 5. sample size: isolation rate of contaminated eggs from infected flocks determined by distribution of values collected from 27 surveys; 6. performance characteristics: NA 7. relevance of data: low
E. Method/Model/Approach	1. general characteristics: 2,000 iteration Monte Carlo simulation using @RISK sampling from distribution below; 2. specific characteristics: log normal and other distributions to calculate number of contaminated eggs and levels of infection in portion of eggs stored at temperatures or durations different from optimal procedures; 3. assumptions: no growth in albumen; ovarian route of transmission (vs. trans-shell) is largely responsible for *S. enteritidis* outbreaks; birds containing the pathogen is best estimated by examining bird ovaries or ovarian tissue and not intestinal tract; *S. enteritidis* numbers in contaminated eggs assumed 0.5 cfu /ml as level of *S. enteritidis* in positive eggs, distribution for time to yolk membrane breakdown was calculated for eggs stored at room temperature for 21days or higher temperatures for shorter time periods; washing, shell sanitation and breaking procedures are effective enough to contribute very little pathogen count to the overall levels in the liquid egg product. 4. limitations: additional information of lag periods existing between growth and pasteurization processes (effects of physiological state of cell and survival adaptations) is needed; further examination of virulence mechanisms and dose-response mechanisms needed. 5. relevance (qualitative judgement of the usefulness of the method to incident-based microbial risk assessment for biothreat agents; high, medium, or low): medium, includes method for modeling pathogen growth and thermal death and development and use of defined scenarios for selected exposure and dose-response conditions could be very useful for incident-based microbial risk assessment, although parameters selected here are not pertinent to EPA's biothreat agents
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: temperature and time were identified as critical factors influencing pathogen containment; scenarios indicate pasteurization temperature effective at reducing pathogen numbers to safe levels when maintained at 60^{o}C and suggests storage temperature highly influences ability of microbial growth. 2. authors' extrapolations from the observed data to other populations or conditions: NA
G. Data Gaps and Proposed Solutions	1. identification of data gaps: prevalence and levels in compartments of shell eggs and growth characteristics 2. assumptions or source of surrogate data to fill gap: NA
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low

	3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: low 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	description of most appropriate uses of method for incident-based microbial risk assessment when evaluating farm-to-table food products; useful for threat scenarios permitting bacterial growth in food process; basis components of model may be useful for examining biothreat agents in buildings.
K. Cross-References	same study in DR, RC

A. Exposure Assessment Study Identification (Food)	Zwietering, M.G. and S.J.C. van Gerwen. 2000. Sensitivity analysis in quantitative microbial risk assessment. Int. J. Food Microbiol. 58: 213-221.
B. Objectives and Type of Study	1. purpose: scientific; future regulatory interest 2. type: EA
C. Publication Attributes	1. sponsors/affiliations: Department of Food Technology and Nutritional Sciences, Wageningen University, The Netherlands 2. peer-review mechanism: full scientific journal review.
D. Data and Study Design	1. type: NA 2. source: published studies for *Salmonella* in poultry 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: An approach for performing sensitivity analysis of microbial risk assessment models is presented. The approach describes three-stages of sensitivity analysis: deterministic, worst-case and stochastic. The approach is illustrated using an example for *Salmonella* contamination of chicken. 2. specific characteristics: 10,000 simulations using distribution listed below; models used to calculate growth and

	inactivation rates was the Cardinal Temperature and pH Model (Rosso et al., 1995) and the D, z model. Triangular distribution for variations in process steps: slaughter time, temperature during pre- and post-cooking storage, and cooking temperature. 3. assumptions: 4. limitations: 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: probability of survival depends on the number of organisms before heating and also on the pre-cooking process. 2. extrapolations: NA
G. Data Gaps and Proposed Solutions	NA
H. Weight of Evidence	1. robustness of method: high 2. representativeness of data: high 3. generalizability or external validity: high 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	1.Useful for determining which process steps are important in controlling exposure to humans via food. 2. other comments by reviewer: This paper provides an overview of quantitative risk assessment (i.e., hazard identification, exposure assessment, hazard characterization, risk characterization, and sensitivity analysis) and presents a phased approach for sensitivity analysis for microbial risk assessment. The second half of the paper implements a sensitivity analysis for *Salmonella* on chicken to determine which process steps are important in the deterministic versus worst-case and stochastic analyses.
K. Cross-References	NA

A.1.2 Ingestion (Water)

Crawford-Brown, D.J. and S. Marquez-Nyarko. 1999. Development of an environmental decision support system (EDSS) for comparing drinking water treatment practices and associated health risks. Report No. 323. Chapel Hill, NC: Water Resources Research Institute of The University of North Carolina. 109

Gale, P., P.A.H. van Dijk and G. Stanfield. 1997. Drinking water treatment increases micro-organism clustering; the implications for microbiological risk assessment. Aqua (Oxford) 46(3): 117-126. 112

Gale, P. 2001. Developments in microbiological risk assessment for drinking water. J. Appl. Microbiol. 91: 191-205..... 114

Medema, G.J., W. Hoogenboezem, A.J. van der Veer, et al. 2003. Quantitative risk assessment of *Cryptosporidium* in surface water treatment. Wat. Sci. Technol. 47(3): 241-247..... 116

Petterson, S.R., and N.J. Ashbolt. 2001. Viral risks associated with wastewater reuse: Modeling virus persistence on wastewater irrigated salad crops. Wat. Sci. Technol. 43(12): 23-26.118

Teunis, P.F.M., G.J. Medema, L. Kruidenier, et al. 1997b. Assessment of the risk of infection by *Cryptosporidium* or *Giardia* in drinking water from a surface water source. Wat. Res. 31(6): 1333-1346..... 120

A. Exposure Assessment Study Identification (Water)	Crawford-Brown, D.J. and S. Marquez-Nyarko. 1999. Development of an environmental decision support system (EDSS) for comparing drinking water treatment practices and associated health risks. Report No. 323. Chapel Hill, NC: Water Resources Research Institute of The University of North Carolina.
B. Objectives and Type of Study	1. purpose: scientific and future regulatory; to present the development of a software tool to aid decision-makers involved in analyzing the various risks associated with disinfection treatment options for drinking water 2. type: EA
C. Publication Attributes	1. sponsors/affiliations: Water Resources Research Institute of The University of North Carolina 2. peer-review mechanism: NA
D. Data and Study Design	1. type: water quality survey data 2. source: survey of Brown Water Treatment Plant 3. extent of data: data from one representative plant were used; water quality data included temperature, pH, total organic carbon, bromide, ammonia, UV absorbance, and raw water concentrations of *Giardia lamba* cysts and *Cryptosporidium parvum* oocysts; information on treatment system characteristics was also collected 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: high
E. Method/Model/Approach	1. general characteristics: exposure to disinfection by-products and microbes is estimated by use of models to predict formation of disinfection by-products and inactivation of waterborne microbes (based on plant water quality measurements and treatment system characteristics), and human exposure factors 2. specific characteristics: formation of disinfectant by-products is predicted from plant water quality measurements and treatment system characteristics using algorithms modified from the EPA (1993) WTP (Water Treatment Plant) model that were developed from chlorination experiments (Harrington, 1992) conducted to measure formation of disinfection by-products under various treatment regimens; inactivation (disinfection) kinetics of microorganisms (*Giardia* and *Cryptosporidium*) are modeled using Chick-Watson first order kinetics, first order kinetics in which disinfectant concentration declines with time, and/or a two-population first order kinetics model (weighted by user), with inputs being the initial concentration of *Giardia* cysts and *Cryptosporidium* oocysts in the water and treatment system characteristics; human exposure factors for water ingestion and body weight are used to calculate doses of disinfection by-products and microbes associated with drinking water concentrations; inputs can be point estimates or user-specified distributions, and if distributions are specified, probabilistic evaluation (Monte Carlo, Median Latin hypercube, or Random Latin hypercube) can be performed to obtain probability distributions for exposure outputs. 3. assumptions: the exposure models assume that each day is a statistically independent exposure to the water with an identical distribution of pathogens 4. limitations: the current model is limited to predicting concentrations of total trihalomethanes, chloroform,

	bromoform, bromodichloromethane, chlorodibromomethane, dichloroacetic acid, and trichloroacetic acid from chlorination and chloramination as a secondary treatment, although the model can be expanded to include other by-products and treatment methods; the current model is limited to predicting disinfection of *Giardia* and *Cryptosporidium*, although the model can be expanded to include other waterborne pathogens; the current model does not address the effects of the water distribution system, which can be significant, on exposure 5. relevance: high
F. Study Conclusions and Extended Applications	1. conclusions: water concentrations of disinfection by-products and microbes at the Brown Water Treatment Plant were consistent with predictions of the model; the model provides a flexible tool to predict drinking water exposure to *Giardia* and *Cryptosporidium* under various water treatment regimens 2. authors' extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: high 2. representativeness of data: high 3. generalizability or external validity: high 4. soundness of study conclusions or internal validity: high 5. defensibility: high
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	same study in DR, RC

A. Exposure Assessment Study Identification (Water)	Gale, P., P.A.H. van Dijk and G. Stanfield. 1997. Drinking water treatment increases micro-organism clustering; the implications for microbiological risk assessment. Aqua (Oxford) 46(3): 117-126.
B. Objectives and Type of Study	1. purpose: scientific, future regulatory interest 2. type: EA
C. Publication Attributes	1. sponsors/affiliations: Department of the Environment 2. peer-review mechanism: full scientific journal review

D. Data and Study Design	1. type: experimental data for presence of aerobic spores in raw water and treated drinking water samples (operational UK drinking water treatment plant) 2. source: published studies 3. extent of data: NA 4. sampling plan:100 L water samples were taken; 150 mL samples were taken every 30 sec for treated water and every minute for raw water from Sterilin on four different days in February 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: examined Poisson distribution and negative normal distribution models for and their ability to provide good fits to microorganisms counts in drinking water 2. specific characteristics: Poisson distribution; negative normal distribution; overdispersed Poisson and Generalized linear modelling (GLM); significance tests on the reduction of spore counts in treated drinking water samples compared to raw water samples 3. assumptions: microorganisms are randomly dispersed in water samples; under non-outbreak conditions consumers are only exposed to one or zero pathogen doses daily; 4. relevance: high
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: water treatment significantly reduces spore viability, and facilitates the clustering of spores that survive; degree of clustering (loose versus tight) will determine how many pathogens are found in each glass of drinking water; spore counts for raw water samples were Poisson distributed; spore counts for treated water samples were over-dispersed; both models (Poisson distribution and negative normal distribution models) provided a good fit for untreated water samples, however negative binomial distribution provided a better fit for treated water samples; even under non-outbreak conditions, it is possible to be exposed to higher doses than just one pathogen as predicted by most RA models 2. authors' extrapolations from the observed data to other populations or conditions: particulates (e.g. carbon, alum) may further promote clustering of microorganisms in drinking water
G. Data Gaps and Proposed Solutions	1. identification of data gaps: Poisson distributions are inflexible to variance above the mean resulting in overdispersion; GLM model is restricted to cases where the value for *k* is known or fixed 2. assumptions or source of surrogate data to fill gap: use of a dispersion statistic to determine if data are Poisson distributed ;fit data to Poisson distribution but allow variances to exceed mean (Over-dispersion Poisson model); Also see E.3. and F.2. above
H. Weight of Evidence	1. robustness of method: high 2. representativeness of data: low 3. generalizability or external validity: high

	4. soundness of study conclusions or internal validity: high 5. defensibility: high
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	description of most appropriate uses of statistical models to best fit data values of spore counts
K. Cross-References	NA

A. Exposure Assessment Study Identification (Water)	Gale, P. 2001. Developments in microbiological risk assessment for drinking water. J. Appl. Microbiol. 91: 191-205.
B. Objectives and Type of Study	1. Purpose: develop microbiological risk assessment models for pathogenic agents in drinking water, primarily *Cryptosporidium parvum*, rotavirus, and Bovine Spongiform Encephalopathy (BSE). 2. EA
C. Publication Attributes	1. sponsors/affiliations: Wrc-NSF, Ltd., Buckinghampshire, UK 2. peer-review mechanism: peer reviewed journal
D. Data and Study Design	1. type: data primarily derived from previously published articles. 2. Source: Gale and Stanfield (2000) *(Cryptosporidium*). Data on surrogate organisms (*Bacillus* spores) were conducted at the sponsoring organization's facility. 3. extent of data: data appear to be well described and appropriately captured for use in this report 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: some high
E. Method/Model/Approach	1. general characteristics: different models applied to predict the exposure of populations to three pathogens that may be present in water supplies 2. specific characteristics: Poisson and negative binomial distribution models were used to generate exposure scenarios. 3. assumptions: surrogate particulates (*Bacillus* spores) were used to model the behavior of *Cryptosporidium* oocysts. The relationship is undescribed.

	4. limitations: NA 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: 2. extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: significant data gaps were reported for the estimation of BSE infection through the consumption of drinking water 2. proposed solutions: the authors suggest that risk assessment models for BSE concentrate on pathway barriers in the infection as opposed to biomedical barriers, the latter of which have considerable uncertainty
H. Weight of Evidence	1. robustness of method: high 2. representativeness of data: high 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility: high
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	promising modeling approaches for describing the likelihood for exposure or infection (e.g., Poisson and negative binomial distribution models used for exposure assessment modeling)
K. Cross-References	NA

A. Exposure Assessment Study Identification (Water)	Medema, G.J., W. Hoogenboezem, A.J. van der Veer, et al. 2003. Quantitative risk assessment of *Cryptosporidium* in surface water treatment. Wat. Sci. Technol. 47(3): 241-247.
B. Objectives and Type of Study	1. purpose: scientific; regulatory 2. type: EA
C. Publication Attributes	1. sponsors/affiliations: Collaborative Research Programme (BTO) of the water companies in The Netherlands 2. peer-review mechanism: scientific journal review
D. Data and Study Design	1. type: water survey data for three case studies; exposure factors 2. source: survey of two water sources and three treatment facilities in The Netherlands; published data used for

	exposure factors 3. extent of data: water survey data comprised 1) concentrations of *Crytosporidium* in raw waters (corrected for recovery efficiency) and 2) removal efficiency of treatment systems (obtained by monitoring removal of spores of sulphite-reducing clostridia [SRC] under full-scale conditions); published data were used for consumption of unheated drinking water in The Netherlands 4. sampling plan: source water sampled each month for a year (for two case studies) and sampled each week for a year (for the third case study) 5. sample size: NA 6. performance characteristics: NA 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: exposure estimated from raw water concentrations of *Crytosporidium*, expected treatment removal efficiency, and expected consumption of unheated drinking water 2. specific characteristics: initial estimates of exposure were based on point estimates for raw water concentrations of *Crytosporidium*, expected treatment removal efficiency, and expected consumption of unheated drinking water for three case studies; for one case study where the point estimate of risk associated with the point estimate of exposure was close to the Netherlands regulatory acceptable health risk of 1/10,000 infections per consumers/year, stochastic modeling was performed in which statistical distributions were fit to the data for *Crytosporidium* concentrations in raw water (negative binomial), removal of SRC during treatment (beta binomial), and consumption of drinking water (log normal) and used in Monte Carlo analysis. 3. assumptions: NA 4. limitations: estimation of inactivation (as opposed to removal) of oocysts by treatment and determination of strain genotype to determine pathogenicity to humans included only in the stochastic case study 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions: point estimates of exposure and risk may be sufficient when the risk estimate is above or below an existing safety level; statistical techniques can be used to determine distribution of exposure and risk when the risk estimate is close to the regulatory level 2. authors' extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: few data available on removal or inactivation of *Crytosporidium* itself under different treatment regimens 2. proposed solutions: on-going studies
H. Weight of Evidence	1. robustness of method: high 2. representativeness of data: high 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: high

	5. defensibility: high
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	same study in DR, RC

A. Exposure Assessment Study Identification (Water)	Petterson, S.R., and N.J. Ashbolt. 2001. Viral risks associated with wastewater reuse: Modeling virus persistence on wastewater irrigated salad crops. Wat. Sci. Technol. 43(12): 23-26.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific; to investigate the implications of over-dispersion and the presence of a very persistent sub-population of viruses for assessing viral illness from the consumption of lettuces and carrots irrigated with secondary treated effluent. 2. type: EA
C. Publication Attributes	1. sponsors/affiliations: University of New South Wales, Victorian Dept of Human Services, and CRC for Waste Management and Pollution Control Ltd. 2. peer-review mechanism: Scientific journal.
D. Data and Study Design	1. type: simulation 2. source: Orange County enterovirus data (Tanaka et al., 1998) 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: standard virus decay modeling, using published and assumed decay coefficients and Monte Carlo simulations 2. specific characteristics: 10,000 Monte Carlo iterations for each of two input distributions to represent the number of viruses on the crop following irrigation, one representing uniform dispersion and the other giving consideration to over-dispersion. The virus decay rates were used; 0.47/d from experimental data and 0.69 (Asano et al., 1992) and a normal distribution (0.47, 0.03) for phage.

	3. assumptions: Over-dispersion–the number of virus on a 100 gram sample follows a discrete distribution, virus decay followed log linear inactivation rate of 0.69/day, consumption occurred 14 days following final irrigation. Persistent sub population–100 viruses/100 gram sample present following final irrigation. For bi-phasic decay the initial fast phase was assumed to be faster than the average value assumed for single phase decay. 4. limitations: the actual values of the risk estimates should only be considered for relative comparison between different model runs. 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: When over-dispersion or clumping of viruses is accounted for, a significant increase in the heterogeneity in the risk estimate arises. Predicted infection rates were significantly underestimated if the presence of a persistent sub-population of viruses was not considered in the decay kinetics of the risk model. Virus decay rate more sensitive to risk estimation than initial density. Virus decay rates highly variable and inappropriate for simple log-linear decay modeling. 2. authors' extrapolations: Both viral clumping and persistence sub-populations should be accounted for in future risk assessments of enteric viruses associated with wastewater reuse.
G. Data Gaps and Proposed Solutions	1. data gaps: viral attachment, adsorption, decay rates 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: high 2. representativeness of data: low 3. generalizability or external validity: high 4. soundness of study conclusions or internal validity: high 5. defensibility: high
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	NA

A. Exposure Assessment Study Identification (Water)	Teunis, P.F.M., G.J. Medema, L. Kruidenier, et al. 1997b. Assessment of the risk of infection by *Cryptosporidium* or *Giardia* in drinking water from a surface water source. Wat. Res. 31(6): 1333-1346.
B. Objectives and Type of Study	1. purpose: scientific, future regulatory interest. This paper focuses on the assessment of the risk of infection by

	Cryptosporidium and *Giardia* via drinking water from a surface water supply. 2. type: EA
C. Publication Attributes	1. sponsors/affiliations: Directorate General for the Environment, Ministry of Housing, Physical Planning and the Environment, The Hague, Netherlands. 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: experimental data for concentration of *Cryptosporidium* and *Giardia* and other relevant parameters were collected at the inlet and outlet of a water storage system; published data (by others) for viability of *Cryptosporidium* and *Giardia* (unknown sampling method); unpublished data from another water treatment facility was used to model treatment efficiency (unknown sampling method); published data for water consumption in the Netherlands (unknown sampling method); 2. source: published and unpublished datasets 3. extent of data: large data sets have been collected representing numbers of viable type cysts or oocysts per 1000 liters of water 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: high
E. Method/Model/Approach	1. general characteristics: A statistical model for the probability of *Cryptosporidium* and *Giardia* infection from treated *surface water* is described. 2. specific characteristics: Negative binomial distribution for counts of *Cryptosporidium* and *Giardia*; beta-binomial distribution for recovery, viability and treatment efficiency; exponential distribution for dose-response model. 3. assumptions: NA 4. limitations: Data needed to model treatment efficiency could not be collected because direct detection of the pathogenic organisms in the treated water was not possible; therefore, data on the removal of spores of surrogate spore former (sulphite reducing *Clostridia*) from another drinking water treatment facility were used. 5. relevance: high
F. Study Conclusions and Extended Applications	1. conclusions: NA 2. authors' extrapolations: surrogate is representative of distribution and survival of pathogens of interest
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: some high

	3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: low 5. defensibility: high
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	Authors suggest that the work described in the paper should be regarded as a preliminary study, mainly to investigate problem areas and to test the feasibility of the chosen approach.
K. Cross-References	NA

A.1.3 Inhalation (Aerosol)

A. Exposure Assessment Study Identification (Aerosol)	Aden, J. and B.R. Scott. 2003. Modeling variability and uncertainty associated with inhaled weapons-grade PuO2. Health Phys 84(6): 726-736.
B. Objectives and Type of Study	1. purpose noted by study authors: evaluate the distribution of radioactivity intake to relatively small numbers of high-specific-activity PuO_2 particles using a stochastic respiratory deposition model 2. type: EA
C. Publication Attributes	1. sponsors/affiliations: Lovelace Respiratory Research Institute, New Mexico; US Dept. of Energy 2. peer-review mechanism: scientific journal review
D. Data and Study Design	1. type: NA 2. source: NA 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: NA
E. Method/Model/Approach	1. general characteristics: development of a stochastic model for the deposition of inhaled radioactive particles within the respiratory tract 2. specific characteristics: The Crystall Ball model is an extension of the Lung Dose Evaluation Program (LUDEP) (ICRP, 1994). Modifications to the LUDEP code include adding a stochastic module that allows the modeling of inter-individual variability in respiratory tract deposition attributes (i.e., model parameters) and uncertainty in the parameters of the statistical distributions that are used to model the variability in the model parameters, and considers particle polydispersivity (i.e., allows particle size to vary); LUDEP and LUDUC assume particles are of one size (monodisperse). Model requires parameter values for height, volumetric flow rate, lung volume, ventilation rate, and other respiratory tract attributes. Distribution for variability and uncertainty for these parameters are from the Lung Dose Uncertainty Code (LUDUC) (Huston, 1995; Jarvis et al., 1996; Bolch et al. 2001). Many of Huston's distributions are based on regression functions that use sex, age, height and body mass index as predictors. The paper presents results of hypothetical exposure scenario of adult male workers exposed to airborne weapons-grade PuO2 from an accidental release. Results are based on 1,000 iterations of the Monte Carlo model. The model predicts the fraction of inhaled particles that are deposited in each of 5 regions of the respiratory tract. 3. assumptions: the radiation dose from beta and gamma radiations is negligible; all inhalation is through nose (although the model appears to be easily modified to consider inhaltion through mouth and nose); the geometric standard deviation of the aerodynamic particle diameter is a function of the median thermodynamic diameter (ICRP, 1994) 4. limitations: no model calibration or validation is discussed, other than that the central tendency estimates

	compare favorably with output from the LUDEP model 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: predicted patterns particle deposition within the respiratory tract are consistent with output from LUDEP (central tendency only) and LUDUC, and those of Scott and Fenel (1999). 2. extrapolations: The distribution of radioactivity intake could be modeled using the output from the model, and probability distributions for airborne particles that the receptor is exposed to. The authors claim the program can be used to model the deposition of other particles (e.g., anthrax) because the deposition model depends only on the aerodynamic properties of the particles.
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	model may be useful for predicting exposure to airborne micro-organisms; model calibration/validation is desirable
K. Cross-References	NA

A. Exposure Assessment Study Identification (Aerosol)	Huston, T.E., E.B. Farfan, W.E. Bolch and W.E. Bolch. 2003. Influences of parameter uncertainties within the ICRP-66 respiratory tract model: A parameter sensitivity analysis. Health Physics 85(5): 553-566.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific; 2. type: EA
C. Publication Attributes	1. sponsors/affiliations: Centers for Disease Control; University of Florida; US Department of Energy 2. peer-review mechanism: full scientific journal review.

D. Data and Study Design	1. type: NA 2. source: published studies 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: Global sensitivity analysis of all 69 input parameters of the ICRP-66 respiratory tract model was performed using the Lung Dose Uncertainty Code (LUDUC) to identify the input parameters that have largest influence on the model output. 2. specific characteristics: Statistical distributions for the 69 model parameters were based on a literature review by author (Huston, 1995). Distributions were sampled 1,000 times using Latin hypercube sampling. Standardized rank regression coefficients (SRRC) and step-wise regression analysis were used to quantify and rank influence of each model parameter on the model output. Case study for sensitivity analysis: adult males 25-34 years old, exposed to PuO_2 aerosols at a light exertion level. 3. assumptions: case study assumed monodisperse aerosols; acute deposition was assumed 4. limitations: not clear how assumption of monodisperse particles affected outcome of sensitivity analysis; conclusions are based on just one exposure scenario involving the 25-34 y male population 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: 50% of the variability in total lung dose of PuO_2 is due to variability in the dose to the alveolar-interstitial (AI) region, and 90% of dose to the AI region explained by variance in ventilation rate, AI deposition fraction, clearance rate constant for slow-phase absorption of deposited material to the blood, and clearance rate from AI_2 to bb_1 compartment 2. extrapolations: Results for similar long-lived, relatively insoluble, primarily alpha emitting materials are expected to be similar to $^{239}PuO_2$; Deposition predictions similar expected to be similar for wide range of exposure scenarios (including different radionuclides and chemical forms)
G. Data Gaps and Proposed Solutions	1. data gaps: additional data on most important variables 2. proposed solutions: refine distributions for most important variables
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility: UN

I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	potentially useful for dosimetry of air-borne particles and adsorbed constituents. The IRP model can be used to model the deposition of any particles within the respiratory tract because the deposition is a function of the aerodynamic properties of the particles, not the agents that are adsorbed onto the particles
K. Cross-References	NA

A. Exposure Assessment Study Identification (Aerosol)	NIOSH. 2001. Exposure and risk assessment for infectious aerosols. Berkeley, CA: National Institute for Occupational Safety and Health. PB2001101415.
B. Objectives and Type of Study	1. purpose: regulatory, future regulatory interest; to develop a quantitative framework for assessing and managing risk of occupational TB transmission in a hospital setting. 2. type: EA
C. Publication Attributes	1. sponsors/affiliations: National Institute for Occupational Safety and Health 2. peer-review mechanism: Report (not specified)
D. Data and Study Design	1. type: epidemiological data on number of TB patients admitted to hospitals annually and number of TB cases among health care workers 2. source: published studies, government datasets 3. extent of data: published information is sparse; study based on available information and a mail questionnaire survey of hospital epidemiologists 4. sampling plan: random 5. sample size: simulations based on 1000 individuals (health care workers); questionnaire survey data from ~200 hospitals 6. performance characteristics: probabilities with standard deviations, percent coefficient of variation reported; adequate analytical and statistical methods; study appears complete 7. relevance: low
E. Method/Model/Approach	1. general characteristics: stochastic 500 simulation model to describe TB infection and disease incidence among a hospital health care worker (HCW) cohort; 100,000 simulation Monte Carlo used in a probabilistic three-state Markov model of infectious particle concentrations in a TB patient isolation room 2. specific characteristics: Poisson random variable model for number of TB patients admitted; turbulent eddy

	diffusion model to describe continuous concentration gradient in Markov models; Markov chain approach to formulate two models to describe dispersion of particles in room air 3. assumptions: an otherwise healthy individual has a 5% chance of developing disease in first year after infection; a diseased worker remains on the job for three calendar weeks while infectious; a diseased worker has 25 close contacts; close contacts have a 22% chance of being infected 4. limitations: Markov models do not independently predict the room air flow patterns and turbulent diffusion coefficient 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions: a binary type of patient infectivity generates substantial variability in infection incidence; infection among immunocompromised HCWs causes only a slight increase in incidence of 2º *M. tb* infection and TB disease at the HCW cohort level2. authors' extrapolations: Engineering elements of the source-pathway-receptor construct for airborne infection can be generalized to other infectious aerosols of occupational concern.
G. Data Gaps and Proposed Solutions	1. data gaps: none stated 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: low 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: high 5. defensibility: high for hospital scenarios
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	potentially useful in modeling fate of airborne infectious particulates in buildings.
K. Cross-References	same study in RC

A. Exposure Assessment Study Identification (Aerosol)	Webb, G.F. and M.J. Blaser. 2002. Mailborne transmission of anthrax: Modeling and implications. PNAS 99(10): 7027-7032.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific; development of model to apply to scenarios that are similar to mailborne transmission of anthrax

	2. type: EA
C. Publication Attributes	1. sponsors/affiliations: National Science Foundation, National Institutes of Health, Department of Veterans Affairs 2. peer-review mechanism: scientific journal review
D. Data and Study Design	1. type: observational data for number of anthrax-contaminated letters, and the number of total letters processed per time 2. source: published government reports (CDC) 3. extent of data: one incident for number of contaminated letters and spore counts 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: very limited data and no statistical analysis 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: development of a deterministic mathematical model to describe the cross-contamination of letters in the postal system by *n* original letters contaminated with spores of *B. anthracis.* 2. specific characteristics: postal system is modeled as series of five nodes: 1-mailbox or other entry point, 2-local postal destination, 3-regional postal facility, 4-local postal facility, 5-final destination; exposure modeled as function of two variables - initial number of contaminated letters introduced into the system and transition matrices that determine the rate of cross-contamination between letters 3. assumptions: originally-contaminated letters contain 10^{10} spores; spores from originally contaminated letters leak, causing cross-contamination of other mail in the postal system; magnitude of exposure = number of spores on letter, i.e., no modeling of the "...aerosolization of letterborne infectious particles..." 4. limitations: very small data set was used to calibrate model; key model parameters were selected to produce the output observed in one anthrax contamination case in 2001 via the US postal system; no model validation was performed 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: no specific conclusions are offered 2. extrapolations: authors describe how the basic model could be extended to apply to larger attacks, and provide model output for this scenario
G. Data Gaps and Proposed Solutions	1. data gaps: data needed to estimate transition matrices that are used in the model to determine the rates at which cross-contamination of letters occurs; studies of the aerosolization of letterborne infectious particles 2. proposed solutions: enhanced dose-reconstruction analysis to measure inhaled doses of surrogate spores
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low or NA

	3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: high for hypothetical scenarios
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	1. method appears to have potential usefulness for incident-based microbial risk assessment of buildings where the agent(s) are introduced into the building via the postal system; much more data and possibly substantial effort would be required for further model development to determine the usefulness of the exposure assessment model described by the authors 2. paper does not include sensitivity analysis for model, which might help focus future model development efforts
K. Cross-References	same study in DR, RC

A. Exposure Assessment Study Identification (Aerosol)	Wein, L.M., D. Craft and E.H. Kaplan. 2003. Emergency response to an anthrax attack. PNAS 100(7): 4346-4351. Supporting Text on www.pnas.org
B. Objectives and Type of Study	1. purpose noted by study authors: scientific, comparison of risk management options 2. type: EA
C. Publication Attributes	1. sponsors/affiliations: Center for Interdisciplinary Research on AIDS (Yale University), National Institutes of Mental Health and Drug Abuse/ Stanford University, Massachusetts Institute of Technology, Yale Schools of Management and Medicine 2. peer-review mechanism: full scientific peer-review
D. Data and Study Design	1. type: NA 2. source: assumptions or literature estimates 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: simplistic Gaussian plume (instantaneous point release) as per (Meselson et al., 1994)

	2. specific characteristics: system of integropartial differential equations; 3. assumptions: release 10^{15} anthrax spores (~1 kg) at 100 m altitude ; dispersion for neutral stability in open air for 200 km (downwind, length of plume) and ~36 km (width plume); uniform population age distribution for urban and rural residents; agent fully dispersed within 48 hours of intentional release 4. limitations: ignores decay of likelihood of deposition and infectivity temporally and spatially, protection of people in buildings, secondary aerosolization, and limits of vertical mixing 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: dispersion is consistent with theory, but largely unvalidated by controlled scientific studies 2. extrapolations: scenario for dispersion useful for selection of appropriate risk management strategies
G. Data Gaps and Proposed Solutions	1. data gaps: actual dispersion dynamics 2. proposed solutions: extend and validate existing model to account for wind, atmospheric influences, time of day for release, stability conditions, form of agent, method of aerosolization , etc.
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: NA
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	authors state Gaussian model perhaps too simplistic for prediction of spatiotheporal dynamics of future outdoor release events under unknown conditions; authors do not address limitations of data or inconsistencies in body of scientific evidence from animal and human sources; the influence of extensive assumptions of mathematical convenience or opinion is not well documented; inferences from poorly documented Sverdlovsk release very influential and merit considerations of alternative assumptions and further analysis
K. Cross-References	same study in RC

A.2 Dose-Response (Hazard Characterization) Assessment Methods

Buchanan, R.L., W.G. Damert, R.C. Whiting and M. van Schothorst. 1997. Use of epidemiologic and food survey data to estimate a purposefully conservative dose-response relationship for *Listeria monocytogenes* levels and incidence of listeriosis. J. Food Protect. 60(8): 918-922. 136

Chen, Y., W.H. Ross, V.N. Scott and D.E. Gombas. 2003. *Listeria monocytogenes*: Low levels equal low risk. J. Food Protect. 66(4): 570-577. 138

Coleman, M. and H. Marks. 1998. Topics in dose-response modeling. J. Food Protect. 61(11): 1550-1559. 140

Coleman, M.E. and H.M. Marks. 2000. Mechanistic modeling of salmonellosis. Quantitative Microbiology 2: 227-247. 142

Coleman, M.E., H.M. Marks, N.J. Golden and H.K. Latimer. 2004. Discerning strain effects in microbial dose-response data. J. Toxicol. Environ. Health 67(8-10): 667-85..... 144

Crawford-Brown, D. J. and S. Marquez-Nyarko. 1999. Development of an environmental decision support system (EDSS) for comparing drinking water treatment practices and associated health risks. Report No. 323. Chapel Hill, NC: Water Resources Research Institute of The University of North Carolina. 147

Englehardt J.D. and J. Swartout. 2004. Predictive population dose-response assessment for *Cryptosporidium parvum*: Infection endpoint. J. Toxicol. Environ. Health, Part A 67(8-10): 651-666. 149

Englehardt J.D. and J. Swartout. 2004. Predictive population dose-response assessment for *Cryptosporidium parvum*: Infection endpoint. J. Toxicol. Environ. Health, Part A 67(8-10): 651-666. 151

Falconer, I.R., M.D. Burch, D.A. Steffensen, et al. 1994. Toxicity of the blue-green alga (Cyanobacterium) *Microcystis aeruginosa* in drinking water to growing pigs, as an animal model for human injury and risk assessment. Environ. Toxicol. Wat. Qual. 9: 131-139. 153

FAO/WHO. 2002b. Risk assessments of *Salmonella* in eggs and broiler chickens. Food and Agriculture Organization/World Health Organization. http://www.who.int/foodsafety/publications/micro/salmonella/en/..... 155

FAO/WHO. 2004. Risk assessment of *Listeria monocytogenes* in ready-to-eat foods. Food and Agriculture Organization/World Health Organization. http://www.who.int/foodsafety/publications/micro/mra_listeria/en/ 157

Farber, J.M., W.H. Ross and J. Harwig. 1996. Health risk assessment of *Listeria monocytogenes* in Canada. Int. J. Food Microbiol. 30(1-2): 145-156. 159

FDA/USDA. 2003. Quantitative assessment of relative risk to public health from foodborne *Listeria monocytogenes* among selected categories of ready-to-eat foods. http://www.foodsafety.gov/~dms/lmr2-toc.html 161

Gale, P. 2001. Developments in microbiological risk assessment for drinking water. J .Appl. Microbiol. 91: 191-205..... 164

Latimer, H.K., L. Jaykus, R.A. Morales, et al. 2001. A weighted composite dose-response model for human salmonellosis. Risk Anal. 21(2): 295-305..... 166

Lindqvist, R. and A. Westoo. 2000. Quantitative risk assessment for *Listeria monocytogenes* in smoked or gravad salmon and rainbow trout in Sweden. Int. J. Food Microbiol. 58(3): 181-196. 168

A. Dose-Response Study Identification	Buchanan, R.L., W.G. Damert, R.C. Whiting and M. van Schothorst. 1997. Use of epidemiologic and food survey data to estimate a purposefully conservative dose-response relationship for *Listeria monocytogenes* levels and incidence of listeriosis. J. Food Protect. 60(8): 918-922.
B. Objectives and Type of Study	1. purpose: regulatory, future regulatory interest; to determine if purposefully conservative dose-response relationships can be estimated on the basis of combining available epidemiologic data with food-survey data for a ready-to-eat product. 2. type: DR
C. Publication Attributes	1. sponsors/affiliations: US Department of Agriculture, Agricultural Research Service 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: data on annual incidence of listeriosis in Germany; levels of *L. monocytogenes* in ready-to-eat smoked fish 2. source: published studies and government datasets 3. extent of data: large nationwide survey of wide variety of foods for presence of *L. monocytogenes;* German estimate of its nationwide extent of listeriosis. 4. sampling plan: random 5. sample size: calculations based on data from analysis of >14,000 food samples and estimated cases of listeriosis per year for the population of Germany. 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: exponential dose-response model to link number of listeriosis cases expected for different *L. monocytogenes* levels enumerated in the smoked fish survey. 2. specific characteristics: estimates the probability of listeriosis per serving. 3. assumptions: levels of *L. monocytogenes* ingested are greater than or equal to levels detected during food survey; listeriosis cases restricted to immunocompromised individuals at increased risk; 20% of German population is at increased risk; smoked fish average serving size is 50 g, and average number of servings per year is 20; immunocompromised individuals consume smoked fish at same rate as general population; all human listeriosis resulted from consumption of smoked fish; dose-response relationship for foodborne human *L. monocytogenes* infections fits exponential dose-response model. 4. limitations: current estimate based on a number of assumptions pertaining to factors that could impact its magnitude. 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions: conservative estimate of the relationship between morbidity and exposure; probability that a high-risk individual will acquire symptomatic listeriosis is extremely low unless high levels of pathogen are consumed. 2. authors' extrapolations: initial focus for risk-management decisions should be prevention of growth of *L.*

	monocytogenes in food to high levels, has greatest public health impact on a cost-benefit basis; similar calculations could be performed for other organisms if sufficient exposure and infection rate data are available.
G. Data Gaps and Proposed Solutions	1. data gaps: study limited to one set each of epidemiologic and microbial survey data. 2. proposed solutions: use additional epidemiologic and microbial survey data sets to enhance accuracy; use frequency distributions based on more quantitative microbial survey data to assess pathogen levels.
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: low 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	NA

A. Dose-Response Study Identification	Chen, Y., W.H. Ross, V.N. Scott and D.E. Gombas. 2003. *Listeria monocytogenes*: Low levels equal low risk. J. Food Protect. 66(4): 570-577.
B. Objectives and Type of Study	1. purpose: future regulatory interest; to derive a dose-response model from food survey and epidemiological data with respect to other variable factors. 2. type: DR
C. Publication Attributes	1. sponsors/affiliations: USDA Cooperative State Research Education and Extension Service; Joint Institute for Food Safety and Applied Nutrition, University of Maryland; National Food Processors Association 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: food survey data representing 8 ready-to-eat (RTE) product categories; illness data from Maryland and northern California FoodNet sites at which the food survey was conducted 2. source: published study; government datasets 3. extent of data: large datasets for both types of data used 4. sampling plan: clustered; samples assigned based on enumeration with Most Probable Number (MPN) pattern.

	5. sample size: 577 positive of 31,705 food samples tested; 106 listeriosis cases for 2-year sampling period given twofold multiplier for underreporting (from higher-risk population of estimated 25% of US population). 6. performance characteristics: NA 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: exponential dose-response model derived on basis of levels of *L. monocytogenes* contamination in foods, number of listeriosis cases in population consuming those foods, size of population of higher risk individuals, number of servings consumed, serving size; purposely conservative risk assessment. 2. specific characteristics: beta distributions of food survey data input into Analytica for 30,000 iteration simulations; categorized frequency data fit to various probability distributions with BestFit and divided into ~65 intervals using 30,000 iteration simulations in Analytica; intervals used to derive exponential model parameter R (risk factor). 3. assumptions: RTE foods are primary source of consumer exposure to *L. monocytogenes*; levels of organism in food did not increase between purchase and consumption; model assumes that a single cell is capable of causing infection, and all cells ingested have an equal probability of causing illness. 4. limitations: no experimental data involving *L. monocytogenes* in humans or animal clinical studies 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions: model gives a direct indication of probability of illness from consumption of a given number of organisms; majority of listeriosis cases were due to consumption of servings contaminated at higher concentrations; most effective efforts to reduce risk of listeriosis in RTE foods will involve targeting heavily contaminated servings. 2. authors' extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: variability in virulence among *L. monocytogenes* subtypes and food matrix effects not modeled in the risk assessment; consistency of exponential model illness probability extrapolation for low dose levels not experimentally proven. 2. proposed solutions: include these variables in another similar risk assessment; try to experimentally prove consistency of model at low dose levels.
H. Weight of Evidence	1. robustness of method: high 2. representativeness of data: low 3. generalizability or external validity: high 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA

J. Reviewer Comments	This method would be useful in situations where human feeding trial and similar data are not available or cannot be obtained for dose-response assessments.
K. Cross-References	Buchanan et al., 1997

A. Dose-Response Study Identification	Coleman, M. and H. Marks. 1998. Topics in dose-response modeling. J. Food Protect. 61(11): 1550-1559.
B. Objectives and Type of Study	1. purpose: scientific; Examination of two data sets for dose-response modeling of illness in adult humans. In particular, the authors seek to show how host, pathogen, and environmental variables have a substantial effect on the probability and severity of illnesses. 2. type: DR
C. Publication Attributes	1. sponsors/affiliations: USDA Food Safety and Inspection Service 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: dose response data on healthy males fed *Salmonella* or *Shigella* strains 2. source: several published studies 3. extent of data: Two data sets were employed: a salmonellosis data set consisting of 163 total observations for healthy adult male volunteers administered nine strains of *Salmonella* from five species or serotypes, and a shigellosis data set consisting of 266 fasting healthy male adult volunteers administered two species (one strain each) from *Shigella dysenteriae* and *Shigella flexneri*. 4. sampling plan: NA 5. sample size: 163 subjects the salmonellosis studies and 266 subjects for the shigellosis studies. 6. performance characteristics: The study provides basic statistics (Chi-square 95% confidence intervals) and model fits to the observed data. 7. relevance: high
E. Method/Model/Approach	1. general characteristics: statistical analysis of data fitted to three different model forms 2. specific characteristics: The study features analysis of variance with its attendant statistics for three types of model forms: logistic, Gompertz, and Beta-Poisson. 3. assumptions: All the treatments are independent. The authors did examine the data that they collected from literature sources for validity. 4. limitations: By the authors own admission, the data sets are sparse and the treatment distributions are not

	balanced. 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions: The modeling exercise needs to be conducted with care because several different model forms can be fit equally well to the same set of data. The choices made need to make sense biologically. 2. authors' extrapolations: *Salmonella* data expected to be more representative of *Shigella* than *Salmonella typhimuriun*
G. Data Gaps and Proposed Solutions	1. data gaps: data are lacking particularly at low doses. 2. proposed solutions: generate mechanistic data considering diverse body of evidence (*in vivo* and *in vitro* methods, animal and human clinical studies, epidemiologic and occupational exposures)
H. Weight of Evidence	1. robustness of method: high 2. representativeness of data: some high 3. generalizability or external validity: high 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	In general the method shown is applicable for assessment of microbial risks in food sources, water systems and buildings. The article is a well reasoned study that is valuable to those who want to understand microbial risk assessment modeling. The authors are careful to define their terms and show how different statistical analyses and model forms can affect predictions.
K. Cross-References	NA

A. Dose-Response Study Identification	Coleman, M.E. and H.M. Marks. 2000. Mechanistic modeling of salmonellosis. Quantitative Microbiology 2: 227-247.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific, future regulatory interest 2. type: DR
C. Publication Attributes	1. sponsors/affiliations: US Department of Agriculture 2. peer-review mechanism: full scientific peer review

D. Data and Study Design	1. type: theoretical; human clinical data; information on mechanisms of pathogens and virulence 2. source: published studies 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: Authors present a mechanistic model that consists of biological events leading from ingestion of *Salmonella* to the development of disease symptoms, to identify a possible biological basis for using a dose-response curve that is convex-shaped in the low dose region; i.e., to support the use of a dose-response model that includes a no response threshold region at low doses 2. specific characteristics: The mechanistic model consists of 7 events: *survival to target, attachment, engulfment, intracellular survival, migration/multiplication, host cell damage,* and *symptoms of gastroenteritis*. Mathematical models are described for attachment, the formation of lesions following engulfment, the distribution of the number of lesions, and the probability of illness. The authors show how these models can lead to a dose-response function that is convex at low doses. Alternatively, the authors describe the interaction between the pathogen and the host defense systems' as a predator-prey relationship, using a system of differential equations to describe the size of the pathogen population over time. The dynamic predator-prey model provides a method for modeling of immunity and disease progression for salmonellosis. 3. assumptions: possible effects of quorum sensing and size of the pathogen colonies are not considered in the derivation of the dose-response functions (which, if considered, could lead to a greater degree of convexity). 4. limitations: little mechanistic data available for model development or selection among empirical models available 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: 2. extrapolations:
G. Data Gaps and Proposed Solutions	1. data gaps: data for evaluating the possible effects of quorum sensing and the size of colonies on the dose-response relationship is lacking 2. proposed solutions: conduct research to generate such data
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high

	5. defensibility: high
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	1. The authors provide a framework that could provide the basis for using dose-response models with low-dose thresholds, and possibly for mechanistic modeling
K. Cross-References	NA

A. Dose-Response Study Identification	Coleman, M.E., H.M. Marks, N.J. Golden and H.K. Latimer. 2004. Discerning strain effects in microbial dose-response data. J. Toxicol. Environ. Health 67(8-10): 667-85.
B. Objectives and Type of Study	1. purpose: scientific; risk assessment methods development for foodborne pathogens of regulatory interest 2. type: DR
C. Publication Attributes	1. sponsors/affiliations: USDA Food Safety and Inspection Service project 2. peer-review mechanism: full scientific journal review
D. Data Description and Study Design	1. type: human clinical data for administration of *Salmonella* strains isolated from spray-dried egg product and human clinical case and *Campylobacter* strains from human clinical cases 2. source: published studies (McCullough & Eisele, 1951a-d; Black et al., 1988) 3. extent of data: 13 strains of six serotypes of *Salmonella* administered to 432 human volunteers with endpoints of fecal excretion and illness; 2 strains of *Campylobacter* administered to 111 human volunteers with endpoints of fecal excretion, diarrhea, fever, volume liquid stool, and serological endpoints 4. sampling plan: 3 or more treatment groups at administered doses from 3 to 10 log counts per volunteer 5. sample size: 5 or 6 volunteers per dose group administered *Salmonella*; 5 to 22 volunteers per dose group administered *Campylobacter* 6. performance characteristics: NA 7. relevance: medium (*Campylobacter* on list of concern and food-borne agent, but study not well controlled for confounding factors such as cellular immunity; non-typhoid *Salmonella* not listed agent, but related to listed agent *Salmonella typhi*)
E. Method/Model/Approach	1. general characteristics: data analysis of body of evidence for two food-borne pathogens including experimental data from human clinical studies and more recent supporting literature 2. specific characteristics: analysis of variance models for logistic and Gompertz (extreme value) distributions,

	testing serotype, strain, and nested effects for salmonellosis referencing previously published study (Coleman and Marks, 1998); 3. assumptions: independent action of bacterial cells unlikely 4. limitations: for *Campylobacter*, inoculum production techniques inappropriate, host variability in immune competency uncharacterized, and sparse and unsymmetrical data for characterizing dose-response relationships for strains, as well as poorly characterized pathogenicity and virulence attributes of strains 5. relevance: medium
F. Study Conclusions and Extended Applications	1. strain effects in human dose-response relationships are supported by the data for these two food-borne pathogens; dose-response models based on human clinical data for *Campylobacter* inappropriate for use in risk assessment due to inconsistencies with more current procedures and more recent evidence from ongoing human clinical trials 2. extrapolation of dose-response models including strain effects to predict illness from consumption of random strains present in servings of foods discussed by study authors
G. Data Gaps and Proposed Solutions	1. data gaps: relative estimates of pathogenicity and virulence for panels of stains (paralleling Toxic Equivalence Factors in chemical risk assessment); distributions of strains that vary in pathogenicity and virulence in foods; mechanisms of survival and invasion 2. proposed solutions: research with genetically engineered animal models as per Lecuit & Cossart (2002) to address normal and susceptible populations, with assumptions or source of surrogate data to fill gaps; expert elicitation
H. Weight of Evidence	1. robustness of method: high 2. representativeness of data: high for *Campylobacter*; low for *Salmonella typhi* 3. generalizability or external validity: high 4. soundness of study conclusions or internal validity: high 5. defensibility: high
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	1. given dose-response data for biothreat agents of interest, analysis of variance (and related non-linear mixed effects modeling) are appropriate and rigorous methods for dose-response modeling in incident-based microbial risk assessment of buildings and water systems; multiple empirical model forms, threshold and non-threshold, would be appropriate to consider for bacterial hazards based on number of volunteers lacking adverse effects after high doses of *Salmonella* and *Campylobacter* 2. might expect bias for highly virulent threat preparations so that strain variability is less important; analysis of variance techniques, particularly for non-linear mixed effects modeling, powerful and underutilized approach in microbial dose-response analyses

	3. both organisms non-spore-forming bacteria expected to be low stability and/or declining in air and water 4. more recent human clinical dataset available for *Campylobacter* (Tribble, Naval Medical Research Center)
K. Cross-References	Oscar, 2004; Coleman and Marks, 2000; Coleman and Marks, 1998

A. Dose-Response Study Identification	Crawford-Brown, D. J. and S. Marquez-Nyarko. 1999. Development of an environmental decision support system (EDSS) for comparing drinking water treatment practices and associated health risks. Report No. 323. Chapel Hill, NC: Water Resources Research Institute of The University of North Carolina.
B. Objectives and Type of Study	1. purpose: scientific and future regulatory; to present the development of a software tool to aid decision-makers involved in analyzing the various risks associated with disinfection treatment options for drinking water 2. type: DR
C. Publication Attributes	1. sponsors/affiliations: Water Resources Research Institute of The University of North Carolina 2. peer-review mechanism: NA
D. Data and Study Design	1. type: experimental data (not further described) 2. source: NA 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: least squares regression was used to fit experimental data to several mathematical models of dose-response for disinfectant by-products and microbes 2. specific characteristics: dose-response parameters for risk of cancer from the disinfection by-products were estimated by fitting experimental data for the individual chemicals to linear (one hit), quadratic (two hit), or beta-Poisson models by least squares regression; dose-response parameters for risk of health effects from *Giardia* and *Cryptosporidium* were estimated by fitting experimental data for the individual microbes to linear (one hit), linear two-population, or beta-Poisson models by least squares regression; for both disinfectant by-products and microbes, the models can be weighted by the user; inputs can be point estimates or user-specified distributions, and if distributions are specified, probabilistic evaluation (Monte Carlo, Median Latin hypercube, or Random Latin hypercube) can be performed to obtain probability distributions for health outcomes.

	3. assumptions: risk of cancer from disinfectant by-products is assumed to be additive, with no synergistic or antagonistic interactions 4. limitations: the current model is limited to predicting the risk of cancer from exposure to chloroform, bromoform, bromodichloromethane, chlorodibromomethane, dichloroacetic acid, and trichloroacetic acid, although the model can be expanded to include other by-products; the current model is limited to predicting risk of adverse health effects from exposure to *Giardia* and *Cryptosporidium*, although the model can be expanded to include other waterborne pathogens 5. relevance: medium
F. Study Conclusions and Extended Applications	1. the model provides a flexible tool to predict risk of health effects due to *Giardia* and *Cryptosporidium* at different exposure levels 2. authors' extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: high 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility: high
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	same study in EA, RC

A. Dose-Response Study Identification	Englehardt J.D. and J. Swartout. 2004. Predictive population dose-response assessment for *Cryptosporidium parvum*: Infection endpoint. J. Toxicol. Environ. Health, Part A 67(8-10): 651-666.
B. Objectives and Type of Study	1. purpose: scientific; A hierarchical predictive population dose-response Bayesian assessment for *C. parvum* is presented for the infection endpoint. 2. type: DR

C. Publication Attributes	1. sponsors/affiliations: University of Miami, EPA 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: Dose-response data for *C. parvum* isolates (Iowa, TAMU, and UCP) by subject serum-antibody status (Ab+ or Ab- to indicate presence or absence of *C. parvum*-specific antibodies in volunteers). 2. source: Dr. Cynthia Chappell, updated from those previously published (Dupont et al., 1995; Chappell et al., 1999) 3. extent of data: NA 4. sampling plan (random, clustered, factorial design, etc.): NA 5. sample size: Eleven doses (as oocysts), ranging from 10 to 1,000,000. The Ab+ individuals comprised 40% of the 49 total observations and were confined to relatively narrow range of dose groups in the higher dose range. 6. performance characteristics: NA 7. relevance: high
E. Method/Model/Approach	1. general characteristics: A parametric bootstrap approach was used to simulate the entire exposed human population 2. specific characteristics: Parametric bootstrap utilizing a closed-form distribution fitted to the original data as the assumed “true” response distribution was used (Shao and Tu, 1995). Sampling is binomial based on the fitted probability of a response, given the number of observation at each dose level. Population-response simulations were conducted for each isolate for the beta-Poisson or exponential response models, depending on the data. All simulations conducted with S-Plus version 4.5 for Windows. The DR model was fit to Ab+ and Ab- individuals. Beta-Poisson used for all except UCP. DR models fit by minimizing the log-likelihood of the respective cumulative probability functions. Goodness of fit was assessed from the asymptotic relationship of the log-likelihood to the chi-square distribution. 3. assumptions: Fraction of sensitive individuals was assumed based on approximate fraction of the US population below 1- and above 70-yr; Responses for Ab- and Ab+ individuals were generated binomially assuming dose-dependent response probabilities based on their respective initial model fits; Responses of sensitive individuals were assumed always positive at the doses tested. 4. limitations: none provided 5. relevance: high
F. Study Conclusions and Extended Applications	1. conclusions: TAMU Ab- fit to beta-Poisson; TAMU Ab+ fit to exponential; Iowa Ab- fit to beta-Poisson; Iowa Ab+ fit to beta-Poisson; and UCP Ab- fit to exponential. 2. authors’ extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: available DR methods, inclusion of secondary transmission 2. proposed solutions: further development of DR methods for pathogens; include secondary transmission

H. Weight of Evidence	1. robustness of method: high 2. representativeness of data: high 3. generalizability or external validity: high 4. soundness of study conclusions or internal validity: high 5. defensibility: high
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	see the other DR template for population response from this same article

A. Dose-Response Study Identification	Englehardt J.D. and J. Swartout. 2004. Predictive population dose-response assessment for *Cryptosporidium parvum*: Infection endpoint. J. Toxicol. Environ. Health, Part A 67(8-10): 651-666.
B. Objectives and Type of Study	1. purpose: scientific; A hierarchical predictive population dose-response Bayesian assessment for *C. parvum* is presented for the infection endpoint. 2. type: DR
C. Publication Attributes	1. sponsors/affiliations: University of Miami 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: Dose-response data for *C. parvum* isolates (Iowa, TAMU, and UCP) by subject serum-antibody status (Ab+ or Ab- to indicate presence or absence of *C. parvum*-specific antibodies in volunteers). 2. source: Dr. Cynthia Chappell, updated from those previously published (Dupont et al., 1995; Chappell et al., 1999) 3. extent of data: NA 4. sampling plan: NA 5. sample size: Eleven doses (as oocysts), ranging from 10 to 1,000,000. The Ab+ individuals comprised 40% of the 49 total observations and were confined to relatively narrow range of dose groups in the higher dose range. 6. performance characteristics: NA 7. relevance: high

E. Method/Model/Approach	1. general characteristics: A hierarchical predictive analysis was conducted to assess population infectivity response. 2. specific characteristics: Assumed beta-Poisson relationship for infection endpoint. To describe variability in *r* based on available information, a predictive Bayesian distribution for *r* was obtained. Computations were conducted using the Markov chain Monte Carlo technique (Gilks et al., 1996) using Matlab version 5.2.0.3084 software. Probability mass functions were plotted in log space. 3. assumptions: That the probability of infection versus dose was described by the exponential distribution in which the exponential parameter, *r*, was variable as described by the beta distribution. 4. limitations: The predictive DR function is a distribution of unconditional probability of illness as a function of dose, based on available information. The distribution is higher in Shannon entropy when less information is available, accounting for both uncertainty and variability. 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions: If no DR information is available for a pathogen, Shannon entropy of the DR function is maximized and the risk is equal to the maximum risk for any pathogen. The unconditional response at any dose, given no DR information is equal to the probability of ingesting one or more organisms. Predictive distributions are sensitive to the form of the sampling distributions. Dose of $6x10^{-6}$ oocysts per exposure corresponds to 10^{-4} infections per capita year. 2. authors' extrapolations: for low-dose risk assessment, which involves extrapolation beyond the range of observations.
G. Data Gaps and Proposed Solutions	1. data gaps: a predictive dose-response function in terms of illness endpoint is needed; effect of secondary transmission should be evaluated if the infection endpoint used to set water quality standards. 2. proposed solutions: develop DR relationships and include secondary transmission.
H. Weight of Evidence	1. robustness of method: high 2. representativeness of data: high 3. generalizability or external validity: high 4. soundness of study conclusions or internal validity: high 5. defensibility: high
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	Methodology for DR would be of use for those pathogens with no or limited DR specific information.
K. Cross-References	NA

A. Dose-Response Study Identification	Falconer, I.R., M.D. Burch, D.A. Steffensen, et al. 1994. Toxicity of the blue-green alga (Cyanobacterium) *Microcystis aeruginosa* in drinking water to growing pigs, as an animal model for human injury and risk assessment. Environ. Toxicol. Wat. Qual. 9: 131-139.
B. Objectives and Type of Study	1. purpose: scientific; This paper describes the use of growing pigs as a model for human injury resulting from *Microcystis* toxins in drinking water. 2. type: DR
C. Publication Attributes	1. sponsors/affiliations: Land and Water Resources Research and Development Corporation, the South Australian Engineering and Water Supply Department, and the University of New England 2. peer-review mechanism: peer-reviewed journal
D. Data and Study Design	1. type: experimental design 2. source: bloom material of *Microcystis aeruginosa* collected from a lake in Australia. Replicate cell counts (3) gave a mean cell content of $2.32x10^6$ cell/ml scum. Mean dry weight of pooled scum was 16.6 $x10^6$ cells/mg dry scum, and the toxin content per cell was 0.2 pg. 3. extent of data: Four dose rates of 374, 227, 80, and 0 mg dry algae/kg body weight/day intake by the pig; average toxin consumption was 1,312, 796, 280, and 0 ug toxin/kg/day for the four groups of pigs. 4. sampling plan: experimental 5. sample size: Four groups of 5 pigs (total 20 male pigs). 6. performance characteristics: NA 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: No statistical models were applies to the dose-response data other than a determination of NOAELs and AELs. 2. specific characteristics: The lowest dose of the toxin in study produced liver injury in 1/5 pigs 3. assumptions: All pigs were equally healthy and exposure to outside influences was equal. 4. limitations: small number of pigs in each group 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions: The liver is the primary target for the toxin, use of pigs for human injury requires additional uncertainty factor, human population will vary in susceptibility; only subchronic effects noted over the 44 days of exposure. 2. authors' extrapolations: A "safe exposure" level was determined by dividing the lowest exposure level, 280 μgtox/kg/day, by an uncertainty factor of 1,000—10 for extrapolating from sunchronic to chronic exposure, 10 for human variations, and 10 for susceptibility and extrapolating from pigs to humans

G. Data Gaps and Proposed Solutions	1. data gaps: lack of human exposure data 2. proposed solutions: large epidemiologic studies required
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	No mathematical models were applied to the dose-response data, but a NOAEL/LOAEL approach was applied to derive estimates of safe exposure. Thus, this paper was not excluded.
J. Reviewer Comments	May be of some use for determining dose-response relationship for the toxin.
K. Cross-References	NA

A. Dose-Response Study Identification	FAO/WHO. 2002b. Risk assessments of *Salmonella* in eggs and broiler chickens. Food and Agriculture Organization/World Health Organization. http://www.who.int/foodsafety/publications/micro/salmonella/en/
B. Objectives and Type of Study	1. purpose: scientific and future regulatory interest; compile currently available information relevant to risk assessment of *Salmonella* in eggs and broiler chickens; identify data gaps; develop example risk assessment models; consider efficacy of some risk management interventions 2. type: DR
C. Publication Attributes	1. sponsors/affiliations: FAO/WHO 2. peer-review mechanism: Technical Report initiated in 1999 and reviewed several times during preparation and after completion through consultations and by an extensive list of selected reviewers and members of the public during a public comment period
D. Data and Study Design	1. type: human clinical trials that administered surrogate pathogens, non-typhoid *Salmonella* and *Shigella*; outbreak information 2. source: published literature 3. extent of data: NA 4. sampling plan: NA

	5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: human clinical data fit to various empirical models; plots of average attack rates and average estimated doses ingested in outbreaks developed for fitting 2. specific characteristics: some consideration of parameter uncertainty by bootstraping;10-fold safety factor assumed for more susceptible sub-population 3. assumptions: DR relationship for surrogate pathogens representative of pathogens of interest; secondary transmission not major factor for salmonellosis; safety factor sufficient to characterize normal and more susceptible subpopulations 4. limitations: sparse and indirect data 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions: predictions of alternative dose-response relationships deviate significantly 2. authors' extrapolations: selected DR relationship is useful for current purpose
G. Data Gaps and Proposed Solutions	1. data gaps: characterization and quantification of the impact of the food matrix effects and host-pathogen interactions and virulence factors and their effect on the likelihood of illness 2. proposed solutions: more rigorous dose-reconstruction analysis for outbreaks and epidemiological data; targeted research on mechanisms of pathogenesis and virulence that affect human dose-response relationships
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: low 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	generic model based on pooled data from multiple sources and countries of origin and assumptions may not support rigorous science-based modeling; 2004 update of US work cited by authors in draft form (USDA/FSIS 1998) is more relevant for compendium review upon release anticipated in October
J. Reviewer Comments	body of evidence and theory does not permit objective unequivocal choice of a DR model for non-typhoid *Salmonella* serotypes
K. Cross-References	NA

A. Dose-Response Study Identification	FAO/WHO. 2004. Risk assessment of *Listeria monocytogenes* in ready-to-eat foods. Food and Agriculture Organization/World Health Organization. http://www.who.int/foodsafety/publications/micro/mra_listeria/en/
B. Objectives and Type of Study	1. purpose: scientific and future regulatory interest; undertaken at request of the Codex Committee on Food Hygiene for scientific advice as a basis for future development of guidelines. 2. type: DR
C. Publication Attributes	1. sponsors/affiliations: FAO/WHO 2. peer-review mechanism: Technical Report reviewed several times during preparation and after completion through consultations and by an extensive list of selected reviewers and members of the public during a public comment period
D. Data and Study Design	1. type: epidemiological data and body of evidence from published literature, including that reviewed in FDA/USDA risk assessment (2003) 2. source: FDA/USDA risk assessment (2003) 3. extent of data: limited human and animal data from published clinical and epidemiologic literature; murine and human dose-response data extensive but conflicting 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: Monte Carlo simulation using simplified exponential dose-response model similar to Buchanan et al. (1997) and Lindqvist and Westöö (2000) 2. specific characteristics: exponential model (non-threshold) implying no “minimum infectious dose”; $r = 5.85 \times 10^{-12}$ for the susceptible population, $r = 5.34 \times 10^{-14}$ for the general healthy population 3. assumptions: the percentage of individuals susceptible to severe *L. monocytogenes* infections; the appropriateness of the exponential model for describing the pathogen’s dose-response relation in humans in the dose range of interest; dose-reconstruction for numbers of *L. monocytogenes* consumed by ill and asymptomatic cases; accuracy of limited survey and outbreak data on the annual rate of severe listeriosis cases. 4. limitations: accuracy of the estimate of the r-value is dependent on the EA from the US risk assessment (FDA/USDA, 2003); size and inclusiveness of the population being considered, reliability of data on the frequency and extent of *L. monocytogenes* contamination in foods 5. relevance: medium
F. Study Conclusions and Extended	1. conclusions: estimated values of r dependent on EA from FDA/USDA risk assessment and assumptions; available contamination and epidemiological data do not permit objective unequivocal choice of r based on

Applications	scientific evidence and theory 2. authors' extrapolations: Estimates of the relative susceptibility of different sub-populations that have specific chronic diseases were derived, assuming different r values based on epidemiological and exposure data, along with professional judgement; provided four example risk assessments for *L. monocytogenes* in which EAs were included for each food product: pasteurized milk, ice cream, fermented meats, and cold-smoked fish. Each EA was different, depending on the data available.
G. Data Gaps and Proposed Solutions	1. data gaps: human DR data; potential effects of the food matrix on the DR relationships 2. proposed solutions: DR relations have been developed and evaluated based on expert elicitation, epidemiological or animal data, or combinations of these
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: low 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	same study in EA, RC; FDA/USDA, 2003 in EA, DR, RC

A. Dose-Response Study Identification	Farber, J.M., W.H. Ross and J. Harwig. 1996. Health risk assessment of *Listeria monocytogenes* in Canada. Int. J. Food Microbiol. 30(1-2): 145-156.
B. Objectives and Type of Study	1. purpose: scientific, regulatory; Major steps used in the formulation of a health risk management for *L. monocytogenes* in foods are discussed. 2. type: DR
C. Publication Attributes	1. sponsors/affiliations: Health Canada, Food Directorate 2. peer-review mechanism: Full Scientific Journal Review
D. Data and Study Design	1. type: expert opinions for infectious dose for 10 and 90% of normal and high risk population 2. source: Krewski and van Ryzin, 1980

	3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: probability of illness of an individual exposed to *L. monocytogenes* is predicted. 2. specific characteristics: flexible dose response model, Weibull model and a modification called Weibull-Gamma model are utilized. 3. assumptions: exposure to a single *Listeria* cell 4. limitations: NA 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: functional relationship between probability of an individual contacting listeriosis and a specified dose, or a level of exposure to virulent strain of *L. monocytogenes.* 2. authors' extrapolations from the observed data to other populations or conditions: NA
G. Data Gaps and Proposed Solutions	1. data gaps: no experimental dose response data on humans available for *Listeria* 2. proposed solutions: comparative analysis of the model and experimental data
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: low 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	same study in EA, RC

A. Dose-Response Study Identification	FDA/USDA. 2003. Quantitative assessment of relative risk to public health from foodborne *Listeria monocytogenes* among selected categories of ready-to-eat foods. http://www.foodsafety.gov/~dms/lmr2-toc.html
B. Objectives and Type of Study	1. purpose: scientific, future regulatory interest; Characterization of the dose-response relationship for *Listeria monocytogenes* 2. type: DR
C. Publication Attributes	1. sponsors/affiliations: US Department of Health and Human Service, Food and Drug Administration's Center for Food Safety and Applied Nutrition (DHHS/FDA/CFSAN) in collaboration with US Department of Agriculture's Food Safety and Inspection Service (USDA/FSIS) 2. peer-review mechanism: Two reviews of previous drafts of the model and its underlying assumptions conducted by the National Advisory Committee on Microbiological Criteria for Foods; draft risk assessment also made available for public comment (6-month period)
D. Data and Study Design	1. type: clinical studies with various laboratory animals and multiple strains, epidemiologic data from active surveillance (FoodNet) and outbreak investigations including three human populations (pregnancy-related or perinatal, elderly over age 60, intermediate age group) 2. source: published scientific literature, government surveys 3. extent of data: limited human data; three experiments in mice administered one strain of pathogen orally for mortality endpoint; 26 experiments in mice administered different strains of the pathogen by intraperitoneal injection to characterize strain virulence variation (range of LD_{50} nearly seven orders of magnitude) 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: multiple adjustments required to extrapolate from animal to human dose-response; mortality in mice, variation in virulence in mice, variation in susceptibility in animal studies, dose-response scaling factor to adjust predictions from animal data to fit human epidemiologic evidence 2. specific characteristics: the shape of the dose-response curve based on mortality data in mice fitted to multiple empirical model forms (best fits used logistic, exponential, Gompertz-log, probit, multihit; poor fits not used included beta Poisson, Gompertz-power, gamma Weibull); strain virulence varied by 5 orders of magnitude in mice; effective dose in simulated servings of foods modified by large dose-response scaling factors (9 to 12.8) to shift dose-response curve to account for greater susceptibility of laboratory animals relative to humans 3. assumptions: Mortality rather than infection is used as an endpoint to model human dose response. Models for variability in strain virulence assumes that the shape of the population dose response function is same for all strains. The susceptible human population is assumed to be nearly as homogenous as a population of laboratory mice. 4. limitations: Lack of extensive genetic and immunological tools in the mouse model. Some of the assumptions

	in the models are unrealistic. 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions: animal dose-response data could be adjusted to predict human epidemiological results for simulated levels of *Listeria monocytogenes* ingested in 23 food categories 2. authors' extrapolations: very large variabilities (host, pathogen, matrix, and interactions) and uncertainties in extrapolating from animals to humans and high dose to low dose; problematic assignment of potential error to exposure assessment or dose-response assessment.
G. Data Gaps and Proposed Solutions	1. data gaps: mechanisms of pathogenicity and virulence in humans and laboratory animals; fractions of strains of high/low virulence strains in foods; diagnostic tests for presence and levels of expression of virulence factors; enhanced epidemiologic investigations for active surveillance and outbreaks to identify source foods and estimate doses for exposed populations of symptomatic and asymptomatic individuals 2. proposed solutions: conduct research
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: low 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: low 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	Interesting study begun in 1999 and completed after multiple rounds of peer review and public comment; extensive add on to and useful discussion of rationale for extrapolations and assumptions; large interest nationally and internationally in pathogen, largely due to ubiquitous distribution, ecological niche and physiological advantage of growth under refrigeration conditions; use of animal clinical data for dose-response and virulence adjusted with human epidemiologic data; the scientific basis for dose-response relationships in animal models and humans weak, as acknowledged by the authors in the Hazard Characterization chapter by the need for large dose-response scaling factors to bridge conflicting sources of data, and in Appendix 11 by identifying needs for further scientific research
K. Cross-References	same study in EA, RC

A. Dose-Response Study Identification	Gale, P. 2001. Developments in microbiological risk assessment for drinking water. J .Appl. Microbiol. 91: 191-205.
B. Objectives and Type of Study	1. purpose: develop microbiological risk assessment models for pathogenic agents in drinking water, primarily *Cryptosporidium parvum*, rotavirus, and Bovine Spongiform Encephalopathy (BSE). 2. type: DR
C. Publication Attributes	1. sponsors/affiliations: Wrc-NSF, Ltd., Buckinghampshire, UK 2. peer-review mechanism: peer reviewed journal
D. Data and Study Design	1. type: data primarily derived from previously published articles. 2. source: Haas et al. (1996) (*Cryptosporidium*), DuPont, et al. (1995) (*Cryptosporidium*), Ward et al. (1996) (rotavirus) and Gale (1998) (BSE). 3. extent of data: data appear to be well described and appropriately captured for use in this report 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: some high
E. Method/Model/Approach	1. general characteristics: different models applied to predict DR for populations to three pathogens that may be present in water supplies. 2. specific characteristics: Beta-Poisson and log-probit models used to generate dose response scenarios. 3. assumptions: Model assumptions were generally sound 4. limitations: NA 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: For risk assessment of *Cryptosporidium* infection, log-probit dose response curve is more representative than a Poisson response. It appears that there is little or no support for an interaction between infectious agents in the likelihood of being infected by one or more of the agents. Protective immunity is an important consideration when evaluating the likelihood for infection from *Cryptosporidium* oocysts 2. extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: significant data gaps were reported for the association of BSE infection with the consumption of drinking water 2. proposed solutions: the authors suggest that risk assessment models for BSE concentrate on pathway barriers in the infection as opposed to biomedical barriers, the latter of which have considerable uncertainty
H. Weight of Evidence	1. robustness of method: high 2. representativeness of data: some high

	3. generalizability or external validity: high 4. soundness of study conclusions or internal validity: high 5. defensibility: high
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	The review discussed the differences between infection occurring via oral exposures to infections that occur by injection. The latter are irrelevant to the objective of the paper (combined infectivity from ingestion of pathogens in drinking water); modeling approaches for describing the likelihood of infection (e.g., Beta-Poisson and log-probit models were used for dose response modeling); more recent human clinical dataset and model available
K. Cross-References	NA

A. Dose-Response Study Identification	Latimer, H.K., L. Jaykus, R.A. Morales, et al. 2001. A weighted composite dose-response model for human salmonellosis. Risk Anal. 21(2): 295-305.
B. Objectives and Type of Study	1. purpose noted by study authors: regulatory, future regulatory interest; to develop a weighted composite dose-response model for human salmonellosis, and to describe the influence of variation in strain virulence and host susceptibility on the shape of the population dose-response relationship 2. type: DR
C. Publication Attributes	1. sponsors/affiliations: USDA, National Research Initiative Competitive Grants Program 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: illness data from feeding trials 2. source: published studies (McCullough and Eisele, 1951, 2 citations; Levine and DuPont, 1973) 3. extent of data: data sets with analysis of 5 strains of non-typhoid *Salmonella* and 1 strain of *Shigella dysenteriae* grouped into high, moderate, and low virulence/pathogenicity categories according to level of dose causing disease 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: high

E. Method/Model/Approach	1. general characteristics: weighted composite dose-response model generated from exponential, two-subpopulation exponential, and Beta-Poisson single-hit models fitted to pooled human feeding trial dose-response data for each of three virulence/pathogenicity categories 2. specific characteristics: three single-hit models (exponential, two-subpopulation exponential, Beta-Poisson) fitted for the strains in the high, moderate, and low virulence categories of pooled data from human feeding studies; parameters determined using maximum likelihood estimation method; selected models evaluated with goodness-of-fit test and for degree of confidence; selected models validated using Chi-square test; degree of confidence used to produce composite model for each virulence/pathogenicity category 3. assumptions: modeling approach assumed the infectivity parameter to be a constant probability that a single microorganism will cause illness; shigellosis dose-response is relevant to dose-response for non-typhoid Salmonellosis 4. limitations: no human feeding study data available for *Salmonella* strains at low doses; no data for major non-typhoid *Salmonella* causing food-borne disease (typhimurium, enteritidis) 5. relevance: medium; model not representative of shigellosis or typhoid fever
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: model acknowledges uncertainty and combines dose-response model with data from expert elicitation for frequencies of different population sensitivity and strain virulence/pathogenicity
G. Data Gaps and Proposed Solutions	1. data gaps: method applied to only one other limited data set 2. proposed solutions: apply method to more data sets
H. Weight of Evidence	1. robustness of method: low; method applied to only pooled data set 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high; acceptable adequacy, completeness, and soundness of conclusions 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	1. description of most appropriate uses of method for incident-based microbial risk assessment of buildings and water systems: method could be used to model dose-response in scenarios involving susceptible populations and/or strains of varying virulence/pathogenicity 2. other comments by reviewer: although this model was constructed using very old data that is not very representative of the current population, its flexibility makes it relevant and useful for incident-based scenario modeling
K. Cross-References	Oscar, T. 2004; Coleman and Marks, 1998a

A. Dose-Response Study Identification	Lindqvist, R. and A. Westoo. 2000. Quantitative risk assessment for *Listeria monocytogenes* in smoked or gravad salmon and rainbow trout in Sweden. Int. J. Food Microbiol. 58(3): 181-196.
B. Objectives and Type of Study	1. purpose noted by study authors: Scientific; To develop a quantitative risk assessment model in which the exposure and risk of acquiring listeriosis from consumption of package smoked or gravad salmon and rainbow trout were estimated. 2. type: DR
C. Publication Attributes	1. sponsors/affiliations: National Food Administration, Uppsala, Sweden 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: An exponential and Weibull-gamma dose response model for *L. monocytogenes*. 2. source: Published literature (Buchanan et al., 1997; Farber et al., 1996; Ross, WH, Health Canada and Bemrah et al., 1998). 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: Two different equations used to estimate probability of adverse effect or illness based on dose. 2. specific characteristics: For the exponential model, $P=1-e^{-RN}$, where P is the probability of an adverse effect, N is the number bacteria consumed (i.e., dose). R is estimated to be $1.18x10^{-10}$ using German data and 5.6x10-10 using Swedish data. The Weibull-Gamma model was given by $P=1-[1+(N^{b})/\beta]^{-\alpha}$, where N is dose, alpha is 0.25, and beta is 10.98 for high risk population and 15.26 for the low-risk population. 3. assumptions: Only foods with a concentration over 10,000 *L. monocytogenes* cfu/g cause illness, and that only members of the high-risk population become ill. Only 1.5% of the servings had concentrations more than 10,000 *L. monocytogenes* cfu/g. High risk population groups (pregnant, elderly, HIV/AIDS) were assumed to be 20% of the total population. Strain virulence was assumed to be 100% pr 1-10% of foodborne strains. 4. limitations: not based on actual animal or human feeding studies. 5. relevance: medium
F. Study Conclusions and Extended	1. conclusions supported by the data: Two dose-response models over-predict annual illnesses in Sweden:

Applications	37 illnesses observed, and 168 or 95,000 were predicted if 100% of strains are virulent
G. Data Gaps and Proposed Solutions	1. data gaps: data based on human or animal studies not included. 2. proposed solutions: design studies and gather data.
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: low 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	same study in EA, RC

A. Dose-Response Study Identification	Marks, H.M., M.E. Coleman, C.-T. J. Lin and T. Roberts. 1998. Topics in microbial risk assessment: Dynamic flow tree process. Risk Anal. 18(3): 309-328.
B. Objectives and Type of Study	1. purpose: scientific, future regulatory interest; a systematic approach to risk assessment, employing data analysis for developing parsimonious models and accounts for variability and uncertainty of model inputs 2. type: DR
C. Publication Attributes	1. USDA Food Safety and Inspection Service project 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: experimental data for dose-response for pathogen administered in human clinical trials 2. source: published studies and government datasets 3. extent of data: no data for dose-response of pathogen of interest in humans (*E. coli* 0157:H7) and inadequate dataset for pathogen of interest in animals (rabbits), so used *Shigella* datasets for DR 4. sampling plan: NA 5. sample size (number of observations by treatment): 266 human volunteers administered one of three strains of *Shigella* (Levine et al., 1973; Dupont et al., 1969; Dupont et al., 1972)

	6. performance characteristics: NA 7. relevance: high
E. Method/Model/Approach	1. general characteristics: non-threshold and threshold beta Poisson dose-response models for shigellosis; Monte Carlo simulation using distributions below 2. specific characteristics: logit p(D), assumed normal for beta Poisson dose-response model for shigellosis; Chi-square for between species and experiment variances for dose-response model; AOV model used to characterize uncertainty and variability 3. assumptions: available data for dose-response assessment sufficiently representative for healthy adult consumers; threshold dose-response models merit consideration 4. limitations: the functional form chosen to model, biologically and mathematically, the DR relationship 5. relevance: high
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: magnitude of differences in annual estimates of illness strongly influenced by limitations of the data as evidenced by large differences between mean and median estimates; threshold of only three pathogen cells surviving cooking associated with 1,000-fold lower annual illness rate than non-threshold model for consumers of hamburgers cooked at recommended temperature 2. authors' extrapolations: the approach can be extended to the most general situation describing birth and death together, and dropping the assumption of the lack of time dependence of the probabilities of birth or death within an increment of time
G. Data Gaps and Proposed Solutions	1. identification of data gaps: ability of small numbers of pathogens, particularly those surviving cooking, to cause illness; appropriateness of shigellosis (invasive pathogen) as surrogate for colitis from O157:H7 (non-invasive attaching and effacing lesions); functional form of dose-response model, including thresholds unlikely to cause illness) 2. assumptions or source of surrogate data to fill gap: limited scenarios defined and linked with alternative surrogate dose-response models
H. Weight of Evidence	1. robustness of method: high 2. representativeness of data: high 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility (scientific judgement of appropriateness of method to incident-based microbial risk assessment of buildings and water systems): high, acknowledges limitations of the available data and offers insights for risk management
I. Criteria for Exclusion from Compendium	NA

J. Reviewer Comments	useful for scenario analysis for two bacterial threat agents as potential contaminants of food and water
K. Cross-References	Marks et al., 1998 also in EA and RC; Cassins et al., 1998

A. Dose-Response Study Identification	Martin, S.A., T.S. Walsten and N.D. Beaulieu. 1995. Assessing the risk of microbial pathogens: Application of a judgement-encoding methodology. J. Food Protect. 58(3): 289-295.
B. Objectives and Type of Study	1. purpose: scientific; To develop a risk-based sampling methodology for imported foods inspected by the US FDA. 2. type: DR
C. Publication Attributes	1. sponsors/affiliations: US FDA 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: The advice of microbiologists was sought. This group was asked to consider a large sample of people who consumed a given dose of a particular pathogen. Information was collected about the experts expectations of the percentage of persons suffering from a given health endpoint. The experts were asked to provide a credible interval (e.g. the percentage that individuals would be expected to suffer from a given health endpoint 50% of the time). Estimates were given for five intervals (1, 25, 50, 75, and 99%). 2. source: panel of 10 scientists from the FDA, CDC and college research centers 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: The experts were asked to provide a credible interval (e.g. the percentage that individuals would be expected to suffer from a given health endpoint 50% of the time). 2. specific characteristics: Vincentization, a technique to average the α percent quartiles of the experts' distributions to construct the α percent quartile of the "consensus". The parameters of the group distribution are the same as the arithmetic averages of the members' distributions' parameters. Hence, the mean of the pooled distributions, is the average of the individual means. Assuming a logical distribution of the probabilities, the median and mean are equal; thus an arithmetic average of the medians is the same as the average of the individual means.

	3. assumptions: pooled opinions can be treated statistically as data sets 4. limitations: expert judgement-encoding methodology cannot substitute for scientifically established dose-response relationships for these microbial pathogens. 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions: This characterization method is useful in the context of food and environmental safety policy. 2. authors' extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: scientific data for dose-response relationships from well-designed and controlled clinical studies 2. proposed solutions: unknown
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: low 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	NA

A. Dose-Response Study Identification	Medema, G.J., P.F.M. Teunis, A.H. Havelaar and C.N. Haas. 1996. Assessment of the dose-relationship of *Campylobacter jejuni*. Int. J. Food Microbiol. 30: 101-111.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific. To describe the dose-response relationship for infection with *Campylobacter jejuni*, based on the feeding study data from Black, R.E. et al. 1988. 2. type: DR
C. Publication Attributes	1. sponsors/affiliations: The general Directorate for the Environment, Ministry of Housing, Physical Planning and the Environment, The Netherlands. 2. peer-review mechanism: full scientific peer review
D. Data and Study Design	1. type: dose-response for *Campylobacter jejuni* with the Beta-Poisson model of infection

	2. source: data obtained in human feeding studies performed by Black, R.E. et.al. 1988 3. extent of data: 2 strains; 3 to 6 dose groups per strain; 5-22 volunteers per dose group, 107 total volunteers; endpoints: fecal positive, liquid stool volume, illness (fever and diarrhea), serology 4. sampling plan: In the weeks after challenge stools and blood were cultured for *Campylobacter jejuni* and serum samples were examined for specific immunoglobulins. 5. sample size: 68 volunteers were included for one-strain model 6. performance characteristics: NA 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: Beta-Poisson probability of infection as a function of the ingested dose 2. specific characteristics: By means of repetitive (5,000 times) resampling the original dataset (bootstrapping) yielding a collection of dose-response curves. 3. assumptions: This model starts form the assumption that the micro-organisms in the inoculum are distributed randomly (Poisson). The probability that an organism that has entered the intestinal tract will cause infection is assumed to be Beta-distributed. Each bacterial cell acts independently to cause infection and disease. 4. limitations: This analysis included only one of two isolates of *Campylobacter jejuni*. This dose response curve does not appear to be typical of all *Campylobacter jejuni* strains. 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: The Beta-Poisson model produces a description of a portion of the human dose-response data for *Campylobacter jejuni*. 2. extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: large amount of uncertainty in the dose-response estimate, especially at low doses 2. proposed solutions: additional dose-response data at low doses are needed
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: high 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: low 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	NA

A. Dose-Response Study Identification	Medema, G.J., W. Hoogenboezem, A.J. van der Veer, et al. 2003. Quantitative risk assessment of *Cryptosporidium* in surface water treatment. Wat. Sci. Technol. 47(3): 241-247.
B. Objectives and Type of Study	1. purpose: scientific; regulatory 2. type: DR
C. Publication Attributes	1. sponsors/affiliations: Collaborative Research Programme (BTO) of the water companies in The Netherlands 2. peer-review mechanism: scientific journal review
D. Data and Study Design	1. type: dose-response data for *Cryptosporidium* 2. source: Ockhuysen et al., 1999; Teunis, personal communication 3. extent of data: data were from 3 strains of *C. parvum* of the bovine genotype 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: constructed dose-response model for *Cryptosporidium* 2. specific characteristics: dose-response model based on combined dose-infection relation for three *C. parvum* strains of the bovine genotype; the best fit exponential model to the dose-response data is described by $P_{inf} = 1 - e^{-dose*0.004005}$ 3. assumptions: NA 4. limitations: NA 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions: NA 2. authors' extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: high 3. generalizability or external validity: NA

	4. soundness of study conclusions or internal validity: NA 5. defensibility: high
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	same study in EA, RC; researchers cite Teunis et al., 1999 as a source for the dose-response assessment

A. Dose-Response Study Identification	Nauta, M.J., E.G. Evers, K. Takumi and A.H. Havelaar. 2001. Risk assessment of Shiga-toxin producing *Escherichia coli* O157 in steak tartare in the Netherlands. RIVM report 257851003. http://www.rivm.nl/bibliotheek/rapporten/257851003.html
B. Objectives and Type of Study	1. purpose: scientific; future regulatory interest 2. type: DR
C. Publication Attributes	1. sponsors/affiliations: Directory Board of RIVM, Netherlands 2. peer-review mechanism: NA
D. Data and Study Design	1. type: food and stool samples following Shiga-toxin producing *E. coli O157* outbreak 2. source: Shinagawa, 1997 (Japanese) 3. extent of data: stool samples were collected from 842 children and 43 teachers following an outbreak of Shiga-toxin producing *E. coli O157* at an elementary school in Morioka city, Japan in Sept 1996; food samples collected from a meal that was preserved for two weeks 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: high
E. Method/Model/Approach	1. general characteristics: models fit to the outbreak data to extrapolate the probability of infection to doses other than the dose estimated for the outbreak 2. specific characteristics: exponential and hypergeometric models used; in the exponential model, there is a constant non-zero risk of infection associated with each pathogen; in the hypergeometric model, the risk of infection from an individual pathogen is described by a beta distribution to take into account variation in virulence

	of pathogens and susceptibility of children, and parameters are estimated by a Markov Chain Monte Carlo algorithm 3. assumptions: pathogens are assumed to act independently to infect a host 4. limitations: NA 5. relevance: high
F. Study Conclusions and Extended Applications	1. conclusions: the exponential model estimates the probability of infection per cfu of ingested microorganism is about 0.01 for children; the hypergeometric model predicts that over 25% of children are more susceptible to infection than the probability estimated in the exponential model; the results indicate that Shiga-toxin producing *E. coli* O157 is highly infectious in humans, in contrast to models based on previous studies of Shiga-toxin producing *E. coli* O157 in rabbits or surrogate microbes in humans 2. authors' extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: high 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility: high
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	same study in EA, RC

A. Dose-Response Study Identification	Oscar, T. 2004. Dose-response model for 13 strains of *Salmonella*. Risk Anal. 24(1): 41-49.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific, future regulatory; to develop a dose-response model for predicting salmonellosis as a function of dose consumed and strain variation, to use the model to investigate the effect of strain variation on the shape of the dose-response curve.

	2. type: DR
C. Publication Attributes	1. sponsors/affiliations: USDA 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: illness data from large feeding trial with healthy men in Chicago (McCullough and Eisele, 1951) 2. source: published studies (McCullough and Eisele, 1951) 3. extent of data: large data sets including analysis of 13 strains of *Salmonella*; data sets for individual strains contain either high and low or intermediate dose responses. 4. sampling plan: multi-dose studies 5. sample size: 64 dose groups with 5-8 men per dose group. 6. performance characteristics: Three-phase linear models of dose-response curves converted into Pert distributions which were used to form the simulation model; Three-phase linear model able to fit incomplete dose-response curves to model dose response; approach verified by simulating original feeding trial. 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: Dose-response simulation model based on three-phase linear models of dose-response curves from a feeding trial; model predictions verified by simulations of original feeding trials for individual strains; 4 feeding trials containing dose groups of 10e4 to 10e10 with increments of 10e0.1 *Salmonella* per dose and 10,000 subjects per dose group simulated to investigate effects of strain variation. 2. specific characteristics: Model prediction verification used @Risk settings of 100 simulations, selection of different random number generator seeds, and Latin Hypercube sampling; strain variation effects simulated feeding trials used settings of 10,000 iterations, one simulation per trial, a seed of one, and Latin Hypercube sampling. 3. assumptions: None stated 4. limitations: data at low doses is required for the three-phase linear model to fit dose-response curves with a minimum illness dose of 1; model predictions only valid for eggnog, healthy men, and the *Salmonella* strains and doses used to develop the model; model predictions only applicable to the very resistant portion of the consumer population, could grossly underpredict the public health risk of salmonellosis if applied to the general consumer population. 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: dose response model predictions were in agreement with the data used to develop the model (predicted median of 69 illnesses vs. 74 illnesses in original trial); predicted dose-response curve does not have a sigmoid shape when multiple strains with different virulence are present. 2. authors' extrapolations from the observed data to other populations or conditions: sigmoid shape of dose-response curves in one strain feeding trials may not accurately reflect dose response in naturally contaminated food where multiple strains may be present; approach used in this study could be used to develop models

	capable of predicting dose response as a function of a matrix of food, pathogen, and host factors.
G. Data Gaps and Proposed Solutions	1. data gaps: high-risk individuals and lower doses not included in the feeding trial; None of the data for individual strains completely defined the dose-response curve (prompted the use of the three-phase linear model which can extrapolate beyond incomplete data to fit dose-response curves); model only applied to one combined data set. 2. proposed solutions: more feeding trials with foods, *Salmonella* strains, and consumers that are more representative of current marketplace; use infection instead of illness as dose-response endpoint to increase feasibility of including high-risk individuals in dose groups; model should be applied to other data sets.
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: high 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	method could be applied to incident-based microbial risk assessments of water if alternative methods were used
K. Cross-References	Coleman and Marks, 1998

A. Dose-Response Study Identification	Slifko T.R., D.E. Huffman, B. Dussert, et al. 2002. Comparison of tissue culture and animal models for assessment of *Cryptosporidium parvum* infection. Exp. Parasitol. 101: 97-106.
B. Objectives and Type of Study	1. purpose: scientific; To compare two models, the microscopically-based immunofluorescent tissue culture assay (i.e., the Foci Detection Method-Most Probable Number Assay) and the neonatal mouse model, for assessing *C. parvum* infectivity 2. type: DR
C. Publication Attributes	1. sponsors/affiliations: Orange County Utilities Laboratory, Orlando Florida 2. peer-review mechanism: peer-reviewed journal
D. Data and Study Design	1. type: infection responses of tissue culture and mice; Oocysts were from the Ames, Iowa isolate of *C. parvum* purchased from Sterling Parasitology Diagnostic Laboratory. Five different oocyst lots used in the study. 2. source: laboratory experiments;

	3. extent of data: The most probable number (MPN) of infectious oocysts per milliliter in tissue cultures and mice were determined. 4. sampling plan: factorial design for both the tissue culture and mouse models. 5. sample size: For tissue culture model, each dilution was put into 6 or 8 replicate wells. For mice, five sets of 4-day old mice were used, one set per oocyst lot. Replicate sets performed for both models. 6. performance characteristics: Data statistically analyzed. The average logit response calculated by using the method of least squares. 7. relevance: high
E. Method/Model/Approach	1. general characteristics: 31 dose-response trials using both tissue culture and mouse models were compared. DR relations were computed for each experiment using the best-fit logistic relationship between oocyst dose per well or mouse. 2. specific characteristics: Calculation of average DR models was determined by averaging individual doses and plotting the respective logit responses. Regression analysis of the average logit dose-response models for cells and mice were conducted. The ID_{50} was calculated when the proportion of infected wells or mice was equal to the proportion of uninfected wells or mice and the response logit was equal to zero. Series of paired *t* tests were performed to determine if differences existed between the two infectivity models. 3. assumptions: oocyst lots are the same with regard to infectivity. 4. limitations: non-specific immune systems and defenses of mice may affect the infectivity ; the methods used to confirm infection in mice also may miss low-level infections; cross-contamination between mouse litters after infection and during laboratory analysis is common; surface area for infection is much larger in the mouse intestine, compared to cell culture chamber wells. 5. relevance: high
F. Study Conclusions and Extended Applications	1. conclusions: Results demonstrated that tissue culture was more sensitive than mice for measuring infection as shown by the lower ID_{50}s. However, rate of infection not different. DR of the tissue culture most similar to the TAMU isolate DR model developed with human volunteers. Different oocyst lots may contribute to experimental variability. 2. authors' extrapolations: Tissue culture can be successfully used to measure *C. parvum* infection and evaluate inactivation in disinfection studies.
G. Data Gaps and Proposed Solutions	1. data gaps: variability associated with the use of different lots and other experimental variability. 2. proposed solutions: acknowledge these variabilities when interpreting data.
H. Weight of Evidence	1. robustness of method: high 2. representativeness of data: high 3. generalizability or external validity: high 4. soundness of study conclusions or internal validity: high

	5. defensibility: high
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	NA

A. Dose-Response Study Identification	Strachan, N.J., G.M. Dunn and I.D. Ogden. 2002. Quantitative risk assessment of human infection from *Escherichia coli* O157 associated with recreational use of animal pasture. Int. J. Food Microbiol. 75:39-51.
B. Objectives and Type of Study	1. purpose: Scientific/Regulatory; use risk assessment to determine the probability of *E. coli* O157:H7 infection following visiting an area grazed by infected livestock. 2. Type of study: DR
C. Publication Attributes	1. sponsor: Department of Plant and Soil Science, School of Physics, and Applied Food Microbiology Group (University of Aberdeen) 2. peer-review mechanism: peer-reviewed journal

D. Data and Study Design	1. type: dose response models from published studies 2. source: Crockett et al., 1996; Cassin et al., 1998; Haas et al., 20003. extent of data: The selected model (Cassin et al., 1998) was based on *Shigella* feeding studies in humans; the Haas et al. (2000) model based on *E. coli* O157 exposure to rabbits was not used. The authors selected the former study because it was more representative. 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: A beta binomial dose response model, estimating the probability of *Shigella* infection as a function of ingested dose 2. specific characteristics: the values used to parameterise the model were calculated from data obtained in three human studies; the uncertainty of the variables is incorporated using study intervariability as a proxy 3. assumptions: the model assumes that only a single organism is required to cause an infection and that each cell is equally infective. 4. limitations: one set of data used, and these data were not considered fully representative. 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: 3 week period of non-livestock use in any pasture that is expected to be visited by the general population. Removal of feces from the field may also reduce the likelihood of exposures. 2. extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: high 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	NA

A. Dose-Response Study Identification	Teunis, P.F.M., O.G. van der Heijden, J.W.B., van der Geissen and A.H. Havelaar. 1996. The dose-response relation in human volunteers for gastro-intestinal pathogens. Report No. 284550002. Leeuwenhoeklaan, The Netherlands: National Institute of Public Health and the Environment.
B. Objectives and Type of Study	1. purpose: scientific; future regulatory; examined previous studies to determine if quantitative relationship between dose and risk of infection could be established 2. type: DR bacteria
C. Publication Attributes	1. sponsors/affiliations: Veterinary Inspectorate (VHI), Public Health Inspectorate (HIGB), and Ministry of Public Health, Welfare, and Sports (VWS) 2. peer-review mechanism: full scientific journal review
D. Data Description and Study Design	1. type: human clinical data for administration of pathogenic bacteria: *Campylobacter jejuni* clinical isolate; *Salmonella meleagridis* and *Salmonella anatum* isolated from spray-dried whole egg powder; *Salmonella newport*, *Salmonella derby*, and *Salmonella bareilly* were isolated from spray-dried whole egg powder; *Salmonella pullorum* was isolated from spray-dried whole egg and one strain from was a human clinical isolate; *Salmonella typhi* clinical isolate; *Plesiomonas shigelloides* clinical isolated from fecal samples; *Shigella flexneri* 2a## clinical isolate; *Shigella paradysenteriae* (*S. flexneri*) unspecified isolate; *Shigella dysenteriae* 1 clinical isolate; *Vibrio cholerae* clinical isolates; *Vibrio cholerae*- deleted mutants were clinical isolates; Enterotoxigenic *Escherichia coli* (ETEC) clinical isolates; Enteroadherent *Escherichia coli* clinical isolate. 2. source: published studies: Black et al., 1988; Mc Cullough and Wesley Eiselle 1951a; Mc Cullough and Wesley Eiselle 1951b; Mc Cullough and Wesley Eiselle 1951c; Hornick et al., 1970; Herrington et al., 1987; DuPont et al., 1969;Shaugnessy et al., 1946; Levine et al., 1973; Cash et al., 1974; Levine et al,., 1988; Evans et al., 1978; Mathewson et al., 1986. 3. extent of data: Two different *Campylobacter jejuni* strains (A3249 and 81-176) were administered individually to 68 and 39 human volunteers, respectively; Three different *Salmonella meleagridis* strains and three different *Salmonella anatum* strains were administered to 118 and 114 human volunteers, respectively; Single strains of *Salmonella newport*, *Salmonella derby*, and *Salmonella bareilly* were administered separately to 20, 30 and 18 human volunteers; Four strains of *Salmonella pullorum* were individually administered to 24, 17, 24, and 30 human volunteers, respectively; A single strain of *Salmonella typhi* was administered to 213 human volunteers; A single strain of *Plesiomonas shigelloides* was administered to 33 human volunteers; A single strain of *Shigella flexneri* 2a## (2457T) was administered to 43 human volunteers; *Shigella paradysenteriae* (*S. flexerni*) was administered to 16 human volunteers; Two strains of *Shigella dysenteriae* 1 (M131 and A-1) were administered to 30 and 10 human volunteers, respectively; Two different serotypes of *Vibrio cholerae* (Inaba 569B and Ogawa 395) were administered with pH buffer to 67 and 25 human volunteers; Deletion mutants of *Vibrio cholerae* (JBK70, CVD101,

	CVD102, CVD104, CVD105) were administered to 14, 18, 5, 6, and 9 human volunteers; Two strains of enterotoxigenic *Escherichia coli* (H10407 – CFA+ and H10407P-CFA-) were administered to 24 and 23 human volunteers, respectively; Two strains of enteroadherent *Escherichia coli* (189 and 221) were administered individually to 8 and 15 human volunteers. 4. sampling plan: *Campylobacter jejuni*: fecal excretion were collected daily for 12 days after inoculation and periodic seriological samples were analyzed for *C. jejuni* specific antibodies for all 6 treatments totaling 68 human volunteers doses ranging from 8.0×10^2 to 1.0×10^8 administered strain A3249 and 3 treatments totaling 39 human volunteers doses ranging from 1.0×10^6 to 2.0×10^9administered 81-176; *Salmonella meleagridis* and *Salmonella anatum*: fecal and blood samples were taken daily for each of two species tested; three strains of *S. meleagridis* were administered individually to 64, 30, and 24 human volunteers doses ranging from 1.2×10^4 to 5.0×10^7 , three strains of *S. anatum* were administered individually to 46, 50, and 18 human volunteers doses ranging from 1.2×10^4 to 6.72×10^7; *Salmonella newport, Salmonella derby* and *Salmonella bareilly*: fecal excretions were examined for infection for all three species, three treatments for *S. newport* were administered to 20 human volunteers doses ranging from 1.52×10^5 to 1.35×10^6, five treatments for *S. derby* were administered to 30 human volunteers doses ranging from 1.38×10^5 to 1.5×10^7, three treatments for *S. bareilly* were administered to 18 human volunteers doses ranging from 1.25×10^5 to 1.7×10^6; four different strains of *Salmonella pullorum* were administered separately in different treatments, *S. pullorumI* was administered in four different treatments to 24 human volunteers doses ranging from 1.0×10^4 to 1.6×10^{10} , *S. pullorumII* was administered in three different treatments to 17 human volunteers doses ranging from 1.38×10^6 to 6.75×10^9 , *S. pullorumIII* was administered in four different treatments to 24 human volunteers doses ranging from 2.3×10^6 to 7.6×10^9 , *S. pullorumIV* was administered in five different treatments to 30 human volunteers doses ranging from 1.88×10^6 to 3.975×10^9; a single strain of Salmonella typhi was administered in five different treatments to 213 human volunteers doses ranging from 1.0×10^3 to 1.0×10^9 with illness symptoms and stool specimens as endpoints; Plesiomonas shigelloides was administered in two series of experiments with endpoints of fecal excretion and blood samples: one where 22 human volunteers were administered bacterial inoculum doses ranging from $1.0x\ 10^3$ to 4.0×10^9 across five different treatments and the second experiment 11 human volunteers were administered bacterial inoculum doses ranging from 1.0×10^5 to 1.0×10^8 across two different treatments after having previously taken an ampicillin dose; *Shigella flexneri* 2a##: a single strain (2457T) was administered to 43 human volunteers through 5 different treatment doses ranging from 1.0×10^4 to 1.0×10^8 with endpoints of daily fecal excretions and weekly serum sample test for antibodies; *Shigella paradysenteriae* (*S. flexneri*) was administered to 16 human volunteers in three different treatments doses ranging from 1.0×10^8 to 1.0×10^{10} with endpoints of fecal excretions; Two strains of *Shigella* dysenteriae 1 were administered with endpoints of rectal swabs and select fecal excretion samples, M131 (strain with multiple resistance to antibiotics) was administered to 30 human volunteers four different doses ranging from 1.0×10^1 to 1.0×10^4 and A-1(antibiotic sensitive strain) was administered to 10 human volunteers two different doses 2.0×10^2 and 1.0×10^4; two different serotypes of *Vibrio cholerae* were examined with endpoint of fecal excretion , preliminary experiments were performed by administering *V. cholerae* Inaba 569 B without pH buffer to 19 human volunteers across 7 different dosage treatments ranging from 1.0×10^4 to 1.0×10^{11}, subsequent comparison of *V. cholerae* Inaba 569 B with three treatments of doses ranging from 1.0×10^4 to 1.0×10^8 to 67 human volunteers to *V.cholerae* Ogawa 395 administered one treatment dose of $1.0x\ 10^6$ to 25 human volunteers; *Vibrio cholerae* deletion mutants: deletion mutant strains were developed (JBK70, CVD101,

	CVD 102, CVD 104, CVD105) and their pathogenicity was examined and compared to original parent strains (*V.cholerae* El Tor Inaba N16961 and *V.cholerae* Ogawa 395), JBK70 was administered to 14 human volunteers three different dosage treatments ranging from 1.0×10^6 to 1.0×10^{10}, CVD101 was administered to 24 human volunteers five different dosage treatments ranging from 1.0×10^4 to 1.0×10^8, CVD102 was administered to 5 human volunteers one treatment dose of 1.0×10^7, CVD104 was administered to 6 human volunteers one treatment dose of 1.0×10^7, CVD105 was administered to 9 human volunteers one treatment dose ranging from 1.0×10^5-10^8, no data regarding bacterial examinations was provided in primary literature; two strains of Enterotoxigenic *Escherichia coli*(CFA+ and CFA-) were administered to 24 and 23 human volunteers three treatments of doses ranging from 1.0×10^6 to 1.2×10^9 with endpoints of fecal excretion; two strains of enteroadherent *E. coli* (189 and 221) were administered to 8 and 15 human volunteers two treatments of doses 7.0×10^8 and 1.0×10^{10} with endpoint of fecal excretion. 5. sample size: *Campylobacter jejuni*: 5-19 volunteers per dose group for strain A3249 and 7-22 volunteers per dose group for strain 81-176; *Salmonella meleagridis* and *Salmonella anatum*: 5-6 volunteers per dose group for all three strains of *S. meleagridis* examined, 5-8 volunteers per dose group for all three strains of *S. anatum* examined; *Salmonella newport, Salmonella derby*, and *Salmonella bareilly*: 6-8 volunteers per dose group for *S. newport*, 6 volunteers per dose group for all treatments for both *S. derby* and *S. bareilly*; *Salmonella pullorum*: 5-6 volunteers per dose group for all four strains examined; *Salmonella typhi*: a wide range of (9-116) volunteers per dose group; *Plesiomonas shigelloides*: 4-7 volunteers per dose group across two experiments; *Shigella flexneri* 2a##: 4-19 volunteers used per dose group; *Shigella paradysenteriae* (*S. flexneri*): 4-8 volunteers per dose group; *Shigella dysenteriae* 1: 4-10 volunteers per dose group for strain M131, 4-6 volunteers per dose group for strain A-1; *Vibrio cholerae*: 1-4 volunteers per dose group for strain Inaba 569 B without pH buffer experiments, 2-52 volunteers per dose group for strain Inaba 569B and 25 volunteers per dose group for strain Ogawa 395 with pH buffer experiments; *Vibrio cholerae* deletion mutants: 4-5 volunteers per dose group for mutant strain JBK 70, 3-6 volunteers per dose group for mutant strain CVD 101, 5 volunteers per dose group for mutant strain CVD 102, 6 volunteers per dose group for mutant strain CVD 104, 9 volunteers per dose group for mutant strain CVD 105; Enterotoxigenic *Escherichia coli*: 7-10 volunteers per dose group for *E. coli* CFA+ strain, 6-10 volunteers per dose group for *E. coli* CFA- strain; Enteroadherent *Escherichia coli*:4 volunteers per dose group for *E. coli* 189 strain, 7-8 volunteers per dose group for *E. coli* 221strain. 6. performance characteristics: NA 7. relevance: medium
E. Method/Model/Approach	Agents of interest: *Campylobacter jejuni, Salmonella typhi, Shigella spp.,* and *Vibrio cholerae* 1. general characteristics: data analysis of experimental data from human clinical studies 2. specific characteristics: experimental data were analyzed with Exponential/ Beta-poisson dose response models to determine best fit model with appropriate confidence range referencing previously published study (DuPont et al., 1995) 3. assumptions: every bacterium that enters host has same probability of causing infection; differences among dose responses for different experiments are likely due to differences in biological factors for each pathogenic organism and/or environmental conditions; factors associated with host(s) are likely to be variable across

	experiments. 4. relevance: medium, method described parameters that may be useful for homeland security and/or agents that are of interest
F. Study Conclusions and Extended Applications	1. Low dose approximations for the above bacteria are: 1.91×10^{-2} , 6.96×10^{-6} , 1.71×10^{-2} to 8.26×10^{-10}, and 1.76×10^{-9}, respectively, as supported by the clinical data from experimental dose-response trials 2. Beta-poisson model is a "single hit" model that can be used when assuming any single microorganism is capable of infection upon entering host; exponential model implies no minimum infective dose.
G. Data Gaps and Proposed Solutions	1. data gaps: class differences among strains of pathogenic organisms are difficult to generalize; unknown if dose-response relationship changes with age or immune status; uncertainty in controlled conditions of experiments. 2. authors propose: Class differences among pathogenic organisms are most difficult to control and examination of different strains for one organism type doesn't necessarily mean it can be applied to other types of organisms; further investigation needed to determine if dose-response relationship changes with age or immune status.
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: some high 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: low 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	most of these studies inoculated volunteers with concentrated amounts of cysts or microorganisms that would not normally be consumed in food; later study (2000) published by first author indicates validity of beta-poisson model is unknown; strain differences no included in models
K. Cross-References	review cited in two other DR other templates including pathogenic viruses and protozoans

A. Dose-Response Study Identification	Teunis, P.F.M., O.G. van der Heijden, J.W.B., van der Geissen and A.H. Havelaar. 1996. The dose-response relation in human volunteers for gastro-intestinal pathogens. Report No. 284550002. Leeuwenhoeklaan, The Netherlands: National Institute of Public Health and the Environment.
B. Objectives and Type of Study	1. purpose: scientific; future regulatory; examined previous studies to determine if quantitative relationship between dose and risk of infection could be established

	2. type: DR protazoans
C. Publication Attributes	1. sponsors/affiliations: Veterinary Inspectorate (VHI), Public Health Inspectorate (HIGB), and Ministry of Public Health, Welfare, and Sports (VWS) 2. peer-review mechanism: full scientific journal review
D. Data Description and Study Design	1. type: human clinical data for administration of pathogenic protozoans: *Giardia lamblia* isolated from human fecal material*, Cyrptosporidium parvum* isolated from fecal material from one-day-old Holstein calves*,* and *Entamoeba coli* clinical human isolate. 2. source: published studies (Rendtorff 1954a, DuPont et al., 1995, and Rendtorff 1954b, respectively) 3. extent of data: A single *Giardia lamblia* strain cysts were administered 40 human volunteers with endpoints of fecal excretion and illness; A single *Cyrptosporidium parvum* strain oocysts were administered to 29 human volunteers who where seronegative (IgG and IgM) with endpoints of fecal excretion, illness, and cryptosporidosis; A single strain of *Entamoeba coli* was administered to 26 male prisoners with endpoints of fecal excretion. 4. sampling plan: *Giardia*: smears of stools were sampled daily for presence of cysts for 8 different treatments administered ranging from 1 to 10^6 cysts; *Cryptosporidium*: stool specimens were collected daily for two weeks followed by 2 days per week for two months for presence of oocysts for 8 different treatments administered ranging from 30 to 10^6 oocysts; *Entamoeba*: stool specimens were collected and examined for presence of cysts or trophozoites for three experiments of 2-4 treatments, each ranging from 0 -10^2 cysts. 5. sample size: 2-20 volunteers per dose group administered *Giardia*; 1-8 volunteers per dose group administered *Cryptosporidium*; 2 or 6 volunteers per dose group administered *Entamoeba*. 6. performance characteristics: NA 7. relevance: low (*Cryptosporidium* only pathogenic protozoan examined here that is pertinent to EPA agent list)
E. Method/Model/Approach	*Cyrptosporidium parvum* 1. general characteristics: data analysis of experimental data from human clinical studies 2. specific characteristics: experimental data were analyzed with Exponential/ Beta-poisson dose response models 3. assumptions: every oocyst that enters host has same probability of causing infection; differences among dose responses for different experiments are likely due to differences in biological factors for each pathogenic organism and/or environmental conditions; factors associated with host(s) are likely to be variable across experiments. 4. relevance: medium
F. Study Conclusions and Extended Applications	1. Low dose approximations for the above protozoans are: 1.99×10^{-2} , 4.00×10^{-3} , 0.359, respectively, as supported by the clinical data from experimental dose-response trials; the exponential model was most appropriate for *Giardia* and *Cryptosporidium* pathogenic protozoans experimental values. 2. Beta-poisson model is a “single hit” model that can be used when assuming any single microorganism is capable of infection upon entering host; exponential model implies no minimum infective dose.
G. Data Gaps and Proposed	1. data gaps: class differences among strains of pathogenic organisms are difficult to generalize; unknown if dose-

Solutions	response relationship changes with age or immune status; uncertainty in controlled conditions of experiments. 2. authors propose: Class differences among pathogenic organisms are most difficult to control and examination of different strains for one organism type doesn't necessarily mean it can be applied to other types of organisms; further investigation needed to determine if dose-response relationship changes with age or immune status; it is possible to control experimental parameters or modify Beta-poisson model to account for uncertainty.
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: some high 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: low 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	most of these studies inoculated volunteers with concentrated amounts of cysts or microorganisms that would not normally be consumed in food; later study (2000) published by first author indicates validity of beta-poisson model is unknown; oocysts were placed in gelatin caplets in order to be administered to volunteers; more recent dataset and models available (Teunis et al., 2002)
K. Cross-References	review cited in two other DR other templates including viruses and bacteria

A. Dose-Response Study Identification	Teunis, P.F.M., O.G. van der Heijden, J.W.B., van der Geissen and A.H. Havelaar. 1996. The dose-response relation in human volunteers for gastro-intestinal pathogens. Report No. 284550002. Leeuwenhoeklaan, The Netherlands: National Institute of Public Health and the Environment.
B. Objectives and Type of Study	1. purpose: scientific; future regulatory; examined previous studies to determine if quantitative relationship between dose and risk of infection could be established 2. type: DR virus
C. Publication Attributes	1. sponsors/affiliations: Veterinary Inspectorate (VHI), Public Health Inspectorate (HIGB), and Ministry of Public Health, Welfare, and Sports (VWS) 2. peer-review mechanism: full scientific journal review
D. Data Description and Study Design	1. type: human clinical data for administration of pathogenic viruses: clinical Rotavirus strain CJN isolated from human fecal material, Echovirus 12 clinical isolate, Polioviruses: Type 1 SM, Sabin Type 1 (LSc2ab), Type 1, 3

	Fox, all strains were clinical isolates , and Norwalk virus clinical isolate. 2. source: published studies (Rotavirus: Ward et al., 1986; Echovirus: Schiff et al., 1984; Polioviruses: Koprowski, 1956; Lepow et al. 1962; Minor et al., 1981; Plotkin et al., 1959; Katz and Plotkin 1967; Norwalk Virus: Graham et al., 1994) 3. extent of data: single Rotavirus strain administered to 62 adult male volunteers (low SNT tiers) with endpoints of fecal excretion, blood samples, and illness symptoms expressed; single Echovirus 12 administered to 149 human volunteers (HAI negative) with endpoint of rectal swab; Single Poliovirus 1 SM administered to 13 adult human volunteers with endpoints of viral shedding; Single Poliovirus 1 (LSc2ab) administered to 272 newborn infants (weighing more than 5lbs and less than 5 days old) with endpoints of fecal excretion; Single Poliovirus type 1 administered to 32 two-month-old infants with endpoints of fecal excretion or rectal swabs; Single Poliovirus 3 Fox administered to 16 premature infants with endpoint of fecal excretion; single Poliovirus 3 Fox administered to 22 premature infants with endpoint of fecal excretion; Norwalk virus administered to approximately 50 volunteers 4. sampling plan: Rotavirus: stool and blood samples collected daily and checked (ELISA) for Rotavirus shedding for 8 different treatments administered ranging from 9×10^{-3} to 9×10^{4};Echovirus 12: rectal swabs examined for viral shedding for 7 different treatments administered ranging from 0 to 3.3×10^{5}; Poliovirus Type 1 SM: undefined samples examined for viral shedding for 4 different treatments administered ranging from 2×10^{-1} to 2×10^{2}; Poliovirus 1 (LSc2ab): fecal specimens were examined on days 6 and 7 for viral isolates for 3 different treatments ranging from $10^{3.5}$ to $10^{5.5}$; Poliovirus type 1: stool samples or rectal swabs collected daily for 10 days and examined for viral isolates for 12 different treatments ranging from 7-280 TCID50; Poliovirus 3 Fox: stool specimens examined before and after administration of treatments at a 3-day interval for 3 different treatments ranging from 10-200 TCID50; Poliovirus 3 Fox: (Kotz and Plotkin 1967) sampling plan not specified; Norwalk virus: methods in primary literature unclear, all volunteers received approximately the same dose amount. 5. sample size:3-11 volunteers per dose group administered Rotavirus; 3-50 volunteers per dose group administered Echovirus 12; 2-4 volunteers per dose group administered Poliovirus Type 1 SM strain; 84-97 volunteers per dose group administered Poliovirus 1(LSc2ab); 1-6 volunteers per dose group administered Poliovirus type 1; 3-9 volunteers per dose group administered Poliovirus 3 Fox; 3-10 volunteers per dose group administered Poliovirus 3 Fox; approximately 50 volunteers received same dose of Norwalk virus. 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: data analysis of experimental data from human clinical studies 2. specific characteristics: experimental data were analyzed with Exponential/ Beta-poisson dose response models to determine best fit model with appropriate confidence range referencing previously published study 3. assumptions: every oocyst that enters host has same probability of causing infection; differences among dose responses for different experiments are likely due to differences in biological factors for each pathogenic organism and/or environmental conditions; factors associated with host(s) are likely to be variable across experiments. 4. relevance: medium
F. Study Conclusions and	1. Low dose approximations for the above viruses are: Rotavirus: 0.60 ; Echovirus 12: 1.76×10^{-3}; Poliovirus 1 SM:

Extended Applications	4.91 x10^{-1}, Poliovirus 1 (LSc2ab):7.2 x10^{-4}, Poliovirus 1: 9.1 x 10^{-3}, Poliovirus 3 Fox:(infants) 0.258, Poliovirus 3 Fox:(premature infants)0.542 as supported by the clinical data from experimental dose-response trials; 2. Beta-poisson model is a "single hit" model that can be used when assuming any single microorganism is capable of infection upon entering host; exponential model implies no minimum infective dose.
G. Data Gaps and Proposed Solutions	1. data gaps: class differences among strains of pathogenic organisms are difficult to generalize; unknown if dose-response relationship changes with age or immune status; uncertainty in controlled conditions of experiments. 2. authors propose: Class differences among pathogenic organisms are most difficult to control and examination of different strains for one organism type doesn't necessarily mean it can be applied to other types of organisms; further investigation needed to determine if dose-response relationship changes with age or immune status; it is possible to control experimental parameters or modify Beta-poisson model to account for uncertainty.
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: NA 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: low 5. defensibility: UN
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	most of these studies inoculated volunteers with concentrated amounts of viruses that would not normally be consumed in food or water; later study (2000) published by first author indicates validity of beta-poisson model is unknown
K. Cross-References	review cited in two other DR templates including bacteria and protazoans

A. Dose-Response Study Identification	Teunis, P.F. and A.H. Havelaar. 2000. The Beta Poisson Dose-Response Model is not a single-hit model. Risk Anal. 20(4): 513-520.
B. Objectives and Type of Study	1. purpose: scientific; A defense is presented for the case of a single-hit model. 2. type: DR
C. Publication Attributes	1. sponsors/affiliations: National Institute of Public Health and The Environment, Bilthoven, The Netherlands 2. peer-review mechanism: peer-reviewed journal

D. Data and Study Design	1. type: historical data in published literature 2. source: human volunteer studies that investigated dose-response for ingestion of rotavirus (Ward et al., 1986), *Campylobacter jejuni* (Black et al., 1998), and *Vibrio cholerae* (Cash et al., 1974) 3. extent of data: dose-response 4. sampling plan: designed experiment 5. sample size: 55 for rotavirus, 68 for *Campylobacter jejuni*, 67 for *Vibrio cholerae* 6. performance characteristics: sound statistical methodology 7. relevance: high
E. Method/Model/Approach	1. general characteristics: beta Poisson approximation compared to exact (hypergeometric) beta Poisson model 2. specific characteristics: comparison of dose-response models, examined behavior of beta Poisson approximation in regions where assumptions of approximations were not met, considers effects of model selection on uncertainty analysis, models fit in Bayesian framework using Markov chain Monte Carlo (MCMC) 3. assumptions: organisms are discrete entities randomly (Poisson) distributed in inoculum, organisms act independently, any organism may cause infection (single hit) 4. limitations: low dose extrapolation necessary for *Campylobacter jejuni*, and *Vibrio cholerae* 5. relevance: high
F. Study Conclusions and Extended Applications	1. conclusions: differences are greatest at low doses, errors may become large in uncertainty estimates 2. authors' extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: low dose exposure data not available 2. proposed solutions: use exact model
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: high 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	Teunis et al., 1999

A. Dose-Response Study Identification	Teunis, P.F., C.L. Chappell and P.C. Okhuysen. 2002. *Cryptosporidium* dose-response studies: Variation between hosts. Risk Anal. 22(3): 475-485.
B. Objectives and Type of Study	1. purpose: scientific; An adaptation of the hit theory model of microbial infection to incorporate covariables, characterizing the immune status of the susceptible host. 2. type: DR
C. Publication Attributes	1. sponsors/affiliations: National Institute of Public Health and The Environment, Bilthoven, The Netherlands 2. peer-review mechanism: peer-reviewed journal
D. Data and Study Design	1. type: historical data in published literature 2. source: human volunteer studies that investigated dose-response for ingestion of *Cryptosporidium parvum* in subjects with low and high preexisting anti-*Cryptosporidium* IgG measured by ELISA 3. extent of data: dose-response for infection and illness 4. sampling plan: designed experiment 5. sample size: 29 low IgG, 17 high IgG 6. performance characteristics: NA 7. relevance: high
E. Method/Model/Approach	1. general characteristics: single hit model adapted to allow IgG level as a covariate, hazard function used to relate duration of infection to probability of illness 2. specific characteristics: infection dose-response with logistic mixture density function, illness dose-response, models fit in Bayesian framework using Markov chain Monte Carlo (MCMC), illness dose-response model with gamma distribution for duration of infection, discussion of health effects 3. assumptions: organisms are discrete entities randomly (Poisson) distributed in inoculum, organisms act independently, any organism may cause infection (single hit), during infection a host has a certain hazard of becoming ill 4. limitations: NA 5. relevance: high
F. Study Conclusions and Extended Applications	1. conclusions: the infectivity and probability of illness given infection appear to correlate with existing IgG levels, there was a 23-fold increase in ID_{50} in subjects with high preexisting anti-*Cryptosporidium* IgG levels 2. authors' extrapolations: results may be used to assess individual susceptibility to illness among human subjects with known anti-*Cryptosporidium* IgG levels

G. Data Gaps and Proposed Solutions	1. data gaps: not all individuals who became ill tested positive for infection 2. proposed solutions: none
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: high 3. generalizability or external validity: high 4. soundness of study conclusions or internal validity: high 5. defensibility: high
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	other immune responses in addition to normal IgG may be important to consider; biological data for modeling progression from colonization/infection to illness may be important
K. Cross-References	Teunis and Havelaar, 2000; Teunis et al., 1999

A. Dose-Response Study Identification	Teunis, P., K. Takumi and K. Shinagawa. 2004. Dose response for infection by *Escherichia coli* O157:H7 from outbreak data. Risk Anal. 24(2): 401-407.
B. Objectives and Type of Study	1. purpose: scientific; Demonstrates how high infectivity limits the uncertainty in the low-dose region. 2. type: DR
C. Publication Attributes	1. sponsors/affiliations: National Institute of Public Health and The Environment, Bilthoven, The Netherlands 2. peer-review mechanism: peer-reviewed journal
D. Data and Study Design	1. type: historical data 2. source: 1996 outbreak of *E. coli* in Japanese elementary school 3. extent of data: both the estimated dose and infection rate were available 4. sampling plan: all exposed subjects were tested 5. sample size: 848 children; 43 adults 6. performance characteristics: case study not reproducible, not repeatable 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: beta Poisson (hypergeometric) model, Bayesian approach, Markov chain Monte Carlo

	(MCMC) 2. specific characteristics: food exposure dose-response relationship estimated from a single data point, exposure dose could be estimated, compared dose-response model to controlled experiments in other species and other organisms 3. assumptions: structure of dose-response model and a single data point are sufficient to estimate dose-response relationship, single hit model applies 4. limitations: dose-response estimated from single data point, food samples held for 8 days prior to testing may affect dose estimates 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions: discrepancy between this dose-response assessment and others considered may be due to species variation, or the strain of *E. coli* that caused the outbreak may be a highly infective strain. 2. authors' extrapolations: none
G. Data Gaps and Proposed Solutions	1. data gaps: dose-response estimated from single data point 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: high 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: low 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	NA

A. Dose-Response Study Identification	Whiting, R.C. and R.L. Buchanan. 1997. Development of a quantitative risk assessment model for *Salmonella enteritidis* in pasteurized liquid eggs. Int. J. Food Microbiol. 36: 111-125.
B. Objectives and Type of Study	1. purpose: scientific and future regulatory interest; construct viable risk assessment model incorporating dose response and food microbiology to quantitatively assess hazards associated with a food process.

	2. type: DR
C. Publication Attributes	1. sponsors/affiliations: US Department of Agriculture 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: NA 2. source: published studies and epidemiological surveys 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance of data: low
E. Method/Model/Approach	1. general characteristics: 2,000 iteration Monte Carlo simulation using @RISK sampling from distribution below; 2. specific characteristics: Beta-poison and exponential models for dose-response for the probability of *Salmonella* infection 3. assumptions: dose-response models merit consideration for species strain effects; 4. limitations: additional information of lag periods (effects of physiological state of cell and survival adaptations) is needed; further examination of virulence mechanisms and dose-response mechanisms needed. 5. relevance (qualitative judgement of the usefulness of the method to incident-based microbial risk assessment for biothreat agents; high, medium, or low): medium, includes method for modeling pathogen growth and thermal death and development and use of defined scenarios for selected exposure and dose-response conditions could be very useful for incident-based microbial risk assessment, although parameters selected here are not pertinent to EPA's biothreat agents
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: NA 2. authors' extrapolations from the observed data to other populations or conditions: NA
G. Data Gaps and Proposed Solutions	1. identification of data gaps: Pathogen species specific dose-response curves; discrepancies among lag and growth rate values not determined by model 2. assumptions or source of surrogate data to fill gap: employed exponential and beta-poison model for *Salmonella* does-response curve
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: low 5. defensibility: low

I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	description of most appropriate uses of method for incident-based microbial risk assessment when evaluating farm-to-table food products; useful for threat scenarios permitting bacterial growth in food process; acknowledges limitations of the available data and uncertain usefulness for microbial risk assessment of buildings and water systems with the parameters examined in this model
K. Cross-References	same study in EA, RC

A.3 Risk Characterization Methods

A.3.1 Disease Transmission

Auranen K., J. Ranta, A.K. Takala and E. Arjas. 1996. A statistical model of transmission of Hib bacteria in a family. Stat. Med. 15: 2235-2252. 207

Bachur, R.G. and M.B. Harper. 2001. Predictive model for serious bacterial infections among infants younger than 3 months of age. Pediatrics 108(2): 311-316. 210

Barnhart, S., L. Sheppard, N. Beaudet, et al. 1997. Tuberculosis in health care settings and the estimated benefits of engineering controls and respiratory protection. J. Occup. Environ. Med. 39(9): 849-854. 212

Beggs, C.B., C.J. Noakes, P.A. Sleigh, et al. 2003. The transmission of tuberculosis in confined spaces: An analytical review of alternative epidemiological models. Int. J. Tuberc. Lung Dis. 7(11): 1015-1026. 215

Brookmeyer, R., E. Johnson and R. Bollinger. 2003. Modeling the optimum duration of antibiotic prophylaxis in an anthrax outbreak. Proc. Nat. Acad. Sci. U S A 100(17): 10129-10132. 217

Chick, S.E., J.S. Koopman, S. Soorapanth and M.E. Brown. 2001. Infection transmission system models for microbial risk assessment. Sci. Total Environ. 274: 197-207. 219

Chowell, G., P.W. Fenimore, M.A. Castillo-Garsow and C. Castillo-Chavez. 2003. SARS outbreaks in Ontario, Hong Kong and Singapore: The role of diagnosis and isolation as a control mechanism. J. Theor. Biol. 224(1): 1-8. 221

Dietz K. and J.A. Heesterbeek. 2002. Daniel Bernoulli's epidemiological model revisited. Math. Biosci. 180: 1-21. 223

Eisenberg, J.N., E.Y.W. Seto, A.W. Olivieri and R.C. Spear. 1996. Quantifying water pathogen risk in an epidemiological framework. Risk Anal. 16(4): 549-563. 225

Eisenberg, J.N., J.A. Soller, J. Scott, et al. 2004. A dynamic model to assess microbial health risks associated with beneficial uses of biosolids. Risk Anal. 24(1): 221-236. 227

Focks, D.A., R.J. Brenner, J. Hayes, et al. 2000. Transmission thresholds for dengue in terms of *Aedes aegypti* pupae per person with discussion of their utility in source reduction efforts. Am. J. Trop. Med. Hyg. 62(1): 11-18. 229

Gani, R. and S. Leach. 2004. Epidemiological determinants for modeling pneumonic plague outbreaks. Emerging Infectious Dis. 10: 608-614. 231

Getoor L., J.T. Rhee, D. Koller and P. Small. 2004. Understanding tuberculosis epidemiology using structured statistical models. Artificial Intelligence Med. 30(3): 233-256. 233

Grasman, J. 1998. Stochastic epidemics: the expected duration of the endemic period in higher dimensional models. Math Biosci. 152(1): 13-27. 235

Ko, G., K.M. Thompson and E.A. Nardell. 2004. Estimation of tuberculosis risk on a commercial airliner. Risk Anal. 24(2): 379-388. 237

Li, X. and P.A. Rossignol. 1998. Probability model on the use of sentinel animal monitoring for arbovirus. Epidemiol. 9(4): 446-451. 239

Lui, K.J. 1998. Interval estimation of the risk ratio between a secondary infection, given a primary infection, and the primary infection. Biometrics 54(2): 706-711. 241

Masuda, N., N. Konno and K. Aihara. 2004. Transmission of severe respiratory syndrome in dynamical small-world networks. Physical Review 69(3 Pt 1): 031917. 243

A. Risk Characterization Study Identification (Disease)	Auranen K., J. Ranta, A.K. Takala and E. Arjas. 1996. A statistical model of transmission of Hib bacteria in a family. Stat. Med. 15: 2235-2252.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific; The model is used to predict prevalence and incidence of Hib carriage in families as a function of family size and age status. 2. type: RC, disease transmission
C. Publication Attributes	1. sponsors/affiliations: The Academy of Finland 2. peer-review mechanism: scientific journal review
D. Data and Study Design	1. type: Data set I - Carriage state of all family members of children with invasive Hib disease at two time points one year apart. Data set II - Carriage state of healthy infants and all family members of healthy infants at six, nine, and twelve months of age. 2. source: Data set I - National Public Health Institute, Helsinki; Data set II - Barbour ML, Mayon-White RT, Coles C, Crook DWM, and Moxon ER 1995. The impact of conjugate vaccine on carriage of Haemophilus influenzae type b (Journal of Infectious Diseases 171:93-98). 3. extent of data: Data set I - Children in Finland with invasive Hib disease in 1985-1986. Data set II - Infants born at two hospitals in Britain in 1991-1992. Only complete families at epochs when none of the family members was yet immunized against Hib were included. 4. sampling plan: Data set I - National surveillance, no sampling. Data set II - Infants included if there was at least one 3-4 year old sibling in the family. 5. sample size: Data set I - 400 individuals in 97 families. Data set II - 487 individuals in 111 families at six months, 393 individuals at nine months, and 258 individuals in 58 families at twelve months. 6. performance characteristics: Data set I - 6.1% of carriage states missing. Data set II - 29% of carriage states missing. 7. relevance: low
E. Method/Model/Approach	1. general characteristics: A two-state (S=susceptible and C=carrier) individual level Markov process (SIS-type epidemic) model is specified to characterize the transmission of Hib among family members. 2. specific characteristics: Two transition probabilities (hazard rates) are modeled, susceptible to carrier (S->C) and carrier to susceptible (C->S). Separate transition probabilities are postulated for children less than 7 years of age and persons 7 years of age and older. Constant hazard rates are assumed for the C->S transition. The S->C transition probability has components for transmission within the family, which is assumed to be proportional to family size, and transmission from the community, which is assumed to be constant. In order to specify the likelihood of the data, from a Markov process, the probability of the initial step must also be specified. The stationary distribution of Hib in families as selected for Data sets I and II, as specified by the two-state Markov process, is derived. The model is applied to Data set I, Data set II, and the combined data. Marginal posterior distributions for model parameters are compared and indicate that all three model fits result in similar conclusions. The datasets are complementary in the sense that Data set I provides strong information about

	within family transmission parameters but little information about community transmission parameters and Data set II provides strong information about community transmission parameters but week information about within family transmission parameters. All models provide similar strong information about stationary prevalence, which is a function of the transmission parameters. 3. assumptions: Within family, infection is modeled as proportional to the number of current infection carriers in the family. Three assumptions are needed to derive the stationary distribution of Hib carriage. 1) The epidemic process is the same in the family of a diseased child as in the family of an asymptomatic carrier, 2) Only the under 7 group can get invasive Hib disease, and 3) The incidence rate of invasive Hib is low compared to the endemic prevalence of Hib carriage. Priors on the parameters of the hazard functions required that younger individuals are more susceptible to becoming carriers than older individuals and prevalences of carriage are higher among younger individuals. 4. limitations: Strong assumptions were made about the steady-state situation of Hib carriage at the initial sampling time. These assumptions might not have been met by families with young infants. 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions: The mean duration of carriage was estimated to be 4.1 and 5.4 months for under 7 years of age and older persons, respectively. The mean durations of non-carrier state in an individual exposed to a single family member carrier are 11.2 and 38.2 months in the two age groups. The mean times until becoming infected by the community are 21 and 56 years for the two age groups. The model quantifies the effect of family size and age structure on the prevalence of Hib carriage in a population of families with small children. Estimates of prevalence of Hib carriage in a number of family configurations are provided. Expected mean time to infection is also estimated for a number of family configurations. 2. authors' extrapolations: The age dependencies observed in transmission rates may be partly explained by changes in social behavior and the physiological development of the mucosa and subsequent differences in adherence of Hib bacteria.
G. Data Gaps and Proposed Solutions	1. data gaps: There were few time points of observations, resulting in wide credible intervals for rates of transmission and sojourn times but many individuals followed resulting in narrower credible intervals for prevalence of Hib carriage. 2. proposed solutions: More observations across time would provide more information on transmission rates and sojourn times.
H. Weight of Evidence	1. robustness of method: high 2. representativeness of data: low 3. generalizability or external validity: high 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from	NA

Compendium	
J. Reviewer Comments	NA
K. Cross-References	NA

A. Risk Characterization Study Identification (Disease)	Bachur, R.G. and M.B. Harper. 2001. Predictive model for serious bacterial infections among infants younger than 3 months of age. Pediatrics 108(2): 311-316.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific; to develop data-derived model for predicting serious bacterial infection (SBI) among febrile infants <3 months old. 2. type: RC, disease transmission
C. Publication Attributes	1. sponsors/affiliations: Children's Hospital, Boston 2. peer-review mechanism: peer-reviewed journal
D. Data and Study Design	1. type: retrospective study in urban emergency department 2. source: retrospective identification of all patients ≤90 days seen in emergency department from 1993 to 1999 with rectal temperature ≥38 degrees C. 3. extent of data: large number of possible patients reviewed to determine confirmation that culture isolate was considered true pathogen and not a contaminant 4. sampling plan: criterion-based 5. sample size: 5279 febrile infants ≤90 days old with various cultures for each; 373 condition of interest 6. performance characteristics: repeatable, reproducible, adequate methods employed, complete 7. relevance: some high
E. Method/Model/Approach	1. general characteristics: model for risk prediction created through binary recursive partitioning (tree-structured analysis by Classification and Regression Tree (CART)), model tested by V-fold cross-validation 2. specific characteristics: SBI or no-SBI used as dichotomous outcome variable, and age, temperature, WBC, UA, absolute nephrile count, and CSF WBC entered as potential predictors. CART determines order and use of variables as well as cut points for any continuous variables. 3. assumptions: unclear 4. limitations: limited definition of SBI to include only meningitis, bacteremia, and UTI, the prevalence of SBI in population was underestimated; not all patients had all cultures performed, underestimating the prevalence of SBI and potentially affecting development of the model; unable to assess value of other predictors (e.g., Gram

	stains of urine) that have been used in other prediction strategies, past medical history of patient not considered in model but potentially important in practice. 5. relevance: high
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: UA found to be single best discriminator for SBI 2. authors' extrapolations from the observed data to other populations or conditions: none
G. Data Gaps and Proposed Solutions	1. data gaps: misclassification of some SBI patients into lower risk group 2. proposed solutions: an outpatient strategy using empiric therapy may be justified
H. Weight of Evidence	1. robustness of method: high (v-fold cross-validation) 2. representativeness of data: high 3. generalizability or external validity: low (good performance when compared to Rochester and Philadelphia strategies but model designed for ≤90 day old infants only so excludes large portion of population) 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	NA

A. Risk Characterization Study Identification (Disease)	Barnhart, S., L. Sheppard, N. Beaudet, et al. 1997. Tuberculosis in health care settings and the estimated benefits of engineering controls and respiratory protection. J. Occup. Environ. Med. 39(9): 849-854.
B. Objectives and Type of Study	1. purpose: scientific; characterization of person-hours and lifetime risks of TB-related morbidity and mortality using a risk assessment of health-care workers at varying levels of exposure, engineering controls, and respiratory protection. 2. type: RC, disease transmission
C. Publication Attributes	1. sponsors/affiliations: National Heart, Lung and Blood Institute 2. peer-review mechanism: peer-reviewed journal
D. Data and Study Design	1. type: published data

	2. source: multiple sources cited in past studies (12 in all) 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: Not highly repeatable or reproducible due to missing information on data selection; adequate methodology employed; incomplete details on data selection from available sources. 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: data from multiple studies was combined in a Poisson probability model 2. specific characteristics: The model predicts risk for Tb infection of healthcare workers in tuberculosis wards (i.e., skin-test conversion from negative to positive). The model is based on understanding that risk is a function of 1) prediction of infectious quanta (particles in air); 2) rate of elimination of infectious quanta in air (due to ventilation and UV germicidal irradiation); 3) minute ventilation of the healthcare workers; and 4) filtering capabilities of respiratory masks worn by the health care workers. The dose-response component of the model assumed that inhalation of one infectious quanta results in a skin-test conversion. 3. assumptions: 1) Assumes steady-state conditions in the room with a random distribution of the infectious quanta, specifically: patient has active pulmonary tuberculosis and is isolated in a room measuring 4 x 4 x 3 meters. 2) The production of infectious particles is set at three levels: (1) average generation of .25 infectious quanta per hour, (2) high generation of 60 infectious quanta per hour, or (3) extreme generation of 249 infectious quanta per hour; 3) inhalation of one infectious particle or quantum results in a skin test conversion. 4) Ventilation rates are set at two levels: (1) baseline ventilation without ultraviolet germicidal irradiation (UVGI) for 6 air exchanges per hour, or (2) ventilation with UVGI equivalent to 25 air exchanges per hour. 5) The health care worker (HCW) has a constant minute ventilation equivalent to (V_e) = 7.5 liters/minute; 6) four different levels of respiratory protection with varying efficacy were considered. The estimated percentage of droplet nuclei (including filter and face seal leakage) penetrating the respirator was based on review of the literature and set equivalent to the values proposed by Nicas. 4. limitations: Limited data on percentage penetration of droplet nuclei, use of published data from various sources may limit the validity of the estimates. Imperfectly mixed air and physical proximity to the patient may increase the risk, thereby showing an underestimation of the benefits of UVGI. 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions: Use of respirator protection is estimated to reduce risks by the following proportions: surgical mask, 2.4-fold; disposable dust, fume, mist, or disposable HEPA-filtering mask, 17.5-fold; elastomeric HEPA cartridge respirator, 45.5-fold; or powered air-purifying respirator, 238-fold. Assuming a lifetime exposure of 250 hours, the risk of a skin-test conversion for workers without respiratory protection is estimated to be 9% indicating HCWs are at a substantial risk for Tb-related morbidity and mortality and that administrative controls, engineering controls, and respirators offer substantial benefits in risk reduction. 2. authors' extrapolations: author does not extrapolate beyond Tb risks

G. Data Gaps and Proposed Solutions	1. data gaps: limited data on percentage penetration of droplet nuclei 2. proposed solutions: no differentiation in the protection is made between disposable dust fume/dust mite, disposable high-efficiency particulate air filtering (HEPA) mask respirators, or the respirators recently certified by NIOSH
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	NA

A. Risk Characterization Study Identification (Disease)	Beggs, C.B., C.J. Noakes, P.A. Sleigh, et al. 2003. The transmission of tuberculosis in confined spaces: An analytical review of alternative epidemiological models. Int. J. Tuberc. Lung Dis. 7(11): 1015-1026.
B. Objectives and Type of Study	1. purpose: analysis and application of 3 epidemiological models used to predict transmission of airborne disease in confined space (Mass Action Model, Riley, Murphy and Riley's Model, and Gammiatoni and Nucci's model), presentation of reported quanta production data 2. type: RC, disease transmission
C. Publication Attributes	1. sponsors/affiliations: Aerobiological Research Group, School of Civil Engineering, University of Leeds, United Kingdom 2. peer-review mechanism: peer-reviewed journal
D. Data and Study Design	1. type: historical data 2. source: historical quanta production rate data for tuberculosis (TB) and measles outbreaks, from various sources 3. extent of data: vast range of quanta rates associated with various TB outbreaks 4. sampling plan: all data from selected reporting papers

	5. sample size: NA 6. performance characteristics: repeatable, reproducible, adequate analytical and statistical methods, complete study 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: Mass Action (MA) Model, Riley, Murphy and Riley's (RMR) Model, and Gammiatoni and Nucci's (GN) model; parametric study 2. specific characteristics: MA states the number of infectious transmission per infected case is a function of the number of susceptible individuals in the population. RMR. model deals with probability of a susceptible person becoming infected by inhaling a quanta of infection. GN model includes the change of quanta level in a room space with time. Parametric study undertaken using GN model to investigate relative impact on infection rates of ventilation rate, room volume, and density of occupation and the dose and infertility of the airborne agent. 3. assumptions: for all models it is assumed that 1) all susceptible individuals have an identical pulmonary ventilation rate, 2) the air in the room space is completely mixed that the infectious agent is evenly distributed throughout the room space, and 3) all susceptible individuals are equally vulnerable to the infectious agent 4. limitations: MA model not well-suited to modeling TB transmission in enclosed spaces. Most comprehensive model is GN model. All models do not automatically allow susceptible individuals to become infectors so to overcome this must apply model for distinct time periods based on incubation period of disease. GN model most suitable for modeling TB transmission in most indoor situations. 5. relevance: high
F. Study Conclusions and Extended Applications	1. conclusions: Overcrowding has strong influence on spread of infection. MA model not suitable for general analysis of TB outbreaks in confined spaces. GN model incorporates RMR. model and is most suitable for simulating TB outbreaks in confined spaces. If concentration of infectious agent in a room air is high, the time period before infection occurs will be short. The greatest risk of TB infections appears to occur in clinical settings as a result of procedures that produce large quantities of aerosol, such a bronchoscopy or intubation. With such procedures the levels of infectious agents released may be so high that normal dilution ventilation alone will not be able to reduce the risk of infection and secondary measures such as respirators or HEPA filter masks will be required to protect health care staff. 2. authors' extrapolations: evaluation of person protection equipment, potential for infection on aircraft.
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: high 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high

	5. defensibility: high
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	NA

A. Risk Characterization Study Identification (Disease)	Brookmeyer, R., E. Johnson and R. Bollinger. 2003. Modeling the optimum duration of antibiotic prophylaxis in an anthrax outbreak. Proc. Nat. Acad. Sci. U S A 100(17): 10129-10132.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific, future regulatory interest A competing-risks model is used to describe the pathogenesis of inhalational anthrax and the impact of antibiotic prophylaxis on attack rate and incubation time. 2. type: RC, disease transmission
C. Publication Attributes	1. sponsors/affiliations: National Institute of Allergy and Infectious Diseases 2. peer-review mechanism: Full scientific journal review.
D. Data and Study Design	1. type: competing-risks model; experimental data from rhesus macaque monkeys from Henderson D.W., Peacock, S, Belton, F.C., 1956, J. Hyg., 54:28-36 2. source: several published studies and theory/theoretical modeling developed by authors 3. extent of data: data interpretation based on some published literature and large number of calculations based on competing-risks model computational analysis. 4. sampling plan: possibly clustered 5. sample size: none reported 6. performance characteristics: none reported 7. relevance: high
E. Method/Model/Approach	1. general characteristics: Competing-risks model to address the duration of antibiotic prophylaxis and the incubation period that accounts for the risks of spore germination and spore clearance. The model predicts the incubation period distribution, which is confirmed by empirical data. 2. specific characteristics: predictive for post exposure prophylaxis that can confer long term immunity; indicative that significant morbidity can occur at high doses of exposure, before antibiotic prophylaxis can be initiated.

	3. assumptions: (a) disease will occur if at least one spore germinates before it is cleared by other mechanisms; (b) antibiotics prevent germination as long as they are administered, but otherwise, they alter neither clearance rate nor the germination rate of spores; (c) probabilistic calculations were based on an underlying Poisson model for the number of spores that germinate in a host 4. limitations: Applicable only to inhalation exposure of anthrax and to no other mode of exposure and to no other organism of interest to EPA 5. relevance: high
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: >4 months of antibiotic prophylaxis are necessary to reduce risk to <1/10,000 for high doses of exposure to anthrax spore via inhalation. 2. authors' extrapolations from the observed data to other populations or conditions: NA
G. Data Gaps and Proposed Solutions	1. data gaps: probability of exposure to spores not provided 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: high 2. representativeness of data: high 3. generalizability or external validity: high 4. soundness of study conclusions or internal validity: high 5. defensibility: high
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	1. Predictions of the model are based on inhalation exposure to anthrax spores which is the most relevant method of exposure. The model does not deal with other modes of exposure and is also limited in application for other threat agents. 2. other comments by reviewer: good scientific paper for future regulatory purpose towards treatment of inhalation exposure to anthrax spores. Antibiotic prophylaxis after exposure is uncertain and is a critical public health question.
K. Cross-References	NA

A. Risk Characterization Study Identification (Disease)	Chick, S.E., J.S. Koopman, S. Soorapanth and M.E. Brown. 2001. Infection transmission system models for microbial risk assessment. Sci. Total Environ. 274: 197-207.

B. Objectives and Type of Study	1. purpose noted by study authors: scientific; presents new models of infection transmission systems being developed as part of a project to quantify risk of microbial infection; models are designed to help inform water treatment system design decisions 2. type: RC, disease transmission
C. Publication Attributes	1. sponsors/affiliations: US EPA NCEA 2. peer-review mechanism: Peer-reviewed journal
D. Data and Study Design	1. type: dynamic system model; *Cryptosporidium parvum* case study 2. source: parameter such as background levels of oocysts in tap water, drinking consumption, the dose-response parameter, duration of infection, and effectiveness of ozone pretreatment and filters were chosen to be compatible with reasonable ranges for *Cryptosporidium* published elsewhere (Eisenberg et al., 1998; Hoxie et al., 1997) 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: infection transmission system model; models exogenous sources of infection, such as human-to-human, and “feedback loops”. 2. specific characteristics: dynamic system model used to describe infection transmission dynamics to model risk from microbial agents; uses the example of *Cryptosporidium* transmission from both drinking water and secondary transmission. Incorporates time-dependent concentration in water. 3. assumptions: Model ignores birth and death, has a homogeneous population susceptible to infection, total population size constant, 4. limitations: Human population dynamics affect transmission dynamics. Other complicating factors include multiple pathogen strains, subpopulations, community makeup, multiple environmental reservoirs, etc. 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: Standard exposure assessment using chemical risk paradigm for microbial risk may give misleading conclusions about effects of hazard reduction intervention. An integrated infection transmission system approach can address special concerns for modeling microbial risk. Case study found that specialized filters on taps to remove *Cryptosporidium* for HIV-infected individuals eliminated risk of infection from drinking water when there is no significant secondary transmission; however, when unsustainable secondary transmission plays a role, *Cryptosporidium* is better controlled by a partially effective centralized ozone pretreatment. 2. authors’ extrapolations: microbial risk assessment is also applicable to agricultural infection control; germ

	warfare preparedness
G. Data Gaps and Proposed Solutions	1. data gaps: role of likelihood and magnitude of exposure not included; other roles of water affecting infection transmission; multiple pathogen strains, multiple subpopulations, multiple environmental reservoirs, other dose response models, etc. 2. proposed solutions: Data gaps should be explored. Sensitivity analysis help to identify those parameters of most importance.
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: high 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility: high for agents with person-to-person transmission
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	article offers example of infection disease transmission systems for risk assessment
K. Cross-References	NA

A. Risk Characterization Study Identification (Disease)	Chowell, G., P.W. Fenimore, M.A. Castillo-Garsow and C. Castillo-Chavez. 2003. SARS outbreaks in Ontario, Hong Kong and Singapore: The role of diagnosis and isolation as a control mechanism. J. Theor. Biol. 224(1): 1-8.
B. Objectives and Type of Study	1. purpose: scientific; to formulate a simple model for SARS outbreaks that captures the effect of average infectiousness and the effect of isolating diagnosed patients. 2. type: RC, disease transmission
C. Publication Attributes	1. sponsors/affiliations: DOE, NSF, NSF, and Sloan Foundation 2. peer-review mechanism: Scientific Journal Article
D. Data and Study Design	1. type: epidemiologic data 2. source: data from the Ontario (Toronto), Hong Kong, and Singapore SARS outbreaks of 2003; data obtained from the Canadian Ministry of Health and World Health Organization. 3. extent of data: three data sets–Toronto, Hong Kong, and Singapore.

	4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: nonlinear system of differential equation. 2. specific characteristics: ten parameters used 3. assumptions: multiple assumptions are made and include contact rate, age-dependent susceptibility, genetic factors, homogeneous mixing, and that diagnosed individuals are handled with care. 4. limitations: model is for single outbreaks and not global spread or long term impact of SARS 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: model results suggest that local outbreaks may follow similar pattern. 2. authors' extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: model not able to handle high levels of variability. 2. proposed solutions: Stochastic model would be desirable.
H. Weight of Evidence	1. robustness of method: high 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: low 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	1. description of most appropriate uses of method for incident-based microbial risk assessment of buildings and water systems: model does not involve buildings or water systems. 2. other comments by reviewer: Study reports a model that predicts local transmission of SARS outbreak.
K. Cross-References	NA

A. Risk Characterization Study Identification (Disease)	Dietz K. and J.A. Heesterbeek. 2002. Daniel Bernoulli's epidemiological model revisited. Math. Biosci. 180: 1-21.
B. Objectives and Type of Study	1. purpose: scientific 2. type: RC, disease transmission
C. Publication Attributes	1. sponsors/affiliations: Netherlands Organization for Scientific Research (NWO) 2. peer-review mechanism: scientific journal review
D. Data and Study Design	1. type: smallpox mortality data from the Hague (1755-1769) 2. source: Lambert, 1772 3. extent of data: age distribution for 1455 smallpox deaths 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: this paper is a reworking of Bernoulli's mathematical model that examines age-specific equilibrium prevalence of immune individuals in an endemic potentially lethal infectious disease, and specifically a mathematical examination of Bernoulli's model to calculate the gain in life expectancy at birth if smallpox were to be eliminated as a cause of death 2. specific characteristics: NA 3. assumptions: risk of dying from the specific infection of interest is independent of risk of dying due to other diseases 4. limitations: NA 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusion: the model can be used to assess gain in life expectancy in a population as a function of the proportion immunized 2. authors' extrapolations: the model is applicable to measles and other viruses whose transmission is associated with potentially fatal infections and permanent immunity in survivors
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: high 3. generalizability or external validity: low

	4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	NA

A. Risk Characterization Study Identification (Disease)	Eisenberg, J.N., E.Y.W. Seto, A.W. Olivieri and R.C. Spear. 1996. Quantifying water pathogen risk in an epidemiological framework. Risk Anal. 16(4): 549-563.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific; to develop a quantitative approach to risk characterization based on a distributional estimate for a population 2. type: RC, disease transmission
C. Publication Attributes	1. sponsors/affiliations: City of Santa Rosa, Irvine Water District, Las Virgenes Municipal Water District, National Water Research Institute, Overheim Municipal Water District, San Diego Water Authority, and Water Resource Center, Grant, University of California. 2. peer-review mechanism: peer-reviewed journal
D. Data and Study Design	1. type: literature based information was used to assign parameter ranges; case study based on *Giardia lamblia* transmission associated with swimming 2. source: several sources of data; surveillance data from non-outbreak conditions in Vermont were used to obtain baseline values for seven of the parameters not associated with water transmission 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: Monte Carlo simulation; binary classification to assess output of each simulation; CART (Classification and Regression Tree) analysis and Regional Sensitivity Analysis 2. specific characteristics: designed and implemented a dynamic model that tracks traditional epidemiological

	variables (susceptible, infected, diseased, and immune) and environmental variables such as pathogen density. Distributions were assumed uniform (incorporating observations or opinion <2 orders of magnitude) or log-uniform. DR assumed single-hit exponential function. Monte Carlo simulations assigned binary classification of the output. Two scenarios, exposure vehicle not reclaimed water or reclaimed wastewater 3. assumptions: the ratio of pathogen concentration in stool is equal to ratio of the rate of shedding; only four disease-state variables involved; both diseased and infected contribute to recreational water contamination, DR model assuming pathogens are randomly distributed in feces and water, a fraction survive and infect swimmers, and survival (and infectivity) are independent of pathogen dose. 4. limitations: no distinction between uncertainty and variability in the values of each parameter; seasonal variation not explored in this study 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: Model predicts likelihood of outbreaks, given data, assumptions, and model structure. Shedding of pathogens by infected swimmers contributed the most uncertainty in risk. Evidence for slowed distributions suggest model could be invalid. 2. authors' extrapolations: Important implications for public health.
G. Data Gaps and Proposed Solutions	1. data gaps: uncertainty and variability in values of each parameter not distinguished; no susceptibility groups 2. proposed solutions: uncertainty can be decreased by more data; variability is inherent but can be better characterized. A more refined model would divide population into different susceptibility groups each with distinct epidemiological parameter values.
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: NA 5. defensibility: NA
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	NA

A. Risk Characterization Study Identification (Disease)	Eisenberg, J.N., J.A. Soller, J. Scott, et al. 2004. A dynamic model to assess microbial health risks associated with beneficial uses of biosolids. Risk Anal. 24(1): 221-236.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific; future regulatory interest; 2. type: RC, disease transmission
C. Publication Attributes	1. sponsors: US EPA Cooperative Agreement CR-825237 through the Water Environment Research Foundation (WERF) 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: NA 2. source: assumed and/or derived parameter values for high and low risk scenarios in an epidemic setting, published literature, and EPA guidance (EPA, 1989); low, medium, and high values from literature (Eisenberg et al., 2003 cited for parameter derivations) 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: Description and demonstration of methodology for assessing risks to human health from pathogen exposure using a population based model that accounts for secondary transmission, immunity, incubation and asymptomatic infection. 2. specific characteristics: Deterministic model for disease transmission consisting of six disease states (susceptible, exposed, carrier, diseased, second carrier, protected state); rates of movement from one state to another simulated using a set of delay equations modeling ingestion, secondary transmission, and immunity; Classification And Regression Tree (CART) analysis was used to compare attributable risk simulation results in sensitivity analysis. Application of the numerical simulation model to predict risk from exposure to biosolids-amended soil contaminated with enterovirus. Transmission routes also include person-to-environment-to-person. A Beta-Poisson dose response function is included to determine the probability: $P=1-(1+d/C2)^{C1}$, where d is the dose, and C1 and C2 are parameters of the model that are identified when the function is fit with dose response data; infection/disease modeled appropriately. 3. assumptions: scenario definition assumed: closed community; homogeneous exposures and susceptibility; endemic enterovirus; only source in environment from infected individuals; homogenous viral populations; pathogens attenuated by defined wastewater treatment processes; single application of biosolids to land; biosolids single source of enterovirus; 40% population susceptible; structure and function of model appropriate 4. limitations: validation of parameters and scenarios uncertain for many environmental and population processes 5. relevance: low

F. Study Conclusions and Extended Applications	1. conclusions supported by the data: assumptions of pathogen dose in biosolids versus other environmental exposures and attenuation by different environmental processes can be important determinants of risk; intermediate rates of shedding may result in higher attributable risk than higher or lower rates of shedding; 2. authors' extrapolations from the observed data to other populations or conditions: The model is applicable for all potential pathways of exposure to pathogens; however, exposure in the model is assumed, not characterized from data. The model is a useful tool for identifying data gaps.
G. Data Gaps and Proposed Solutions	1. data gaps: rigorous studies needed to validate parameters of the model; surveillance data for pathogen prevalence and densities in the environmental scenarios of interest; survival models for natural and treatment effects under variable environmental conditions, including humidity and temperature; person-to-person transmission rates and immunity; strain effects on immunity; 2. proposed solutions: conduct research
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: NA 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: low 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	May be useful if person-to-person transmission and immunity are important and data are available for biothreat agents of concern
K. Cross-References	Soller et al., 2004

A. Risk Characterization Study Identification (Disease)	Focks, D.A., R.J. Brenner, J. Hayes, et al. 2000. Transmission thresholds for dengue in terms of *Aedes aegypti* pupae per person with discussion of their utility in source reduction efforts. Am. J. Trop. Med. Hyg. 62(1): 11-18.
B. Objectives and Type of Study	1. purpose: scientific; attempt to estimate transmission thresholds for dengue viruses in terms of *Aedes aegypti* per person in the environment 2. type: RC, disease transmission
C. Publication Attributes	1. sponsors/affiliations: Pollution Prevention Project, Strategic Environmental Research and Development Program and EPA-USDA Interagency Agreement

	2. peer-review mechanism: full scientific peer review
D. Data and Study Design	1. type: previously derived parameter estimates and field and laboratory observations 2. source: parameter estimates and field and laboratory observations on which they are based presented earlier by Focks et al., 1993 3. extent of data: key determinates are number, size, and timing of viral introductions during year, seroprevalence of anti-body to dengue, and temperature 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: two stochastic, simulation models, CIMSiM and DENSiM 2. specific characteristics: Two, interrelated simulation models, CIMSiM and DENSiM, are used to estimate transmission thresholds. CIMSiM is an accounting program of vector dynamics and DENSiM is corresponding account of human dynamics. 3. assumptions: Vector competence is adequate, blood feeding by *Aedes aegypti* occurs primarily on humans, and essentially all hosts are at risk of being bitten. 4. limitations: unknown 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions: Probability of significant transmission was only slightly influenced by the size of the introduction, meaning that any of the computed thresholds could be used for risk assessment. 2. authors' extrapolations: developing software to provide spatially based risk assessment and guidance for control of dengue
G. Data Gaps and Proposed Solutions	1. data gaps: Only one field estimate exists with which to verify model estimates. 2. proposed solutions: Estimates are consistent with the only field estimate available and await further validation from the results of the 5-year, NIH-funded study conducted in Peru.
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA

J. Reviewer Comments	NA
K. Cross-References	NA

A. Risk Characterization Study Identification (Disease)	Gani, R. and S. Leach. 2004. Epidemiological determinants for modeling pneumonic plague outbreaks. Emerging Infectious Dis. 10: 608-614.
B. Objectives and Type of Study	1. purpose noted by study authors: The objective of this paper was to test different approaches for modeling the transmission and infectivity of *Yersinia pestis* outbreaks 2. type: RC, disease transmission
C. Publication Attributes	1. sponsors/affiliations: The Health Protection Agency, United Kingdom (http://www.hpa.org.uk/) 2. peer-review mechanism: peer reviewed journal
D. Data and Study Design	1. type: secondary data derived from several published scientific articles 2. source: several sources of data from well-documented outbreaks 3. extent of data: transmission data were derived from outbreaks occurring between 1907 and 1997 4. sampling plan: NA 5. sample size: number of cases of primary pneumonic plague per outbreak ranged from 5 to 42 6. performance characteristics: NA 7. relevance: high
E. Method/Model/Approach	1. general characteristics: Modeling applied to (rare) infection/outbreak data to predict likelihood for infection that occurred under different conditions 2. specific characteristics: Markov chain models used to predict likelihood for infections following different exposures of susceptible individuals to infected individuals. Models were able generally applicable to predict outcomes under different exposure scenarios 3. assumptions: 1) model assumes that a person, once infected experiences a non-infective latency period followed by a symptomatic infective period. If untreated, the infected person dies. 4. limitations: data for outbreaks were rare. To address different possible transmissability scenarios, probability functions were applied to the data (Poisson and geometric). Model predictions gave fairly good estimates of outcomes. 5. relevance: high

F. Study Conclusions and Extended Applications	1. conclusions supported by the data: risk of secondary infection is lowered by rapid detection of outbreak events and the accurate identification of infected individuals. 2. extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: high 2. representativeness of data: high 3. generalizability or external validity: high 4. soundness of study conclusions or internal validity: high 5. defensibility: high
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	This report offers some real utility in its ability to generate an estimated exposure that may result in plague infection. Somewhat insufficient model documentation to demonstrate viable and credible modeling approaches; the Markov Chain model and other components were not explicitly stated in the report
K. Cross-References	NA

A. Risk Characterization Study Identification (Disease)	Getoor L., J.T. Rhee, D. Koller and P. Small. 2004. Understanding tuberculosis epidemiology using structured statistical models. Artificial Intelligence Med. 30(3): 233-256.
B. Objectives and Type of Study	1. purpose: scientific; examines the use of Bayesian models to analyze tuberculosis epidemiology 2. type: RC, disease transmission
C. Publication Attributes	1. sponsors/affiliations: National Science Foundation Grant (ITR ACI-0082554) , Office of Naval Research contract (N66001-97-C-8554), American Lung Association, National Institutes of Health grant (AI-34238) and National Science Foundation grant (ITR ACI-0082554). 2. peer-review mechanism: scientific journal review
D. Data and Study Design	1. type: study population of tuberculosis patients 2. source: San Francisco Department of Public Health Division 3. extent of data: from 1991-1999; data includes *Mycobacterium tuberculosis* strains and data on contact

	investigations, as well as demographic information for patients. 4. sampling plan: published elsewhere (Small et al., 1994) 5. sample size: 2516 tuberculosis cases, 1879 of which were culture-positive 6. performance characteristics: NA 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: Bayesian network (BN) analysis and statistical relational model (SRM) analysis conducted using the patient data to determine risk factors. 2. specific characteristics: BN model learned using patient data only, with 10 variables included; SRM incorporated same patient data, as well as strains and contact data. The BN model attempts to distinguish between direct and indirect influence. 3. assumptions: data derived from sound study design, selection of variables sound 4. limitations: analysis of the results requires knowledge of tuberculosis, the underlying data, and an understanding of the potential relationships between variables. 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions: the resulting statistical relation model corroborated previously reported findings and revealed several novel associations. The models revealed relationships that may not be apparent using conventional statistical approaches. 2. authors' extrapolations: excellent starting point for generating hypotheses for further investigation.
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: high 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	First half of paper provides methodological overview of Bayesian networks and structured statistical models, including statistical relational models (SRM). Answering queries using SRMs and SRM construction was discussed prior to providing the evaluation of the TB cases. Evaluations based on historical perspective, not current biothreat.
K. Cross-References	NA

A. Risk Characterization Study Identification (Disease)	Grasman, J. 1998. Stochastic epidemics: the expected duration of the endemic period in higher dimensional models. Math Biosci. 152(1): 13-27.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific; Estimating the fraction of vaccinated individuals or otherwise eliminated susceptibles necessary to prevent an infectious disease outbreak. 2. type: RC, disease transmission
C. Publication Attributes	1. sponsors/affiliations: Agricultural University, the Netherlands. 2. peer-review mechanism: scientific journal review
D. Data and Study Design	1. type: NA 2. source: NA 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: NA
E. Method/Model/Approach	1. general characteristics: Analytical approximations to the duration of the endemic period of a stochastic epidemic process are derived, evaluated, and applied to several infectious diseases. 2. specific characteristics: Three analytical, increasingly coarse, approximations to the duration of the endemic period of a stochastic epidemic process (SIR-model) are developed and compared with simulation results from the full stochastic system. Analytical approximations are developed sequentially by 1) dimension reduction and diffusion approximation, 2) Laplace approximation, and 3) elimination of higher order terms. The relative ability of the three approximations to reproduce stochastic simulation results is illustrated for a range of population sizes. The approximations are more accurate for larger populations. The generalization of the approximations to an SIER-model and a spatial (two populations with migration) SIR-model are provided. The expected durations of endemic periods of several SIERl and spatial SIR-models, as estimated by full stochastic simulation, are compared to the final analytical approximation (based on all three approximating steps) for a range of population sizes. The final analytical approximation is applied to several infectious diseases, including Poliomyelitis and Measles. Population size necessary for the approximation to be appropriate is discussed. Approximation can be used to estimate fraction of the population that must be vaccinated or otherwise eliminated from the susceptible to achieve an acceptable epidemic duration. 3. assumptions: SIR- and SIER-models are appropriate to characterize epidemic process.

	4. limitations: Analytical approximations are only appropriate when population sizes are sufficiently large. Sufficient population size depends on parameters of the SIR- and SIER-models. 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: The analytical approximation does well for a range of SIR- and SIER-model parameters. Compared with simulation, the analytical approximation can be numerically evaluated very quickly. 2. authors' extrapolations from the observed data to other populations or conditions: NA
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: high 2. representativeness of data: low 3. generalizability or external validity: high 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	Methods applicable to stopping the spread of infection.
K. Cross-References	NA

A. Risk Characterization Study Identification (Disease)	Ko, G., K.M. Thompson and E.A. Nardell. 2004. Estimation of tuberculosis risk on a commercial airliner. Risk Anal. 24(2): 379-388.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific. To estimate the risk of tuberculous transmission on a typical commercial airliner using a simple one box mode and a sequential box model. 2. type: RC, disease transmission
C. Publication Attributes	1. sponsors/affiliations: University of Texas Health Science Center at Houston, School of Public Health, Houston Texas. Harvard School of Public Health and Harvard Center for Risk Analysis, Boston, MA. Pulmonary Medicine, Cambridge Hospital, and Department of Infectious Diseases and Social Change, Harvard Medical School, Boston, MA. 2. peer-review mechanism: full scientific peer review

D. Data and Study Design	1. type: epidemiological investigations conducted by the CDC and to characterize the pattern of TB transmission on airliners. 2. source: data generated in a CDC study (Kenyon et al., 1996). 3. extent of data: The model was based on a 1996 CDC investigation where 249 people flew in an airliner (Boeing 747-400) with four passenger cabins with an infectious source seated in cabin 4. Cabin four contained 148 seats, however only 8 people occupied seats in that cabin. 4. sampling plan: No detailed information on the seat locations of these 68 passengers in the 148 seat cabin existed so it was assumed that the passengers were evenly distributed throughout the cabin. 5. sample size: 249 passengers on an airliner. 6. performance characteristics: The results of the deterministic one box model and the sequential box model were computed using ExcelK™ (Microsoft). Best Fit™ (Palisade Corp, Newfield, NY) was used to fit the distribution to the epidemiological data, estimate the best fitting parameter using MLE, and perform the goodness-of-fit test. The group performed simulations to characterize the variability of TB risk within the same cabin using @RISK™ (Palisade Corp.) Latin Hypercube Sampling with 20,000 iterations. 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: Two methods were used: a one box model and a deterministic sequential box model to estimate the concentration of infectious Tuberculosis aerosols and the risk of infection. 2. specific characteristics: The one box method assumes an equal concentration of infectious particles (uniform mixing) throughout the airliner cabin and the same risk of Tuberculosis infection for all passengers regardless of their seating locations. In the sequential box model the group modeled the airliner as a series of four passenger cabins, each cabin uniformly mixed within, but potentially differing in concentration from the other three cabins. 3. assumptions: It was assumed that the 68 passengers in the 148 passenger cabin were evenly distributed throughout the cabin since no detailed information on the seat locations of these passengers was available. 4. limitations: The one box model has more limitations given it is very unlikely for all air to be distributed evenly throughout the entire cabin of the aircraft. 5. relevance: high
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: Almost all Tuberculosis risk to the passengers on commercial airliners appears to occur in the same cabin with the infectious Tuberculosis source case, and that within the same cabin the risk appears to decrease exponentially with distance from the source. This indicates that most Tuberculosis cases probably occur within several rows of the Tuberculosis patient and for any given passenger the risks of getting Tuberculosis on a commercial flight remain very small even on long flights. 2. authors' extrapolations from the observed data to other populations or conditions: NA
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA

H. Weight of Evidence	1. robustness of method: high 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	description of most appropriate uses of method for incident-based microbial risk assessment of buildings and water systems: This general method may be used as a model to determine the risk of an individual to an agent dispersed through the air in an enclosed environment, such as an airplane.
K. Cross-References	NA

A. Risk Characterization Study Identification (Disease)	Li, X. and P.A. Rossignol. 1998. Probability model on the use of sentinel animal monitoring for arbovirus. Epidemiol. 9(4): 446-451.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific 2. type: RC, disease transmission
C. Publication Attributes	1. sponsors/affiliations: Washington State University, Oregon State University 2. peer-review mechanism: scientific journal review
D. Data and Study Design	1. type: NA 2. source: NA 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: NA
E. Method/Model/Approach	1. general characteristics: the authors propose statistical models (from the exponential family of distributions) for the relationships between parameters that are used to describe arbovirus transmission from vectors to sentinel

	animals 2. specific characteristics: Poisson distribution for the rate of positive blood sample (i.e., the rate of seroconversion); exponential distribution for estimating the blood sampling frequency required to maintain probability of superinfection (two or more infective bites prior to seroconversion; i.e., prior to detection by positive blood sample) below selected rate; exponential distribution to estimate the number of sentinel animals required to achieve selected number of positive blood samples; formula for maximum likelihood estimate of the vector infection rate (assuming Poisson distribution); exponential distribution to estimate the risk of human infection (assuming hosts have an equal chance of being bitten), and for the number of infections per year; gamma distribution to model the distribution of vector bites on humans if the assumption of equal probability is not valid; suggests an approach for comparing the rate of positive blood test results collected at different times or geographic locations 3. assumptions: arbovirus vectors select hosts randomly or, alternatively, selection follows a gamma distribution 4. limitations: approach does not consider the effect of environmental factors on disease transmission 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: conclusions are based on model, and limited comparison of model predictions to data: if infection rate and biting rate are low, the observed rate of positive blood samples could vary greatly, even with a constant vector density; even if a large number of animals are used, the observed rate of positive blood samples could be 0 or very low; given the preceding conclusions, it may be unrealistic to use sentinel animals to estimate virus transmission intensity, or for early warning of virus transmission 2. extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	1. no data are provided or discussed in detail in this paper; the authors indicate their model is consistent with data gathered by others 2. simple, concise model that could be useful for designing monitoring plan for arbovirus
K. Cross-References	NA

A. Risk Characterization Study Identification (Disease)	Lui, K.J. 1998. Interval estimation of the risk ratio between a secondary infection, given a primary infection, and the primary infection. Biometrics 54(2): 706-711.
B. Objectives and Type of Study	1. purpose: scientific 2. type: RC, disease transmission
C. Publication Attributes	1. sponsors/affiliations: Agency for Health Care Policy and Research Grant R01-HS07161 2. peer-review mechanism: scientific journal review
D. Data and Study Design	1. type: data from literature 2. source: Agresti, 1990 3. extent of data: calves classified according to whether they developed primary pneumonia infection within 60 days of birth, and then again according to whether they developed secondary pneumonia infection within 2 weeks of recovery from the primary infection 4. sampling plan: NA 5. sample size: 156 calves 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: interval estimation of relative risk (RR) between secondary infection and primary infection under three asymptotic closed-form interval estimators (Wald's test statistic, logarithmic transformation, Fieller's theorem) 2. specific characteristics: contingency tables constructed based on probabilities of primary and secondary infections 3. assumptions: different models might be more applicable for large v. small sample sizes 4. limitations: need to use log transformation for small samples 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusion: when probability of primary infection is high ($\geq$0.80), all 3 interval estimators perform well; when probability of primary infection is low (0.2) or medium (0.3-0.5), the interval estimator using the log transformation outperforms the others; the interval estimator using the log transformation is recommended for general use 2. authors' extrapolations: NA
G. Data Gaps and Proposed	1. data gaps: NA

Solutions	2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	Good potential for applying a more developed model to a variety of pathogens, especially those with known characteristics about secondary transmission.
K. Cross-References	NA

A. Risk Characterization Study Identification (Disease)	Masuda, N., N. Konno and K. Aihara. 2004. Transmission of severe respiratory syndrome in dynamical small-world networks. Physical Review 69(3 Pt 1): 031917.
B. Objectives and Type of Study	1. purpose: Scientific; to propose a dynamic network model for SARS epidemic spread. 2. type: RC, disease transmission
C. Publication Attributes	1. sponsors/affiliations: Japan Society for the Promotion of Science and Advanced and Innovational Research Program in Life Sciences, the Japanese government. 2. peer-review mechanism: Journal article
D. Data and Study Design	1. type: theoretical modeling using small-world, scale-free, and 2-dimensional regular lattice networks 2. source: NA 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: NA
E. Method/Model/Approach	1. general characteristics: theoretical simplified spatial model to indicate how interplay between network structure

	and individual factors affects epidemics. 2. specific characteristics: Three types of individuals are modeled: susceptible, infected but not a super spreader (non-SS), and a super spreader (SS). The infected non-SS and SS are modeled with different rates of infection. An infected turns an adjacent susceptible into infected non-SS or SS at assumed parameter values. The parameter values depend on the definition of a SS, the network structure, and the time scales. 3. assumptions: Total mixing of the individuals. 4. limitations: some parameters invalidated by data 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions: A dynamic network model for SARS epidemics was proposed to explain interplay between network structure and individual factors influencing epidemics. Combined effects of superspreaders and their possible tendencies to haunt potentially contagious places, such as hospitals, accounts for amplification and disease spread. 2. authors' extrapolations: To avoid mass transmission in hospitals, treat suspected cases without hospitalizing them. Models such as this can establish strategies for tracing, quarantine, isolation, and regulating social behavior to help control disease spread. Authors note super spreader mechanism also holds for Ebola, measles, and tuberculosis for biological and serological reasons.
G. Data Gaps and Proposed Solutions	1. data gaps: unclear how many parameters are data-derived 2. proposed solutions: collect data from other regions regarding transmission and causation for contact cases
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: low 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	Authors note that SARS seems to fit the pattern of small-world networks associated with human contacts rather than epidemic model of sexually transmitted diseases and computer virus that typically fit scale-free networks. Further, use of small-world networks has fewer unknown parameters than dynamic compartmental models, also successful in explaining observed data and determining reproductive number.
K. Cross-References	NA

A. Risk Characterization Study Identification (Disease)	McKenna, S.A. 2000. Development of a discrete spatial-temporal SEIR simulator for modeling infectious diseases. Albuquerque, NM: Sandia National Laboratories.
B. Objectives and Type of Study	1. purpose: scientific; SEIR (Susceptible, Exposed, Infectious, Recovered) type model to simulate the spatial, as well as temporal, evolution of disease 2. type: RC, disease transmission
C. Publication Attributes	1. sponsors/affiliations: Sandia Corporation, Lockheed Martin 2. peer-review mechanism: NA
D. Data and Study Design	1. type: NA 2. source: NA 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: NA
E. Method/Model/Approach	1. general characteristics: SEIR model concept extended to work on a population of discrete individuals located on a two-dimensional grid 2. specific characteristics: likelihood of exposure for an individual is described as a function (spherical, exponential, and Gaussian likelihood functions are developed in the paper) of proximity to an infectious individual and efficiency of transmission of the disease from the infectious individual 3. assumptions: NA 4. limitations: NA 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusion: spatial variation in the initial levels of susceptibility can drastically affect the spread of a disease 2. authors' extrapolations: SEIR parameters for common diseases or diseases that could be introduced in a terrorist attack can be used to develop the spatial-temporal spread of these specific diseases across a population
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: NA 3. generalizability or external validity: low

	4. soundness of study conclusions or internal validity: high 5. defensibility: high for biothreat agents with person-to-person transmission
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	one possible use would be to discriminate common outbreaks from terrorist attacks
K. Cross-References	NA

A. Risk Characterization Study Identification (Disease)	Mugglin, A.S., N. Cressie and I. Gemmell. 2002. Hierarchical statistical modelling of influenza epidemic dynamics in space and time. Stat. Med. 21: 2703-2721.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific/emergency planning. Development of a spatially descriptive, temporally dynamic hierarchical model that fits data describing spread of infection. 2. type: RC, disease transmission
C. Publication Attributes	1. sponsors/affiliations: US Environmental Protection Agency and Office of Naval Research 2. peer-review mechanism: Peer-reviewed journal
D. Data and Study Design	1. type: Counts of influenza hospital admissions 2. source: Emergency admissions with ICD9 code 487 3. extent of data: Scotland, 1989-1990 4. sampling plan: Data were not collected for this study. Admissions are spatially resolved to the postcode sector. There are 895 postcode sectors in Scotland. 5. sample size: There were about 500 cases in all of Scotland in the winter of 1989-1990. 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: Authors build a hierarchical Bayesian model of Scottish influenza cases by district and week. 2. specific characteristics: The chief purpose of the model is to describe the evolution of an influenza epidemic as a three stage process with stability, growth, and decline states. Influenza admission counts by district and week are modeled as Poisson counts. The expected counts by district and week are modeled as multiplicative deviations from the expected number of influenza admissions in the district. (Expected influenza admissions for

	each district were estimated and considered fixed values based on historical data.) The deviations were modeled in a manner to capture spatial and temporal variability, as well as the systematic effects of covariates (temperature and lags of temperature, which varied by district and week, and a standardized morbidity ratio capturing propensity for sickness, which varied by district). The model postulates spatial and temporal dependence between districts and their neighboring districts via two components, a conditional auto-regressive (CAR) epidemic-forcing term and an auto-regressive (AR(1)) coefficient matrix. 3. assumptions: The onset of an epidemic is assumed to be global, with no spatial heterogeneity. Thus, the spread of infection is captured in the spatial dependence component of the model. 4. limitations: The use of a spatial dependence structure defined by political boundaries arbitrarily affects study results, i.e., changing influenza counts defined over a different geography may change results. The times of epidemic onset and departure are specified a priori and are not determined by the model. Thus, this model is suitable for description of the epidemic but could not be used to forecast an epidemic. 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions: The Bayesian model produces spatially smoothed estimates of relative risk of infection. Relative risk of infection is estimated with less uncertainty when influenza incidence is higher. For this particular influenza epidemic in Scotland, the disease is shown to first appear along a southwest-northeast corridor of high population density that includes Glasgow, Edinburgh, and Dundee. The disease progresses perpendicularly away from the corridor. It dies out first along the corridor of onset and departs last from the eastern coastline. Posterior investigation of the effect of an epidemic onset on eventual relative risk reveals that the effect on relative risk of influenza is spatially heterogeneous with higher risk estimated for two clusters, one north and one south of the high population corridor. The posterior predictive distribution for influenza counts by district and week is examined. This is used to assess what could have happened in this epidemic, i.e., how many influenza admissions there could have been. 2. authors' extrapolations: The authors believe the spatially smoothed estimates of relative risk of infection are more sensible than the rougher estimates produced by looking at standardized morbidity ratios. The authors believe that the posterior predictive distribution could be used for planning for future influenza epidemic hospital bed needs.
G. Data Gaps and Proposed Solutions	1. data gaps: Many persons with influenza do not become sick enough for hospital admission. Thus, the influenza counts do not include these persons. The spatial (postcode sector) and temporal (daily) resolution of the data results in many zero counts. 2. proposed solutions: Hospital influenza admissions are used anyway. The model aggregates hospital influenza admissions to districts and weeks to deal with the sparseness of the data.
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: high

	5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	1. Model can be used to understand the likely spatial and temporal progression of infection based on previous epidemic data. 2. Aggregating the data to districts (56 in Scotland) from postcode sectors (895 in Scotland), may exacerbate issues associated with the definition of spatial dependence in terms of political divisions.
K. Cross-References	NA

A. Risk Characterization Study Identification (Disease)	Nicas, M. and E. Seto. 1997. A simulation model for occupational tuberculosis transmission. Risk Anal. 17(5): 609-616.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific; To develop a simulation model to capture the dynamics of *M tb.* infection and morbidity among hospital employees; also account for secondary sources of infection. 2. type: RC, disease transmission
C. Publication Attributes	1. sponsors/affiliations: Grant No K01-OH00155-01, National Institute for Occupational Safety and Health and California Department of Health Services 2. peer-review mechanism: full journal peer review
D. Data and Study Design	1. type: hypothetical data for simulation 2. source: NA 3. extent of data: NA 4. sampling plan: Stratified by degree of patient contact, i.e., physical separation from patient care, e.g., records clerks; presence in TB patient care areas but no direct patient contact; provision of services directed to TB patients, e.g., physicians, nurses 5. sample size: NA 6. performance characteristics: NA 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: simulation 2. specific characteristics: Complexity added to model in a stepwise fashion; scenarios examined for 5 or 50 TB

	patients admitted annually. Simulations based on 1000 individuals; in first scenario, 600 low risk, 300 medium risk, 100 high risk; in second scenario, 850 high risk, 100 medium risk, 50 low risk. 3. assumptions: Daily infection risk attributed to a given TB patient treated as identical for all members of a risk group, i.e., if two TB patients were in the hospital, daily risks doubled 4. limitations: TB patients may not be admitted in a uniform fashion over time 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: In first scenario, with 5 TB patients per year, expected value is 12.5 occupational infections per year; with 50 TB patients, jumps to 103.7 occupational infections. As expected, fewer occupational infections when fewer staff receive high exposure. Secondary infection rates dependent on how long a diseased worker remains on the job and how many close contacts s/he has. 2. authors' extrapolations from the observed data to other populations or conditions: Model could be used outside of healthcare environments.
G. Data Gaps and Proposed Solutions	1. data gaps: Population based TB cases that are hospitalized is unknown. 2. proposed solutions: None
H. Weight of Evidence	1. robustness of method: high 2. representativeness of data: high 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	model has other applications for pathogens with similar aerosol transmission patterns and virulence mechanisms
K. Cross-References	NA

A. Risk Characterization Study Identification (Disease)	NIOSH. 2001. Exposure and risk assessment for infectious aerosols. Berkeley, CA: National Institute for Occupational Safety and Health. PB2001101415.
B. Objectives and Type of Study	1. purpose: regulatory, future regulatory interest; to develop a quantitative framework for assessing and managing risk of occupational TB transmission in a hospital setting

	2. type: RC, disease transmission
C. Publication Attributes	1. sponsors/affiliations: National Institute for Occupational Safety and Health 2. peer-review mechanism: Report (not specified)
D. Data and Study Design	1. type: epidemiological data on number of TB patients admitted to hospitals annually and number of TB cases among health care workers 2. source: published studies, government datasets 3. extent of data: published information is sparse; study based on available information and a mail questionnaire survey of hospital epidemiologists 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: stochastic 500 simulation model to describe TB infection and disease incidence among a hospital HCW cohort; component reliability analysis of a hospital TB control program to identify the most important control measures 2. specific characteristics: analytical risk model developed to examine cost-efficacy of alternative screening intervals for new HCW infections; source-pathway-receptor engineering construct developed to assess efficacy of alternative control measures (primarily environmental) 3. assumptions: an otherwise healthy individual has a 5% chance of developing disease in first year after infection; a diseased worker remains on the job for three calendar weeks while infectious; a diseased worker has 25 close contacts; close contacts have a 22% chance of being infected 4. limitations: NA 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions: a binary type of patient infectivity generates substantial variability in infection incidence; infection among immunocompromised HCWs causes only a slight increase in incidence of 2º *M. tb* infection and TB disease at the HCW cohort level 2. authors' extrapolations: none stated
G. Data Gaps and Proposed Solutions	1. data gaps: cost of false positive errors in skin testing is not included; daily infection risks could not be extrapolated because of insufficient detail in data 2. proposed solutions: consider false positive skin tests in risk characterization
H. Weight of Evidence	1. robustness of method: high 2. representativeness of data: low

	3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	other applications for modeling pathogens with similar aerosol transmission patterns and virulence mechanisms
K. Cross-References	same study in EA

A. Risk Characterization Study Identification (Disease)	Pascual, M., M. J. Bouma and A. P. Dobson. 2002. Cholera and climate: Revisiting the quantitative evidence. Microbes and Infection 4: 237-245.
B. Objectives and Type of Study	1. purpose: Scientific. Authors developed evidence for climate-cholera interaction with a restriction to the endemic dynamics of cholera in order to identify areas requiring quantitative analysis. 2. type: RC, disease transmission
C. Publication Attributes	1. sponsors/affiliations: Joint Program on Climate Variability and Human Health, NOAA, EPA, NASA, NSF, EPRI, conducted in part at the National Center for Ecological Analysis and Synthesis 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: theoretical epidemiologic model for cholera disease transmission 2. source: NA 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: high
E. Method/Model/Approach	1. general characteristics: mathematical models using 4 differential equations for disease dynamics and climatic influences 2. specific characteristics: state variables, susceptibilities (S), infection (I), fomites (F) (equations described by Codeco, 2000), and water volume (W) (equation described by the author as a modification of the saturation transmission function). A 5th equation was derived to describe the force of infection. Used the equations to

	describe R_o as the basic reproductive number of cholera. 3. assumptions: ”W” was included to consider changes that affect or alter the concentration of the organism which influences infection. 4. limitations: some parameters unvalidated by data 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions: Based on the mathematical model, both increasing temperatures and water volume temper each others’ effects for influencing outbreaks of cholera near water. R_o varies with climatic factors which directly alter the concentration of the pathogen. 2. authors’ extrapolations: The set of differential equations presented could be used in a model to predict the basic reproductive number for cholera and how it is affected by concentration of the organism growth and survival, strain variation, and populations structure.
G. Data Gaps and Proposed Solutions	1. data gaps: unclear how many parameters are data-derived or validated by outbreak data 2. proposed solutions: further studies
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: UN
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	NA

A. Risk Characterization Study Identification (Disease)	Smith, P.J., T.J. Thompson and J.A. Jereb. 1997. A model for interval-censored tuberculosis outbreak data. Stat. Med. 16(5): 485-496.
B. Objectives and Type of Study	1. purpose: scientific; characterize risk of tuberculin skin test as a function of health care workers’ job type, using and comparing simulation with hospital outbreak data. 2. type: RC, disease transmission

C. Publication Attributes	1. sponsors/affiliations: Centers for Disease Control and Prevention (CDC) 2. peer-review mechanism: peer-reviewed by top tier journal
D. Data and Study Design	1. type: epidemiological/observational data for single hospital outbreak of TB 2. source: published studies 3. extent of data: Data limited to one hospital and to seroconversion between 1978 and 1992 4. sampling plan: NA 5. sample size: 260 health care workers 6. performance characteristics: NA 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: Proportional hazards model estimated by simulation (Monte Carlo) and as a member of the family of general linear models (GLM). 2. specific characteristics: Proposed model is an extension of Efron's model for censored survival data. Proposed model is appropriate for longitudinal data. Differentiation between *non-synchronized* and *synchronized interval* censored data, i.e., *synchronized interval* model is appropriate when all persons are measured for seroconversion at the same time for each subject. Data on hospital workers with different levels of risk, based on job type, e.g., nurses, housekeepers (high risk) v. secretaries, etc. Simulation study (500 repetition at 6 sample sizes) performed to estimate bias, mean squared error, and loss of efficiency in estimating treatment effects due to interval-censoring. 3. assumptions: model depends on parametric, non-parametric, and semi-parametric modeling assumptions 4. limitations: population characteristics limited by jobs, length of time of exposure, i.e., length of time working in hospital. 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions: Relative Risk (RR) and probability of infections declined with job proximity to patents; model for interval censored data 11% efficient as compared to model where event times and distributions are known. Bias becomes negligible as same size increases 2. authors' extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: length of employment unknown 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high

	5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	Proportional hazards model is an acceptable starting point to derive GSM for internal censored data, but less effective as time between observations is long.
K. Cross-References	NA

A. Risk Characterization Study Identification (Disease)	Torgerson, P.R. and D.D. Heath. 2003. Transmission dynamics and control options for *Echinococcus granulosus*. Parasitology 127: S123-S158.
B. Objectives and Type of Study	1. purpose: scientific; Summary of developments of mathematical models describing the transmission of the parasite. 2. type: RC, disease transmission
C. Publication Attributes	1. sponsors/affiliations: INTAS, National Institutes for Health (USA), and The National Science Foundation (USA) 2. peer-review mechanism: peer reviewed journal
D. Data and Study Design	1. type: a knowledge of the parasite's biology and observational studies of its epidemiology 2. source: published literature 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: Mathematical models developed to describe the transmission dynamics of *E. granulosus* and to predict epidemiology. 2. specific characteristics: Roberts et al. (1986 and 1987) and Torgerson et al. (2002) derived models to describe the variation of parasite prevalence with the age of the host. A set of four differential equations used for prevalence variation: infected but immune, infected but not immune, not infected and immune, and not infected and not immune. ODE function using a 4^{th} order Runge-Kutta algorithm to integrate the series of differential equations used. In addition, a binomial likelihood function with the ODE function was used to estimate certain

	parameters. 3. assumptions: based on theoretical ideas of parasite-host relationships 4. limitations: available epidemiological data and present theoretical ideas 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions: Based on various epidemiological data, determined various mean time to exposure to dogs and mean survival time of infection of parasites; provided indications of parasite-induced immunity given degrees of infection; was also used to estimate infection pressure in dogs. 2. authors' extrapolations: models could be used to predict outcomes of interventions.
G. Data Gaps and Proposed Solutions	1. data gaps: information for parameterization of the models 2. proposed solutions: none provided
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	May be useful method to test intervention methods.
K. Cross-References	NA

A. Risk Characterization Study Identification (Disease)	Wolleswinkel-van, B.J., N.J. Nagelkerke, J.F Broekmans, et al. 2002. The impact of immigration on the elimination of tuberculosis in The Netherlands: A model based approach. Int. J. Tuberc. Lung Dis. 6(2): 130-136.
B. Objectives and Type of Study	1. purpose: scientific; to determine whether elimination of tuberculosis in Dutch population can be achieved by 2030, taking in to account impact of immigration 2. type: RC, disease transmission
C. Publication Attributes	1. sponsors/affiliations: Royal Netherlands Tuberculosis Association 2. peer-review mechanism: peer-reviewed journal

D. Data and Study Design	1. type: historical data, estimates of future infection rate, estimations of relative risks, population data, immigration information 2. source: annual risk of tuberculosis infection (ARTI) (1910-1979) available from tuberculin surveys, age-specific relative risks of infection estimated based on study by Sutherland and Fayers, annual risk for years 1980-2030 estimated from model using contact rate in Dutch population and incidence of infection calculation, population data obtained from Statistics Netherlands for 1997-2015, past data and projections on first generation immigrants living in Netherlands 3. extent of data: data for Dutch population 1910-2030, four possible scenarios of immigration considered in model 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: life-table model with 4 immigrant scenarios 2. specific characteristics: life-table model used to estimate incidence of tuberculosis in Dutch population cohort; number of infectious cases times contact rate from simple immigration scenarios yielded additional number of newly infected individual in Dutch population of which 14 % assumed to develop primary tuberculosis 3. assumptions: most parameter values accepted from Dye et al. 4. limitations: immigration scenarios underestimated or overestimated the observed number of cases based on different assumptions of uncertain contact rates 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions: tuberculosis as public health problem in Dutch population will have been achieved by 2030 (defined as infection prevalence of less then 1% which continues to decline) but incidence of smear-positive tuberculosis will remain above 1 per million based on all immigrant scenarios explored, proportion of Dutch cases resulting from transmission from a foreign source case expected to become substantial over time, tuberculosis control needs to shift its attention to immigrants to address estimated problem. 2. authors' extrapolations: none
G. Data Gaps and Proposed Solutions	1. data gaps: immigration and tuberculosis incidence 2. proposed solutions: gather more data
H. Weight of Evidence	1. robustness of method: high 2. representativeness of data: low 3. generalizability or external validity: high 4. soundness of study conclusions or internal validity: high

	5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	NA

A.3.2 Other Risk Characterization Methods

Barker, C.M., W.K. Reisen and V.L. Kramer. 2003. California State Mosquito-Borne Virus Surveillance and Response Plan: A retrospective evaluation using conditional simulations. Am. J. Trop. Med. Hyg. 68(5): 508-518. 265

Bemrah N., M. Sanaa, M.H. Cassin, et al. 1998. Quantitative risk assessment of human listeriosis from consumption of soft cheese made from raw milk. Prev. Vet. Med. 37(1-4): 129-145. 267

Brown, M.H., K.W. Davies, C.M.-P. Billon, C. Adair and P.J. McClure. 1998. Quantitative microbiological risk assessment: principles applied to determining the comparative risk of salmonellosis from chicken products. J. Food Protect. 61(11): 1446-1453. 269

Buchanan, R.L., J.L. Smith and W. Long. 2000. Microbial risk assessment: Dose-response relation and risk characterization. Int. J. Food Microbiol. 58: 159-172. 271

Cassin, M.H., G.M. Paoli and A.M. Lammerding. 1998. Simulation modeling for microbial risk assessment. J. Food Protect. 61(11): 1560-1566. 273

Christensen, B., H. Sommer, H. Rosenquist, et al. 2001. Risk assessment on *Campylobacter jejuni* in chicken products. The Danish Veterinary and Food Administration. 275

Crawford-Brown, D. J. and S. Marquez-Nyarko. 1999. Development of an environmental decision support system (EDSS) for comparing drinking water treatment practices and associated health risks. Report No. 323. Chapel Hill, NC: Water Resources Research Institute of The University of North Carolina. 278

FAO/WHO. 2002b. Risk assessments of *Salmonella* in eggs and broiler chickens. Food and Agriculture Organization/World Health Organization. http://www.who.int/foodsafety/publications/micro/salmonella/en/ 281

FAO/WHO. 2004. Risk assessment of *Listeria monocytogenes* in ready-to-eat foods. Food and Agriculture Organization/World Health Organization. http://www.who.int/foodsafety/publications/micro/mra_listeria/en/ 283

Farber, J.M., W.H. Ross and J. Harwig. 1996. Health risk assessment of *Listeria monocytogenes* in Canada. Int. J. Food Microbiol. 30(1-2): 145-156. 285

FDA-CVM. 2001a. The human health impact of fluoroquinolone resistant *Campylobacter* attributed to the consumption of chicken. US Food and Drug Administration Center for Veterinary Medicine. October 18, 2000. Revised: January 5, 2001. http://www.fda.gov/cvm/antimicrobial/Risk_asses.htm 287

FDA/USDA. 2003. Quantitative assessment of relative risk to public health from foodborne *Listeria monocytogenes* among selected categories of ready-to-eat foods. http://www.foodsafety.gov/~dms/lmr2-toc.html 290

Gale, P. 2001. Developments in microbiological risk assessment for drinking water. J. Appl. Microbiol. 91: 191-205. 293

Glass, G.E., J.E. Cheek, J.A. Patz, et al. 2000. Using remotely sensed data to identify areas at risk for hantavirus pulmonary syndrome. Emerging Infectious Dis. 6(3): 238-247. 295

Havelaar, A.H., M.J. Nauta and J.T. Jansen. 2004. Fine tuning food safety objectives and risk assessment. Int. J. Food Microbiol. 93: 11-29. 297

Hope, B.K., A.R. Baker, E.D. Edel, et al. 2002. An overview of the *Salmonella enteritidis* risk assessment for shell eggs and egg products. Risk Anal. 22(2): 203-218. 299

Hurd, H.S., S. Doores, D. Hayes, et al. 2004. Public health consequences of macrolide use in food animals: A deterministic risk assessment. J. Food Protect. (67)5: 980-992. 301

Lindqvist, R. and A. Westoo. 2000. Quantitative risk assessment for *Listeria monocytogenes* in smoked or gravad salmon and rainbow trout in Sweden. Int. J. Food Microbiol. 58(3): 181-196. 303

Marks, H.M., M.E. Coleman, C.-T. J. Lin and T. Roberts. 1998. Topics in microbial risk assessment: Dynamic flow tree process. Risk Anal. 18(3): 309-328. 305

Medema, G.J., W. Hoogenboezem, A.J. van der Veer, et al. 2003. Quantitative risk assessment of *Cryptosporidium* in surface water treatment. Wat. Sci. Technol. 47(3): 241-247. 308

Nagelkerke N., S. Heisterkamp, M. Borgdorff, et al. 1999. Semi-parametric estimation of age-time specific infection incidence from serial prevalence data. Stat. Med. 18(3): 307-320. 310

Nauta, M.J., E.G. Evers, K. Takumi and A.H. Havelaar. 2001. Risk assessment of Shiga-toxin producing *Escherichia coli* O157 in steak tartare in the Netherlands. RIVM report 257851003. http://www.rivm.nl/bibliotheek/rapporten/257851003.html 312

Perz, J.F., F.K. Ennever and S.M. LeBlancq. 1998. *Cryptosporidium* in tap water. Comparison of predicted risks with observed levels of disease. Am. J. Epidemiol. 147(3): 289-301. 314

Petterson, S.R., N.J. Ashbolt and A. Sharma. 2001. Microbial risks from wastewater irrigation of salad crops: A screening-level risk assessment. Wat. Environ. Res. 72 (6): 667-672. 316

Ross, T. and J. Sumner. 2002. A simple spreadsheet-based food safety risk assessment tool. Int. J. Food Microbiol. 77(1-2): 39-53. 318

Rusin, P.A., J.B. Rose, C.N. Haas, et al. 1997. Risk assessment of opportunistic bacterial pathogens in drinking water. Rev. Environ. Contam. Toxicol. 152: 57-83. 320

Sanaa, M., L. Coroller and O. Cerf. 2004. Risk assessment of listeriosis linked to the consumption of two soft cheeses made from raw milk: Camembert of Normandy and Brie of Meaux. Risk Anal. 24(2): 389-399. 322

Stewart, C.M., B. Cole and D.W. Shaffner. 2003. Managing the risk of staphylococcal food poisoning from cream-filled baked goods to meet a food safety objective. J. Food Protect. 66(7): 1310-1325. 324

Strachan, N.J., D.R. Fenlon and I.D. Ogden. 2001. Modelling the vector pathway and infection of humans in an environmental outbreak of *Escherichia coli* O157. FEMS Microbiol. Lett. 203(1): 69-73. 326

Teunis, P.F.M., G.J. Medema, L. Kruidenier, et al. 1997b. Assessment of the risk of infection by *Cryptosporidium* or *Giardia* in drinking water from a surface water source. Wat. Res. 31(6): 1333-1346. 328

USDA/FSIS. 2003. Risk assessment for *Listeria monocytogenes* in deli meats. US Department of Agriculture/Food Safety and Inspection Service. www.fsis.usda.gov/OPPDE/rdad/FRPubs/97-013F/ListeriaReport.pdf 331

Wein, L.M., D. Craft and E.H. Kaplan. 2003. Emergency response to an anthrax attack. PNAS 100(7): 4346-4351. Supporting Text on www.pnas.org 333

Westrell, T., O. Bergstedt, T.A. Stenstrom and N.J. Ashbolt. 2003. A theoretical approach to assess microbial risks due to failures in drinking water systems. Int. J. Environ. Health Res. 13: 181-197. 335

Whiting, R.C. and R.L. Buchanan. 1997. Development of a quantitative risk assessment model for *Salmonella enteritidis* in pasteurized liquid eggs. Int. J. Food Microbiol. 36: 111-125. 337

A. Risk Characterization Study Identification (other)	Barker, C.M., W.K. Reisen and V.L. Kramer. 2003. California State Mosquito-Borne Virus Surveillance and Response Plan: A retrospective evaluation using conditional simulations. Am. J. Trop. Med. Hyg. 68(5): 508-518.
B. Objectives and Type of Study	1. purpose: scientific; Evaluation of California Mosquito-Borne Virus Surveillance and Response Plan model for western equine encephalomyelitis (WEE) and St. Louis encephalitis (SLE) 2. type: RC
C. Publication Attributes	1. sponsors/affiliations: Office of Global Programs, National Oceanic and Atmospheric Administration 2. peer-review mechanism: peer-review journal
D. Data and Study Design	1. type: historical, environmental 2. source: historical climate data, historical mosquito abundance and virus activity data, total precipitation, total runoff, and mean temperatures, female vector mosquito abundance, vector infection rates, sentinel chicken seroconversion rates, equine disease cases, human disease cases, degree of urbanization in areas where virus detected 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: repeatable and reproducible, adequate methods, complete study 7. relevance: low
E. Method/Model/Approach	1. general characteristics: California Mosquito-Borne Virus Surveillance and Response Plan (the Plan) 2. specific characteristics: The Plan quantifies the focal risk for WEE and SLE cases and provides appropriate response recommendations using bi-weekly or cumulative methods. The semi-quantitative plan assessed risk of WEE or SLE in a geographical area, assigning each of the risk factors (see source above) a risk score between 1 and 5. The values were averaged to obtain an overall risk on a scale of 1 to 5. 3. assumptions: NA 4. limitations: NA 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions: Risk estimates were calculated with several different methods (e.g., cumulative temp., rainfall, and runoff levels over a season vs. biweekly assessments based on the previous half month) and were compared with actual historical data for cases of WEE and SLE in several California locations. Methods which best predicted risk differed for WEE and SLE. 2. authors' extrapolations: none
G. Data Gaps and Proposed Solutions	1. data gaps: Poor sensitivity of current passive case detection system, including case recognition, laboratory confirmation, and reporting. Missed cases or delays in diagnoses would artificially reduce the risk level during epidemic or enzootic periods. Risk based on perceived lack of human cases during the epidemic would have

	underestimated the actual risk and mostly likely limited the emergency response. 2. proposed solutions: vigilance in compiling cases
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	NA

A. Risk Characterization Study Identification (other)	Bemrah N., M. Sanaa, M.H. Cassin, et al. 1998. Quantitative risk assessment of human listeriosis from consumption of soft cheese made from raw milk. Prev. Vet. Med. 37(1- 4): 129-145.
B. Objectives and Type of Study	1. purpose: scientific; To quantify risk of exposure to *L. monocytogenes* from consumption o f soft cheese made from raw milk from a public health perspective. 2. type: RC
C. Publication Attributes	1. sponsors/affiliations: Epidemiology and Animal Health Management Laboratory, Alfort Veterinary School, Maisons-Alfort, France 2. peer-review mechanism: peer-reviewed journal
D. Data and Study Design	1. type: data published on the different sources of milk contamination (environment and mastitis) and bacterial growth. 2. source: published literature 3. extent of data: quantitative data of raw milk contamination and growth in cheese; Each one of the exposure variables is discussed and the range of values provided in the literature is discussed. Variables include those associated with milk production, cheese processing, consumption, and a brief review of the data for dose response. Distributions of all variables summarized in this paper. 4. sampling plan: NA

	5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: to estimate the risk of infection by *L. monocytogenes* in a single serving 2. specific characteristics: Risk estimated using the results of the dose response. The Weibull-Gamma equation that predicts the percentage of the population responding to a particular dose was used. Vulnerability of the hosts were included in the evaluation based on population percentages for high and low-risk groups. Individual annual cumulative risk calculated as a combination of the probability of illness linked to the consumption of one cheese serving and the number of servings per year. Probability of illness calculated using the DR equation times the probability that the consumed strains were virulent. Milk and cheese contamination derived using 10000 iterations using Latin Hypercube sampling implemented with @RISK software. 3. assumptions: made for milk production (number of farms, herd size, and milk volume per cow); cheese making process (did not account for contamination during transportation of raw milk, cheese making, ripening, distribution, and in households); consumption considered similar in susceptible and general populations; triangular distributions used when exact distributions unknown; Poisson distribution used for organisms distribution in homogeneous liquid; dose response same for different groups in the population; proportion of virulent strains was 0.1. 4. limitations: data retrieved were more than six years old and did not account for recent improvements in hygiene; dose response data. 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions: Concentrations of *L. monocytogenes* in milk before cheese processing ranged from 0-32.68 CFU/ml. The probability of contaminated milk was 67%. Model predicted that 99% of the concentrations before cheese processing would be less than 14 CFU/ml. Estimated probability of consuming a contaminated cheese serving was 65.3%. Risk of illness varied from 0 to 3.73×10^{-4}. Risks provided for high risk and low risk populations. Number of expected deaths for each group also provided. 2. authors' extrapolations: can be used to study the influence on morbidity and mortality of realistic management options; useful tool for cheese manufacturers as well as those in public health practices.
G. Data Gaps and Proposed Solutions	1. data gaps: indicated by the assumptions that had to be used in E3. 2. proposed solutions: research needed for areas having no available data
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility: low

I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	NA

A. Risk Characterization Study Identification (other)	Brown, M.H., K.W. Davies, C.M.-P. Billon, C. Adair and P.J. McClure. 1998. Quantitative microbiological risk assessment: principles applied to determining the comparative risk of salmonellosis from chicken products. J. Food Protect. 61(11): 1446-1453.
B. Objectives and Type of Study	1. purpose: future regulatory interest; to use existing mathematical models as a Quantitative Risk Assessment (QRA) tool to provide transparent, model-based QRA to allow effective risk communication within food manufacturing business 2. type: RC
C. Publication Attributes	1. sponsors/affiliations: Unilever Research Laboratory 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: surveys conducted in the EU and theory 2. source: experimental data, published and unpublished studies cited 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: mathematics given in sufficient detail to use on any suitable platform; analytical and statistical methods appear to be adequate; authors state that accuracy could be improved by using better numerical integration method 7. relevance: low
E. Method/Model/Approach	1. general characteristics: estimate of risk of salmonellosis due to undercooked chicken consumption, obtained by integration with respect to time, microbial distribution, and distance fo heat penetration into product 2. specific characteristics: dose response characterized by Beta-Poisson distribution (Todd 1978 cited; no details provided); what-if scenarios testable with sliders 3. assumptions: infection encompasses all degrees of human response; microbial survivors of heat treatment are infectious

	4. limitations: dose-response assessment precision limited by increment size used in the integration; imprecise nature of infection function does not allow for accurate predictions 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions: authors show change in individual parameters required to reduce risk from one per million servings to one per ten million servings and adverse consequences of parameter changes; risk of infection is very sensitive to "product and cooking attributes"
G. Data Gaps and Proposed Solutions	1. data gaps: dose response of children 2. proposed solutions: use larger dataset for dose response in children in dose response assessment; apply method to data from other sources and studies; use smaller increments in dose-response assessment integration to improve precision
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: low 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	same study in EA

A. Risk Characterization Study Identification (other)	Buchanan, R.L., J.L. Smith and W. Long. 2000. Microbial risk assessment: Dose-response relation and risk characterization. Int. J. Food Microbiol. 58: 159-172.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific and future regulatory; Continued examination of food safety through risk assessment. 2. type: RC
C. Publication Attributes	1. sponsors/affiliations: Food and Drug Administration 2. peer-review mechanism: scientific peer review
D. Data and Study Design	1. type: review and dosimetry method development cited from various sources

	2. source: NA 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: dosimetry 2. specific characteristics: Three compartments (1) gastric acidity barrier (Buchanan et al., 1998a); (2) attachment/infectivity; and (3) morbidity/mortality. 3. assumptions: For animal models, assumes mechanism of infection same as humans, the animal's physiological and immune response similar to humans, and relationship same for infectivity, morbidity and mortality as humans. 4. limitations: dose-response data from human volunteer feeding studies generally conducted only on healthy adult males, use non-life threatening diseases, are given to small numbers of test subjects, and use relatively high doses. 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions: risk characterizations may require dosimetry and more mechanistic studies to address variations in disease triangle effects (host, pathogen, matrix) and interactions 2. authors' extrapolations: Alternative models may be required used for toxigenic microorganisms.
G. Data Gaps and Proposed Solutions	1. data gaps: data pertinent to entire population and host-pathogen interactions 2. proposed solutions: mechanistic model (see E above)
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: low 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	Chen et al., 2003

A. Risk Characterization Study Identification (other)	Cassin, M.H., G.M. Paoli and A.M. Lammerding. 1998. Simulation modeling for microbial risk assessment. J. Food Protect. 61(11): 1560-1566.
B. Objectives and Type of Study	1. purpose: scientific and potential future regulatory interest; Paper describes general approach for risk modeling using Monte Carlo simulation, with the main objective of improving tools available to decision makers. 2. type: RC, review of usefulness of probabilistic risk assessment models
C. Publication Attributes	1. sponsors/affiliations: International Life Sciences Institute-North America Technical Committee on Food Microbiology 2. peer-review mechanism: peer-reviewed journal
D. Data and Study Design	1. type: *E. coli* 0157:H7 in ground beef used as an example for the model simulations; however, this information not the focus. 2. source: published literature 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: NA
E. Method/Model/Approach	1. general characteristics: Process Risk Model (RPM) using Monte Carlo simulations to describe variability and uncertainty in many parameters 2. specific characteristics: A model using Monte Carlo simulations conducted with @Risk or Crystal Ball. Results are probability distributions of model outcomes that reflect underlying nature of the phenomena. The distributions generated this way converge with increasing interactions toward the distributions that would otherwise be generated analytically. Rank correlation is provided to quantify the strength of the association between two variables. A probabilistic model for *E. coli* 0157:h7 in hamburgers was used to illustrate the utility of such models to identify research needs and predict the risk reduction effects of various practices to control prevalence and numbers of microbial agents in food. 3. assumptions: probability distribution of parameters 4. limitations: Results are predictions, not observations; limited to the amount of data available for use as input parameters; limited in general applicability and do not approach true complexity. 5. relevance: medium
F. Study Conclusions and Extended	1. conclusions: sensitive to the specific probability distributions; results are predictions, not observations

Applications	2. authors' extrapolations: can provide method to make more effective decisions about foodborne pathogen risk reduction, proposed control strategies can be initially evaluated using the model as a predictive tool.
G. Data Gaps and Proposed Solutions	1. data gaps: information about consumer preferences is lacking, or information is inaccurate 2. proposed solutions: obtain data
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: NA 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	Can be useful to evaluate "what if" scenarios under various mitigating practices
K. Cross-References	NA

A. Risk Characterization Study Identification (other)	Christensen, B., H. Sommer, H. Rosenquist, et al. 2001. Risk assessment on *Campylobacter jejuni* in chicken products. The Danish Veterinary and Food Administration.
B. Objectives and Type of Study	1. Purpose: scientific; risk assessment as a part of strategy to control pathogenic micro-organism of current and future regulatory interest 2. Type: RC
C. Publication Attributes	1. sponsors/affiliations: Danish Veterinary and Food Administration, Institute of Food Safety and Toxicology, Division of Microbiological Safety 2. peer-review mechanism: Government document that did not specify peer review process
D. Data and Study Design	1. type: survey of consumption data and prevalence of pathogen (*Campylobacter jejuni, C. jejuni*) in chicken products; dose-response investigations in volunteers; seasonal variation data 2. source: published studies and EU government data sets. 3. extent of data: large databases for consumption and prevalence in chicken products (Danish, chilled, frozen, and imported); sparse data for dose-response of pathogen of interest in humans and sparse data set for pathogen of interest in other animals (cattle, pigs, turkeys); insufficient data related to time/temperature variations

	through slaughter house processes, storage, distribution, and food handling 4. sampling plan: broilers chickens (carcasses) analyzed for presence and prevalence of the pathogen; modeling: baseline model defined as the processing of fresh carcasses from both the positive and negative flocks (the within flock prevalence is either 100% or 0%); scenario analysis, where alterations to the baseline are studied by changing one or more model parameters (temperature, level of contamination). 5. sample size: for slaughter house model often more than 40,000 broilers 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: Penner serotyping and pulsed field gel electrophoresis of restriction enzyme-produced DNA fragments on isolates of human and veterinary cases, raw milk, chicken and untreated water (from a restricted geographical area) (Hudson et al.,1999); model estimating concentration of *Campylobacter* cells on chicken carcasses, and probability of illness (look at variations by age/sex groups; hygiene level). 2. specific characteristics: various statistical procedures used including semi-quantitative method; Bartlett's test for testing the quality of variances; one-way variance analysis for testing whether there is significant difference between flocks; D normal distribution for input concentration on broilers at entrance to slaughterhouse; estimation of the variance component to estimate changes in *Campylobacter* concentration throughout plant processes; sensitivity analysis**;** simulation methods include @RISK analysis on Excel platform; Zhao et al. (1998) reported in level *of cross-contamination* from contaminated raw chicken to a cutting board and from the cutting board to the salad. 3. assumptions: *Campylobacter* contaminated chicken are assumed to be an important source of human campylobacteriosis; number of Campylobacter in salad or chicken serving is assumed to be Poisson distributed; 4. limitations: uncertainty about the true estimates of the exposure levels and probabilities of illness and the relationship between dose and response, uncertainty related to the behavior of the person who prepares the meal, uncertainty of the impact of undercooking (due to insufficient heat during cooking processes) and the impact of cross-contamination during food preparation or to other food products via raw chicken liquids or direct contact. 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: Cross-contamination in private kitchens from *Campylobacter* infected chickens seems to be an important source of infection. Simulation showed a linear correlation between the flock prevalence and the probability of illness. 2. extrapolations: N/A
G. Data Gaps and Proposed Solutions	1. identification of data gaps: for exposure assessment [concentration of *Campylobacter* during the slaughter processes from entrance of slaughtered broiler flocks to final packaged chilled/frozen product; the effect of different scalding temperatures; the effect of chilling method (water chilling versus air chilling); different packing methods (e.g. packing in modified atmosphere); the actual cross-contamination between positive and negative flocks and within positive flocks during the different slaughter house processes], and for dose-response

	assessment [whether probability of illness is dependent on ingesting frozen or chilled chicken; survival of Campylobacter on other food products; cross-contamination to other food products; number of people eating contaminated food products] 2. proposed solutions: N/A
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: high 3. generalizability or external validity: high 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	Useful for consideration as a potential food contaminant. Published data from countries other than Denmark used in the slaughter house model since only few Danish data exist.
K. Cross-References	NA

A. Risk Characterization Study Identification (other)	Crawford-Brown, D. J. and S. Marquez-Nyarko. 1999. Development of an environmental decision support system (EDSS) for comparing drinking water treatment practices and associated health risks. Report No. 323. Chapel Hill, NC: Water Resources Research Institute of The University of North Carolina.
B. Objectives and Type of Study	1. purpose: scientific and future regulatory; to present the development of a software tool to aid decision-makers involved in analyzing the various risks associated with disinfection treatment options for drinking water. 2. type: RC
C. Publication Attributes	1. sponsors/affiliations: Water Resources Research Institute of the University of North Carolina 2. peer-review mechanism: NA
D. Data and Study Design	1. type: water quality survey data 2. source: survey of Brown Water Treatment Plant 3. extent of data: data from one representative plant were used; water quality data included temperature, pH, total organic carbon, bromide, ammonia, UV absorbance, and raw water concentrations of *Giardia* and *Cryptosporidium*; information on treatment system characteristics was also collected.

	4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: high
E. Method/Model/Approach	1. general characteristics: competing risks of cancer due to exposure to disinfection by-products and health effects due to waterborne pathogens are estimated using models to predict formation of disinfection by-products and inactivation of waterborne microbes (based on plant water quality measurements and treatment system characteristics), human exposure factors, and dose-response models for carcinogenicity of disinfection by-products and health effects from *Giardia* and *Cryptosporidium*. 2. specific characteristics: formation of disinfectant by-products is predicted from plant water quality measurements and treatment system characteristics using algorithms modified from the EPA (1993) WTP (Water Treatment Plant) model that were developed from chlorination experiments (Harrington, 1992) conducted to measure formation of disinfection by-products under various treatment regimens; inactivation (disinfection) kinetics of microorganisms (*Giardia* and *Cryptosporidium*) are modeled using Chick-Watson first order kinetics, first order kinetics in which disinfectant concentration declines with time, and/or a two-population first order kinetics model (weighted by user), with inputs being the initial concentration of *Giardia* cysts and *Cryptosporidium* oocysts in the water and treatment system characteristics; human exposure factors for water ingestion and body weight are used to calculate doses of disinfection by-products and microbes associated with drinking water concentrations; dose-response parameters for risk of cancer from the disinfection by-products were estimated by fitting experimental data for the individual chemicals to linear (one hit), quadratic (two hit), or beta-Poisson models (weighted by user) by least squares regression; dose-response parameters for risk of health effects from *Giardia* and *Cryptosporidium* were estimated by fitting experimental data for the individual microbes to linear (one hit), linear two-population, or beta-Poisson models (weighted by the user) by least squares regression; inputs can be point estimates or user-specified distributions, and if distributions are specified, probabilistic evaluation (Monte Carlo, Median Latin hypercube, or Random Latin hypercube) can be performed to obtain probability distributions for exposure and risk estimates. 3. assumptions: the exposure models assume that each day is a statistically independent exposure to the water with an identical distribution of pathogens; risk of cancer from disinfectant by-products is assumed to be additive, with no synergistic or antagonistic interactions 4. limitations: the current model is limited to predicting exposure and cancer risk for chloroform, bromoform, bromodichloromethane, chlorodibromomethane, dichloroacetic acid, and trichloroacetic acid following water treatment by chlorination and chloramination, although the model can be expanded to include other by-products and treatment methods; the current model is limited to predicting exposure and risk of adverse health effects for *Giardia* and *Cryptosporidium*, although the model can be expanded to include other waterborne pathogens 5. relevance: high
F. Study Conclusions and Extended Applications	1. conclusions: estimated health risks due to *Giardia* and *Cryptosporidium* at the Brown Water Treatment Plant may exceed recommended levels; the model provides a flexible tool to predict drinking water exposure to *Giardia*

	and *Cryptosporidium* and associated health risk under various water treatment regimens 2. authors' extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: high 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility: high
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	The report describes a software tool that can be used to compare competing risks associated with drinking water treatment. Essentially the tool embeds several models in a flow chart to assist the analyst to evaluate the consequences of treatment decision. A similar approach to this could be of value in developing a tool to assess microbial risks to water supplies, food or buildings.
K. Cross-References	same study in EA, DR

A. Risk Characterization Study Identification (other)	FAO/WHO. 2002b. Risk assessments of *Salmonella* in eggs and broiler chickens. Food and Agriculture Organization/World Health Organization. http://www.who.int/foodsafety/publications/micro/salmonella/en/
B. Objectives and Type of Study	1. purpose: scientific and future regulatory interest; compile currently available information relevant to risk assessment of *Salmonella* in eggs and broiler chickens; identify data gaps; develop example risk assessment models; consider efficacy of some risk management interventions 2. type: RC
C. Publication Attributes	1. sponsors/affiliations: FAO/WHO 2. peer-review mechanism: Technical Report initiated in 1999 and reviewed several times during preparation and after completion through consultations and by an extensive list of selected reviewers and members of the public during a public comment period

D. Data and Study Design	1. type: non-typhi human feeding trials, surrogate pathogen, and outbreak information 2. source: published literature 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: Monte Carlo simulation model predicting risk of salmonellosis for hypothetical exposures to contaminated servings of eggs and broilers, linked to a dose-response model 2. specific characteristics: “generic” risk assessment model “deliberately configured and parameterized NOT to represent any one country 3. assumptions: contamination of hens and eggs occurs at constant frequency independent of host, bacterial strain, and environmental, seasonal, regional, and demographic factors; flocks of hens and eggs are homogeneous; contamination is random and independent of hen/egg age and other host, bacterial, or environmental factors; DR relationship for surrogate pathogens representative of pathogens of interest; secondary transmission not major factor for salmonellosis; safety factor sufficient to characterize normal and more susceptible subpopulations 4. limitations: influential parameters based on expert opinion or assumption unvalidated 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions: risk of salmonellosis predicted from 2 illnesses per 10 million to 45 illnesses per 10 million shell egg servings; 2. authors’ extrapolations: the general framework and analysis may be adapted to a country or region with development and inclusion of country-specific data for model inputs
G. Data Gaps and Proposed Solutions	1. data gaps: prevalence and levels of the pathogen from representative national surveys; preparation and consumption patterns among consumers, validation of predictive microbiology models for growth and survival; including times and temperatures of storage; characterization and quantification of the impact of the food matrix effects and host-pathogen interactions and virulence factors and their effect on the likelihood of illness; biology of host-pathogen interaction for hens (and humans) 2. proposed solutions: conduct targeted research; elicit expert opinion; generate more rigorous dose-reconstruction analysis for outbreaks and epidemiological data; targeted research on mechanisms of pathogenesis and virulence that affect human dose-response relationships
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: low 3. generalizability or external validity: NA

	4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	generic model based on pooled data from multiple sources and countries of origin and assumptions may not support rigorous science-based modeling; 2004 update of US work cited by authors in draft form (USDA/FSIS 1998) is more relevant for compendium review upon release anticipated in October
J. Reviewer Comments	NA
K. Cross-References	NA

A. Risk Characterization Study Identification (other)	FAO/WHO. 2004. Risk assessment of *Listeria monocytogenes* in ready-to-eat foods. Food and Agriculture Organization/World Health Organization. http://www.who.int/foodsafety/publications/micro/mra_listeria/en/
B. Objectives and Type of Study	1. purpose: scientific and future regulatory interest; undertaken at request of the Codex Committee on Food Hygiene for scientific advice as a basis for future development of guidelines. 2. type: RC
C. Publication Attributes	1. sponsors/affiliations: FAO/WHO 2. peer-review mechanism: Technical Report reviewed several times during preparation and after completion through consultations and by an extensive list of selected reviewers and members of the public during a public comment period
D. Data and Study Design	1. type: epidemiological data and detailed exposure assessment 2. source: FDA/FSIS risk assessment (2003) 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: risk of severe listeriosis was estimated for hypothetical exposures to contaminated servings of milk, ice cream, fermented meat, and fish, linked to a simplified dose-response model also dependent on EA data (FDA/USDA, 2003)

	2. specific characteristics: Monte Carlo simulation in Analytical using Latin hypercube sampling typically for 32,000 interations; "what if" scenarios, using different consumption rates, sensitive subpopulations, prevalence data, etc. 3. assumptions: serving size and frequency of consumption by sub-population; distribution of the pathogen in foods; the percentage of individuals susceptible to severe *L. monocytogenes* infections; the appropriateness of the exponential model for describing the pathogen's dose-response relation in humans in the dose range of interest; dose-reconstruction for numbers of *L. monocytogenes* consumed by ill and asymptomatic cases; accuracy of limited survey and outbreak data on the annual rate of severe listeriosis cases. 4. limitations: EA largely hypothetical; DR dependent on US EA model; accuracy of the estimate of the r-value is dependent on the size and inclusiveness of the population being considered; available contamination and epidemiological data do not permit objective unequivocal choice of r based on scientific evidence and theory 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions: mean estimated cases predicted per 10 million people per year and per million servings, respectively, were: 9.1 and 0.005 for milk; 0.012 and 0.000014 for ice cream; 0.46 and 0.021 for smoked fish; and 0.00066 and 0.00000025 for fermented meats; interventions to prevent high levels of contamination would have large impact on number of cases; relative susceptibility of humans with underlying conditions that compromise immunity appear to be approximately 8 to 3,000 times more sensitive to the pathogen than normal healthy people without an underlying medical condition; controlling frequency and magnitude of contamination and growth important 2. authors' extrapolations: what-if scenarios useful to evaluate the likely impact of different risk management options
G. Data Gaps and Proposed Solutions	1. data gaps: Dose-response data from human volunteer studies with *L. monocytogenes* or from volunteer studies with a surrogate pathogen do not exist. 2. proposed solutions: There is a clear need in future outbreaks for exposure levels, immune status of the patients and strain characteristics to all be investigated so that these dose response models can be further refined and validated.
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: low 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: high 5. defensibility: high
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	provides various "what if" scenarios to answer regulatory issue concerns, demonstrating utility of methods to

	address relative risks for specific scenarios of concern
K. Cross-References	same study in EA, DR; FDA/USDA, 2003 in EA, DR, RC

A. Risk Characterization Study Identification (other)	Farber, J.M., W.H. Ross and J. Harwig. 1996. Health risk assessment of *Listeria monocytogenes* in Canada. Int. J. Food Microbiol. 30(1-2): 145-156.
B. Objectives and Type of Study	1. purpose: scientific, regulatory; major steps used in the formulation of a health risk management for *L. monocytogenes* in foods are discussed. 2. type: RC
C. Publication Attributes	1. sponsors/affiliations: Health Canada, Food Directorate 2. peer-review mechanism: Full Scientific Journal Review
D. Data and Study Design	1. type: Computational analysis 2. source: published studies and computational analysis 3. extent of data: few data points 4. sampling plan: none reported 5. sample size: none reported 6. performance characteristics: none reported 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: substantial level of consistency between computed and reported data 2. specific characteristics: The impact of growth on the probability of illness of *L. monocytogenes* is predicted. Incidence expressed mathematically as: $cpu_1[nP_{I,N} +(1-n)P_{I,H}]=I_{u2}$, where p= incidence, c=consumption, u_1=proportion virulent, n=proportion with normal risk exposed, $P_{I,N}$=average probability of illness for normal risk group, $P_{I,H}$=average probability of illness for high risk group, I=annual incidence, and u_2=rate of under reporting. 3. assumptions: none reported 4. limitations: none reported 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: The incidence of listeriosis is expressed symbolically by considering the incidence of *L. monocytogenes* in soft and semi-soft cheese. Economic and social consequences of estimated risks are costed to be around 111 to 126 million dollars for human listeriosis cases.

	2. authors' extrapolations from the observed data to other populations or conditions: None reported
G. Data Gaps and Proposed Solutions	1. data gaps: none identified 2. proposed solutions: none
H. Weight of Evidence	1. robustness of method: low, *L. monocytogenes* is not on the EPA list of biological threat agents of concern. 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: low 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	Useful for predicting ID 10 and ID 90 (dose causing illness in 10 and 90% of population) in normal and high risk populations; useful for predicting average probability of illness
K. Cross-References	same study in EA, DR; Farber and Peterkin, 1991; Roberts, 1989; Todd, 1989

A. Risk Characterization Study Identification (other)	FDA-CVM. 2001a. The human health impact of fluoroquinolone resistant *Campylobacter* attributed to the consumption of chicken. US Food and Drug Administration Center for Veterinary Medicine. October 18, 2000. Revised: January 5, 2001. http://www.fda.gov/cvm/antimicrobial/Risk_asses.htm
B. Objectives and Type of Study	1. purpose: future regulatory interest. 2. type: RC
C. Publication Attributes	1. sponsors/affiliations: Food and Drug Administration. Center for Veterinary Medicine (FDA-CVM) 2. peer-review mechanism: report
D. Data and Study Design	1. type: Estimated future number of reportable cases to the CDC's active surveillance system extrapolated from present FoodNet catchment sample area data of number of culture confirmed cases reported in a given year. 2. source: Published data and government sources. 3. extent of data: CDC obtained large data sets through regional active surveillance, surveys and case control studies, which were used to extrapolate national data for the risk characterization model 4. sampling plan: random 5. sample size: large, e.g. 3,884 *Campylobacter* cultured-confirmed cases in 1999 used for extrapolating the

	model's estimated data set 6. performance characteristics: Extensive statistics used in the data analysis and the risk assessment model are provided. 7. relevance: high
E. Method/Model/Approach	1. general characteristics: The model was run for 10,000 iterations to produce relative frequency plots and statistics. It was run for 300 iterations to produce points on spider plots sufficient in number to provide stable means. All models used Latin Hypercube sampling from distributions below. 2. specific characteristics: Gamma distributions for expected observable reportable cases, beta for expected total number of cases, uniform and beta for resistant *Campylobacter* cases attributable to chicken and treated with fluoroquinolone, and beta for quantity of resistant *Campylobacter*-contaminated chicken consumed. A sensitivity analysis has been performed on the risk assessment model to determine which parameters are contributing to the model output's total uncertainty. 3. assumptions: The model assumes that the presence of resistant *Campylobacter* on the animal carcass was due to antimicrobial drug use and that the FoodNet catchment populations are representative of the US population. The model also assumes that resistant bacteria pass through the food supply, infect humans and are treated in the same manner as susceptible bacteria. A complete list of assumptions with associated discussions are provided in the appendix B of the report. 4. limitations: The model has limited ability to include inter-individual variability, stochastic variability, and uncertainty as compared to a traditional farm-to-fork risk characterization, thus increasing necessary assumptions incorporated in the model. A complete list of limitations with associated discussions are provided in the appendix B of the report. 5. relevance: high
F. Study Conclusions and Extended Applications	1. conclusions: this risk assessment has quantitatively demonstrated that resistance development in bacteria from food-producing animals presents a risk to human health. 2. authors' extrapolations: Although the FDA-CVM model described in this report is not an attempt at a full microbial food safety risk assessment, it can be used to predict future human health impact by resistant *Campylobacter* prevalence in poultry.
G. Data Gaps and Proposed Solutions	1. data gaps: Additional studies to define the rate at which people with campylobacteriosis seek care would be helpful and would provide a more accurate estimate, and incomplete knowledge of the sensitivity and specificity of culturing specimens for *Campylobacter* exists. Also, data are not currently available on the distribution ratio between susceptible and resistance *Campylobacter* on a carcass but would be extremely useful for risk characterization. Further, the data describing rates or cases of invasive disease seeking care, requests for diagnostics tests, and the sensitivity of diagnostics procedure, such as blood culture, are not available. More data gaps are provided in detail in the appendix B of the report. 2. proposed solutions: The model as it stands provides a quickly and continuously updateable method of estimating the current human health impact. There is considerable uncertainty in estimating the ratio K(res) (i.e.,

	mean number of resistant *Campylobacter* cases from chicken/amount of resistant *Campylobacter*-contaminated chicken consumed) because of imperfect data, but further data and more years of monitoring would improve this estimate.
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: high 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	1. Useful for risk characterization of threat scenarios in which *Campylobacter*-contaminated chicken is the vehicle. 2. Useful precedent for future risk characterization models regarding bacterial infections. 3. Innovative modeling approach but needs to be verified against traditional modeling methods.
K. Cross-References	NA

A. Risk Characterization Study Identification (other)	FDA/USDA. 2003. Quantitative assessment of relative risk to public health from foodborne *Listeria monocytogenes* among selected categories of ready-to-eat foods. http://www.foodsafety.gov/~dms/lmr2-toc.html
B. Objectives and Type of Study	1. purpose: Future regulatory. Systematically examine available data and information to estimate relative risks (serious illness and death) associated with different ready-to-eat food categories contaminated with *L. monocytogenes.* 2. type: RC
C. Publication Attributes	1. sponsors/affiliations: US Department of Health and Human Service, Food and Drug Administration's Center for Food Safety and Applied Nutrition (DHHS/FDA/CFSAN) in collaboration with US Department of Agriculture's Food Safety and Inspection Service (USDA/FSIS). 2. peer-review mechanism: Two reviews of previous drafts of the model and its underlying assumptions conducted by the National Advisory Committee on Microbiological Criteria for Foods; draft risk assessment also made available for public comment (6-month period)
D. Data and Study Design	1. type: comparative risk; predicted annual servings at various contamination levels over all 23 food categories

	linked with mouse dose-response model and adjusted for large differences in human susceptibility for three populations of concern 2. source: published and unpublished studies; government and industry databases 3. extent of data: some food categories with sufficient and some with sparse data; murine and human dose-response data extensive but conflicting; some associations between food commodities causing illness weak or inconsistent 4. sampling plan: NA 5. sample size: large for some variables, sparse for others 6. performance characteristics: NA. 7. relevance: low
E. Method/Model/Approach	1. general characteristics: Monte Carlo simulation linking predicted outputs of EA and DR. 2. specific characteristics: a) EA used 2 dimensional Monte Carlo Simulation (100,000 variability and 300 uncertainty iterations); DR scalling factor adjusted so sum of murine DR model and predicted doses from EA equaled CDC estimates for annual cases of listeriosis; DR used 2 dimensional Monte Carlo Simulation (100,000 variability and 300 uncertainty iterations) and 1 dimensional (4,000 uncertainty iterations) for each food category by selecting one of the 300 dose bins from EA. Qualitative ranking for relative risk of each of 23 food categories determined for each of 4,000 simulations. b) RC output analyzed: by nonparametric analysis of variance (Kruskal-Wallis test) followed by multiple comparison procedures for per serving and per annum risks; and by cluster analysis to objectively identify similar groups of food categories considering both predicted relative risk rankings per serving and per annum. c) “What if” scenarios developed to address risk management concerns. 3. assumptions: contamination in 23 food categories accounted for all human listeriosis cases in US; expert opinions and assumptions used in EA and DR valid 4. limitations: data sparse for many variables, though available body of evidence is extensive and well presented 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions: analysis supported five risk designations for the 23 food categories: a) very high risk (deli meats and frankfurters (not reheated)); b) high risk (pate, unpasteurized and pasteurized milk, smoked seafood, high fat dairy products, soft unripened cheese); c) moderate risk (cooked crustaceans, deli salads, fermented sausages, frankfurters (reheated), fresh soft semi-soft, and soft ripened cheeses, fruits, vegetables); d) low risk (preserved fish, raw seafood); and e) very low risk (cultured milk products, hard cheese, ice cream, processed cheese). 2. authors’ extrapolations: “what if” scenarios demonstrated importance of five factors related to exposure assessment for ready-to-eat foods and potential control points for interventions or risk mitigation strategies: amount and frequency of consumption; frequency and levels of pathogen; growth potential in food; storage temperature; duration of storage prior to consumption. A variety of foods will need to be considered to control listeriosis with some requiring more attention.

G. Data Gaps and Proposed Solutions	1. data gaps: Data on consumer storage practices was not generally available 2. proposed solutions: Storage times based on expert judgement and USDA recommended practices.
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: high 5. defensibility: high
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	Interesting study begun in 1999 and completed after multiple rounds of peer review and public comment; extensive and useful discussion of rationale for extrapolations and assumptions; large interest nationally and internationally in pathogen, largely due to ubiquitous distribution, ecological niche and physiological advantage of growth under refrigeration conditions; approach sensitive to the nuances of consumption and microbial growth as they affect the final exposure; general approach for relative ranking well considered, potential for indirect application to incident based risk assessment for biothreat agents
K. Cross-References	same study in EA, DR

A. Risk Characterization Study Identification (other)	Gale, P. 2001. Developments in microbiological risk assessment for drinking water. J. Appl. Microbiol. 91: 191-205.
B. Objectives and Type of Study	1. Purpose: develop microbiological risk assessment models for pathogenic agents in drinking water, primarily *Cryptosporidium parvum*, rotavirus, and Bovine Spongiform Encephalopathy (BSE). 2. RC
C. Publication Attributes	1. sponsors/affiliations: Wrc-NSF, Ltd., Buckinghampshire, UK 2. peer-review mechanism: peer reviewed journal
D. Data and Study Design	1. type: data primarily derived from previously published articles. 2. source: Gale and Stanfield (2000) (*Cryptosporidium*), Haas et al. (1996) (*Cryptosporidium*), DuPont, et al. (1995) (*Cryptosporidium*), Ward et al. (1996) (rotavirus) and Gale (1998) (BSE). Data on surrogate organisms (*Bacillus* spores) were conducted at the sponsoring organization's facility.

	3. extent of data: data appear to be well described and appropriately captured for use in this report 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: different models applied to predict the exposure of populations to three rare pathogens that may be present in water supplies. 2. specific characteristics: Poisson and negative binomial distribution models were used to generate exposure and negative exponential, Beta-Poisson and log-probit models used to generate dose response scenarios. 3. assumptions: Model assumptions were generally sound, with two exceptions. First, the exposure data did not usually fit typical exposure models very well, and second, surrogate particulates (*Bacillus* spores) were used to model the behavior of *Cryptosporidium* oocysts. The latter relationship is undescribed. 4. limitations: The review discussed the differences between infection occurring via oral exposures to infections that occur by injection. The latter are irrelevant to the objective of the paper (combined infectivity from ingestion of pathogens in drinking water) 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: For risk assessment of *Cryptosporidium* infection, it appears that the use of Poisson log normal and Poisson distributions are of the same quality for predicting infections, but that the log-probit dose response curve is more representative than a Poisson response. It appears that there is little or no support for an interaction between infectious agents in the likelihood of being infected by one or more of the agents. Protective immunity is an important consideration when evaluating the likelihood for infection from *Cryptosporidium* oocysts 2. extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: significant data gaps were reported for the estimation of BSE infection through the consumption of drinking water 2. proposed solutions: the authors suggest that risk assessment models for BSE concentrate on pathway barriers in the infection as opposed to biomedical barriers, the latter of which have considerable uncertainty
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: high 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from	NA

Compendium	
J. Reviewer Comments	This paper provides good information regarding the need for use of the correct modeling approaches for describing the likelihood for exposure or infection (e.g., Poisson and negative binomial distribution models were used for exposure assessment modeling, and negative exponential, Beta-Poisson and log-probit models were used for dose response modeling); exposure data did not fit typical distribution data. Conclusions drawn from the analysis of these data therefore need to be interpreted with caution
K. Cross-References	NA

A. Risk Characterization Study Identification (other)	Glass, G.E., J.E. Cheek, J.A. Patz, et al. 2000. Using remotely sensed data to identify areas at risk for hantavirus pulmonary syndrome. Emerging Infectious Dis. 6(3): 238-247.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific; to test hypothesis that the 1993 hantavirus pulmonary syndrome (HPS) outbreak could be attributed to environmental conditions and increased rodent populations caused by unusual weather in 1991-1992. A retrospective epidemiological approach to risk assessment. 2. type: RC
C. Publication Attributes	1. sponsors/affiliations: CDC, US EPA, NASA 2. peer-review mechanism: Scientific journal article
D. Data and Study Design	1. type: retrospective epidemiologic analysis performed as a case-control study 2. source: monthly precipitation data from the US National Oceanic and Atmospheric Administration's National climatic Data Center; archived Landsat Thematic Mapper images recorded mid-June 1992 3. extent of data: 30 sites with confirmed cases of hantavirus pulmonary syndrome 4. sampling plan: two cases excluded due to inability to confirm proper geographic site or site of likely exposure. Controls of 170 people with different residential addresses were randomly selected. 5. sample size: NA 6. performance characteristics: NA 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: odds ratios of the environmental characteristics were used to estimate the population's relative risk for HPS. 2. specific characteristics: elevation was dichotomized at the median elevation for case and control sites. Logical

	regression analysis to identify the best combination of Thematic Mapper bands and environmental variables associated with hantavirus pulmonary syndrome. The logistic model was evaluated with the Deviance and the Hosmer-Lemeshow goodness of fit statistics for deciles of risk. Sensitivity and specificity was evaluated by creating a Receiver Operator Characterization function. 3. assumptions: cased in the study represent all cases, controls represent the general population, and the disease is rare. 4. limitations: NA 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: preliminary analyses show a good relationship between hantavirus pulmonary syndrome risk predicted from satellite imagery and *P. maniculatus* population abundance (r=0.92). 2. authors' extrapolations from the observed data to other populations or conditions: General assumption to assume a relationship between climate variability and infectious outbreaks, few studies have evaluated if presumed relationship actually exists. This study indicates that if these relationships do occur, they are modulated by a number of poorly understood ecological and social conditions that require substantial detailed studies.
G. Data Gaps and Proposed Solutions	1. data gaps: broad regions of moderate to high risk areas did not relate to vegetation index and the logistic regression model did not perform well. 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: low 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	description of most appropriate uses of method for incident-based microbial risk assessment of buildings and water systems: Not applicable to buildings or water systems
K. Cross-References	NA

A. Risk Characterization Study Identification (other)	Havelaar, A.H., M.J. Nauta and J.T. Jansen. 2004. Fine tuning food safety objectives and risk assessment. Int. J. Food Microbiol. 93: 11-29.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific, regulatory, future regulatory interest, etc. 2. type: RC
C. Publication Attributes	1. sponsors/affiliations: National Institutes for Public Health and the Environment, Food and Non-food Authority, The Netherlands (RIVM) 2. peer-review mechanism: peer reviewed journal
D. Data and Study Design	1. type: published data for *E. coli* O157:H7 in steak tartare, epidemiologic data from Japanese outbreak 2. source: extensive documentation of data in Nauta et al., 2001 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: high
E. Method/Model/Approach	1. general characteristics: developed tiered approach (simple deterministic model, simple stochastic model accounting for variability, more complex stochastic model accounting for variability and uncertainty) to define relationship between quantitative microbial risk assessment and food safety objective (FSO) for “tolerable” risk of illness; RC example developed predicting *E. coli* O157:H7 illness in scenarios depicting consumption of contaminated steak tartare servings 2. specific characteristics: explanations/derivations provided for calculations to develop tiered models and their relationships with an assumed FSO 3. assumptions: for generating P-D equivalence curve (linear approximation of dose-response model; linear approximation for relationship between probability of infection per serving and incidence of infection in population; number of annual servings consumed by population; prevalence and mean dose per contaminated serving); additional assumptions for risk assessment model documented in Nauta et al., 2001 4. limitations: suggested approach for controversial topic intended to continue and clarify international deliberations of complex nature before utility of approach to decision makers can be demonstrated 5. relevance: high
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: approach more consistent with variability and uncertainty associated with microbial risk assessment requires new operational definition for FSO 2. extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: NA.

	2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: high 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: high 5. defensibility: high
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	approaches applicable to incident based approaches for water or buildings
K. Cross-References	Nauta et al., 2001 in EA, DR, RC

A. Risk Characterization Study Identification (other)	Hope, B.K., A.R. Baker, E.D. Edel, et al. 2002. An overview of the *Salmonella enteritidis* risk assessment for shell eggs and egg products. Risk Anal. 22(2): 203-218.
B. Objectives and Type of Study	1. purpose noted by study authors: regulatory, future regulatory interest; to establish baseline risk of foodborne illness from *Salmonella enteritidis* (SE), to identify and evaluate potential risk mitigation strategies, to identify data gaps related to future research efforts 2. type: RC
C. Publication Attributes	1. sponsors/affiliations: USDA, Food Safety and Inspection Service 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: national public health surveillance by CDC; human clinical data for shigellosis, salmonellosis cited in report 2. source: published studies and government datasets and expert opinion 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low

E. Method/Model/Approach	1. general characteristics: model built of 5 separate modules in Excel spreadsheet to generate baseline results 2. specific characteristics: Monte Carlo simulation performed with @Risk comprised 1,000 iterations; each iteration performed calculations with randomly selected values from each distribution within model using Latin Hypercube sampling; Public Health Outcomes module calculates number of human illnesses resulting from exposure to meals containing varying levels of SE per serving, links exposure to SE with adverse health outcomes of morbidity and mortality that may arise from ingestion of SE bacteria; uses Pascal distribution to estimate mean number of cases/year for comparison of baseline risk assessment model and public health surveillance 3. assumptions: susceptible subpopulation estimated to consist of 20% of US population; shigellosis dose-response model is representative of salmonellosis 4. limitations: static model that does not incorporate possible changes in SE over time as either host, environment, or agent factors change; data limited or non-existent for many variables; model does not yet separate uncertainty from inherent variability of the system; Public Health Outcomes module does not evaluate economic costs of illness and economic costs and benefits of mitigation activities; model limited to describing SE illnesses caused by consumption of eggs internally contaminated with SE, does not account for other sources of human SE illness in US 5. relevance: medium; data is of medium relevance, describes directly aspects needed for incident based scenario modeling for fate and transport for foodborne hazards
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: predicted average risk is 3.5 SE illnesses per 1 million egg-containing servings per year; mitigation elasticity >1 only when separate mitigations were combined 2. authors' extrapolations from the observed data to other populations or conditions: a policy directed solely at one segment of farm-to-table continuum will be less effective than a more broad-based approach
G. Data Gaps and Proposed Solutions	1. data gaps: epidemiology of SE on farms, bacteriology of SE in eggs, human behavior in food handling and preparation; neither distribution for illnesses predicted by baseline model or from public health reporting can be verified 2. proposed solutions: more research in these areas is needed
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: low 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	summary of draft risk assessment (1998) updated and expanded in 2003; revision unavailable for compendium

	review as USDA is addressing peer review comments
K. Cross-References	same study in EA

A. Risk Characterization Study Identification (other)	Hurd, H.S., S. Doores, D. Hayes, et al. 2004. Public health consequences of macrolide use in food animals: A deterministic risk assessment. J. Food Protect. (67)5: 980-992.
B. Objectives and Type of Study	1. purpose: scientific; to conduct a risk assessment for human illness from *Camplobacter* spp. or *Enterococcus faecium* attributable to consumption of contaminated poultry, pork, or beef from animals treated with a macrolide-class antibiotic 2. type: RC
C. Publication Attributes	1. sponsors/affiliations: Elanco Animal Health, Indianapolis, IN 2. peer-review mechanism: full scientific peer review
D. Data and Study Design	1. type: the probabilities or frequencies were based on available experimental data 2. source: published studies and government data sets 3. extent of data: large data sets 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: Several pathway of events leading to the risk of foodborne human illness with a resistant organism due to antibiotic treatment of food animals have been assessed. 2. specific characteristics: Several nodes or events (nine) have been modeled. For each event, the likely probabilities or frequencies were modeled based on available data. When numbers were uncertain, a more conservative, or higher risk estimate was used. 3. assumptions: (a) Resistance determinants (RzD) must move from the intestinal or fecal material in the treated animal and contaminate the carcass, rinse fluids and neighboring carcasses during slaughter and processing operations. (b) 100% of the 2.3kg poultry, if contaminated, was assumed to produce contaminated infective servings. (c) A single macrolide treatment was assumed to be equivalent to long-term feeding for growth promotion, thereby inflating the estimated effects on some animals exposed to the macrolides. 4. limitations: (a) Limited to only two macrolides; (b) commodities limited to swine, poultry, and non-dairy beef

	cattle; (c) independent assessment of “at-risk” population (e.g., young, old, or immuno-compromised) was not undertaken. 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions: Use of tylosin and tilmicosin in food animals presents a very low risk of human treatment failure. 2. authors’ extrapolations: probability of contamination is extrapolated to be less than 1 in 10 million for *Campylobacter*-derived and approximately 1 in 3 billion for *E. faecium*-derived risk.
G. Data Gaps and Proposed Solutions	1. data gaps: none 2. proposed solutions: none
H. Weight of Evidence	1. robustness of method: high 2. representativeness of data: high 3. generalizability or external validity: high 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	method applicable only to certain risk types (e.g., macrolide-treated animals that are used for food consumption)
K. Cross-References	NA

A. Risk Characterization Study Identification (other)	Lindqvist, R. and A. Westoo. 2000. Quantitative risk assessment for *Listeria monocytogenes* in smoked or gravad salmon and rainbow trout in Sweden. Int. J. Food Microbiol. 58(3): 181-196.
B. Objectives and Type of Study	1. purpose noted by study authors: Scientific; To develop a quantitative risk assessment model in which the exposure and risk of acquiring listeriosis from consumption of contaminated fish were estimated. 2. type: RC
C. Publication Attributes	1. sponsors/affiliations: National Food Administration, Uppsala, Sweden 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: Prevalence data and concentration data for *L. monocytogenes* in fish from a number of surveys. Consumption (i.e., serving size) data for cold cuts and salmon. Two dose response models for *L. monocytogenes*

	from published sources were also applied. 2. source: Prevalence and concentration data from 6 surveys. Consumption data based on two studies. Dose response data and models from Farber et. al. (1996) and Buchanan et al. (1997). 3. extent of data: For prevalence, a cumulative distribution assuming a minimum and maximum prevalence of 1 and 25%; For concentration data, two surveys with different detection limits used to describe a cumulative distribution assuming minimum and maximum level of 1 and 10^6 cfu g^{-1}, respectively. Consumption data ranged from 50 to 175 g based on servings for cold cut meats and specific salmon products. The distribution for serving sizes was described by a modified triangular distribution. Dose response models were based on epidemiological data and assumptions. 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: Model used to estimate probability of illness per serving and to calculate the annual cumulative risk based on weekly or monthly exposures, and an annual number of predicted listeriosis cased in Sweden. Excel spreadsheet-based, incorporating Monte Carlo simulations to evaluate uncertainty and variability. 2. specific characteristics: using Latin Hypercube sampling, until the convergence criteria were met (<1.5% change or 10,000 iterations) in the @RISK® 3.5.1 Software. Cumulative risk calculated using: $CR=1-(1-P_{ill})^n$ or binomial distribution. 3. assumptions: according to central limit theorem. Thus, the probability of illness was approximated by a normal distribution with the same mean and standard deviation as the parent distribution. 4. limitations: Growth or inactivation of pathogen not addressed in model 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: The use of point estimates for risk is inappropriate. Assumptions in absence of data lead to large uncertainties in simulations of risk. 2. extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: prevalence and concentration of *L. monocytogenes* in the specific fish products, dose response data, and quantitative information on the proportion of virulent strains 2. proposed solutions: gather more quantitative data
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: low

	5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	same study in EA, DR

A. Risk Characterization Study Identification (other)	Marks, H.M., M.E. Coleman, C.-T. J. Lin and T. Roberts. 1998. Topics in microbial risk assessment: Dynamic flow tree process. Risk Anal. 18(3): 309-328.
B. Objectives and Type of Study	1. purpose: scientific, future regulatory interest 2. type: RC
C. Publication Attributes	1. sponsor/affiliations: USDA Food Safety and Inspection Service 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: experimental data for growth and decline of pathogen and dose-response for related surrogates administered in human clinical trials; survey data for consumption data and prevalence of pathogens in ground beef; outbreak investigation data for initial densities of pathogen 2. source: published studies and government datasets 3. extent of data: large databases for consumption and prevalence in ground beef; adequate experimental studies for growth and decline of pathogen; sparse data for initial densities of pathogen in ground beef; no data for dose-response of pathogen of interest in humans and inadequate dataset for pathogen of interest in animals (rabbits); no data on frequency for scenarios of time/temperature incubation throughout production, distribution, and food handling 4. sampling plan: factorial design for bacterial growth studies; 3-day food diary for CSFII; random and targeted sampling for FSIS prevalence survey; 5. sample size (number of observations by treatment): 12,000 observations for consumption in CSFII database (USDA Continuing Survey of Food Intake by Individuals, 1989, 1991); 184 growth curves for pathogen in culture media (ARS Pathogen Modeling Program); 38 ground beef patties for cooking study (Juneja et al., 1997); 9,821 ground beef samples in FSIS database for prevalence (FSIS, www.fsis.usda.gov/OA/topics/o157.htm#3) ; 6 ground beef samples for initial density (Johnson et al.,

	1995; Doyle personal communication, 1996); 266 human volunteers administered one of three strains of *Shigella* (Levine et al., 1973; Dupont et al., 1969; Dupont et al., 1972) 6. performance characteristics: limited statistical results (mean or geometric mean and confidence limits for prevalence in ground beef; Most Probable Number or MPN assuming perfect method for quantitation of pathogen in ground beef 7. relevance: some high
E. Method/Model/Approach	1. general characteristics: various statistical procedures, including analysis of variance and seemingly unrelated regression (SUR) with variance/covariance matrices to address variability and uncertainty; model for simple stochastic birth process for growth of pathogen before and after cooking; non-threshold and threshold beta Poisson dose-response models for shigellosis; discrete modeling of scenarios of exposure for consumers of rare, medium, and well-done hamburgers for baseline, temperature abuse, and intervention models; Monte Carlo simulation using distributions below 2. specific characteristics: Burr Type XII for consumption of ground beef; beta for prevalence in ground beef; log/t-(7df) for initial density of pathogen in ground beef; multivariate normal for expected relative growth of pathogen in ground beef; normal for expected relative decline of pathogen in ground beef; negative binomial for likelihood of growth; logit p(D), assumed normal for beta Poisson dose-response model for shigellosis; Chi-square for between species and experiment variances for dose-response model 3. assumptions: available data for exposure assessment and dose-response assessment sufficiently representative for healthy adult consumers of 114-gram hamburger meals prepared outside the home to rare, medium, or well-done states; available data insufficient to define explicitly farm-to-fork exposure assessment (growth and decline) for population of US consumers; threshold dose-response models merit consideration 4. limitations: weak dose-response model based on *Shigella* as a weak potential surrogate pathogen; invasive mechanism of pathogenesis inconsistent with non-invasive agent of interest (*E. coli* O157:H7) 5. relevance: high; methods for development and use of defined scenarios for selected exposure and dose-response conditions could be very useful for incident-based microbial risk assessment of buildings and water systems
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: magnitude of differences in annual estimates of illness strongly influenced by limitations of the data as evidenced by large differences between mean and median estimates; threshold of only three pathogen cells surviving cooking associated with 1,000-fold lower annual illness rate than non-threshold model for consumers of hamburgers cooked at recommended temperature 2. extrapolations: rate of illness per million meals extrapolated to population of consumers using mean

	and median estimates (11,000 and 45 annual illnesses estimated from consuming hamburgers prepared away from home)
G. Data Gaps and Proposed Solutions	1. identification of data gaps: for exposure assessment (verification of binomial distribution for pathogen survival of cooking; test of independence of survival, infectivity, and initial density per serving; continuous modeling of growth and decline using thermal heat transfer equations; validation of predictive microbiology models in ground beef) and for dose-response assessment (ability of small numbers of pathogens, particularly those surviving cooking, to cause illness; appropriateness of shigellosis (invasive pathogen) as surrogate for colitis from O157:H7 (non-invasive attaching and effacing lesions); functional form of dose-response model, including thresholds unlikely to cause illness) and for risk characterization (fractions of annual US consumption for rare, medium, and well-done hamburgers prepared at home and away from home, with time-temperature histories from production, distribution, and food handling) 2. proposed solutions: limited scenarios defined and linked with alternative surrogate dose-response models
H. Weight of Evidence	1. robustness of method: high 2. representativeness of data: high 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	1. useful for scenario analysis for two listed bacterial threat agents as potential contaminants of food and water 2. acknowledges limitations of the available data and offers insights for risk management
K. Cross-References	same study in EA, DR; Cassins et al., 1998 in EA, DR, RC

A. Risk Characterization Study Identification (other)	Medema, G.J., W. Hoogenboezem, A.J. van der Veer, et al. 2003. Quantitative risk assessment of

	Cryptosporidium in surface water treatment. Wat. Sci. Technol. 47(3): 241-247.
B. Objectives and Type of Study	1. purpose: scientific; regulatory 2. type: RC
C. Publication Attributes	1. sponsors/affiliations: Collaborative Research Programme (BTO) of the water companies in The Netherlands 2. peer-review mechanism: scientific journal review
D. Data and Study Design	1. type: water survey data and exposure factors for the exposure assessment; dose-response data for the dose-response assessment 2. source: for the exposure assessment, collected survey data for two water sources and three treatment facilities in The Netherlands and used published data for exposure factors; for the dose-response assessment, data were taken from the literature (Ockhuysen et al., 1999; Teunis, personal communication) 3. extent of data: water survey data comprised 1) concentrations of *Crytosporidium* in raw waters and 2) removal efficiency of treatment systems (obtained by monitoring removal of spores of sulphite-reducing clostridia [SRC] under full-scale conditions); published data were used for consumption of unheated drinking water in The Netherlands; dose-response data were from 3 strains of *C. parvum* of the bovine genotype; human clinical data for two strains 4. sampling plan: source water sampled each month for a year (for two case studies) and sampled each week for a year (for the third case study) 5. sample size: NA 6. performance characteristics: NA 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: risk of infection calculated for three case studies 2. specific characteristics: for all three case studies, the point estimate of exposure was fed into the dose-response model to estimate risk of infection; for one case study, a distribution of expected exposures was found by Monte Carlo analysis in which statistical distributions fit to the data for *Crytosporidium* concentrations in raw water (negative binomial), removal of SRC during treatment (beta binomial), and consumption of drinking water (log normal) replaced point estimates, and was fed into the dose-response model to derive a distribution of risk estimates 3. assumptions: NA 4. limitations: NA

	5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions: quantitative risk assessment can be used in tiered approach; point estimates of risk may be sufficient when the risk estimate is above or below required safety level; statistical techniques can be used to determine distribution of risk when risk estimate is close to the regulatory level. 2. authors' extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: high 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	Teunis et al., 1999 in EA, DR

A. Risk Characterization Study Identification (other)	Nagelkerke N., S. Heisterkamp, M. Borgdorff, et al. 1999. Semi-parametric estimation of age-time specific infection incidence from serial prevalence data. Stat. Med. 18(3): 307-320.
B. Objectives and Type of Study	1. purpose: scientific; To estimate age and time specific incidence with proportional hazards models from a series of prevalence surveys about immune responses, using tuberculosis as an example. 2. type: RC
C. Publication Attributes	1. sponsors/affiliations: National Institute of Public Health, Netherlands 2. peer-review mechanism: peer-reviewed journal
D. Data and Study Design	1. type: statistical modeling of survey data

	2. source: TB surveys of school children (data used as an example for the model) 3. extent of data: NA 4. sampling plan: Survey from 1966-1973 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: semi-parametric proportional hazards model 2. specific characteristics: birth year and sex used as covariates 3. assumptions: test assumption that force of infection remains constant over time 4. limitations: deals only with limited population 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusion: proportional hazards models applies to the cohort and age specific incidence density (hazard rate), with year of birth as a covariate. 2. authors' extrapolations: generalizability limited to data that are not both left and right censored
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	Method useful, but not applied to EPA priority agent
K. Cross-References	NA

A. Risk Characterization Study Identification (other)	Nauta, M.J., E.G. Evers, K. Takumi and A.H. Havelaar. 2001. Risk assessment of Shiga-toxin producing *Escherichia coli* O157 in steak tartare in the Netherlands. RIVM report 257851003. http://www.rivm.nl/bibliotheek/rapporten/257851003.html
B. Objectives and Type of Study	1. purpose: scientific; future regulatory interest 2. type: RC
C. Publication Attributes	1. sponsors/affiliations: Directory Board of RIVM, Netherlands 2. peer-review mechanism: NA
D. Data and Study Design	1. type: data from literature 2. source: published and unpublished studies, and expert opinion from a workshop conducted on 30 Jan 2001 at RIVM Bilthoven for exposure assessment; Shinagawa, 1997 (Japanese) for dose-response assessment 3. extent of data: for exposure assessment, extensive sets of data from multiple sources on prevalence and concentration of Shiga-toxin producing *E. coli* O157 in cattle at the farm, slaughterhouse, and retail, food consumption in the Netherlands, and food handling processes; for dose-response assessment, stool samples were collected from 842 children and 43 teachers following an outbreak of Shiga-toxin producing *E. coli O157* at an elementary school in Morioka city, Japan in Sept 1996, and food samples were collected from a meal that was preserved for two weeks 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: high
E. Method/Model/Approach	1. general characteristics: Quantitative microbiological risk assessment (QMRA) of Shiga-toxin producing *E. coli O157* in steak tartare in the Netherlands conducted using the Modular Process Risk Model concept 2. specific characteristics: probability distributions of exposure for several exposure scenarios obtained from the exposure assessment were linked with models from the dose-response assessment to estimate risk of infection and illness due to Shiga-toxin producing *E. coli* O157 in steak tartare in the Netherlands; the food pathway is modeled as a series of 9 steps starting with animals at the farm and ending with consumption of steak tartare; although they occur throughout the entire pathway, growth and inactivation are modeled only at three stages along the food pathway - during the time between carcass halving and carcass trimming, during storage after tartare production, and during preparation

	of tartare patties - due to lack of critical information (e.g., process time, temperature) for other stages of the pathway; model parameters were estimated for two different types of slaughterhouses, two different types of butchers, three different patty preparation styles (raw, medium, well done), and three different age classes of consumers; model parameters estimated as distributions rather than point estimates to the extent possible; Monte Carlo simulations (up to 50,000 iterations each) were run for the various exposure scenarios to derive distributions of expected exposures; exponential and hypergeometric models used for dose-response assessment; in the exponential model, there is a constant non-zero risk of infection associated with each pathogen; in the hypergeometric model, the risk of infection from an individual pathogen is described by a beta distribution to take into account variation in virulence of pathogens and susceptibility of children, and parameters are estimated by a Markov Chain Monte Carlo algorithm 3. assumptions: 55% of infected people take ill 4. limitations: NA 5. relevance: high
F. Study Conclusions and Extended Applications	1. conclusions: predicted illness rate of 8 per 100,000 person-years in the Netherlands, which is high in relation to epidemiological data; risk estimates highly uncertain due to data gaps in the exposure model; intervention at the farm or at slaughter would be more efficient way to reduce health risks than intervention at the consumer stage 2. authors' extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: high 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility: high
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	same study in EA, DR

A. Risk Characterization Study Identification (other)	Perz, J.F., F.K. Ennever and S.M. LeBlancq. 1998. *Cryptosporidium* in tap water. Comparison of predicted risks with observed levels of disease. Am. J. Epidemiol. 147(3): 289-301.
B. Objectives and Type of Study	1. purpose: scientific study with future regulatory interest 2. type: RC
C. Publication Attributes	1. sponsors/affiliations: National Institutes of Health (International Collaborative Infectious Disease Research Program) 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: average tap water intake, infectivity data, and epidemiological data for cryptosporidiosis outbreaks in Las Vegas, NV (1994) and for tap water-related outbreaks in New York, NY (1995) 2. source: published studies and government data 3. extent of data: Several published studies and government reports on *Cryptosporidium* outbreaks are used as background; modeling compared to one dataset. 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: A risk assessment model employing a hybrid approach combining multiplicative components with Monte Carlo analysis. 2. specific characteristics: The model consists of two parts. The first part predicts the incidence of *Cryptosporidium parvum* infection from tap water (exposure-infection model). The second part predicts the probability that cases will be reported (infection-outcome model). The second part includes an exponential infectivity model developed with dose-response data from an infectivity experiment with human volunteers, and employment that modeled the sequence of events from infection to case reporting as series of conditional probabilities. Different infectivity parameters were used for subpopulations varying in susceptibility (e.g., adults and children with or without AIDS). 3. assumptions: A low occurrence of *Cryptosporidium parvum* (1/1000 liters) in tap water is assumed. It is assumed that cryptosporidiosis cases usually will not be reported unless they are debilitating. The analysis assumes that cryptosporidiosis cases in AIDS patients will tend to be more debilitating than in

	the normal population and that such cases will be reported at a higher rate. 4. limitations: The hard data available correlating endemic infection rates to tap water are few. Also limited are data on *Cryptosporidium parvum* numbers in tap water. The model results are characterized by rather large 95% confidence intervals. 5. relevance: medium, the approach deals with an organism on the biothreat list and a transmission route of interest
F. Study Conclusions and Extended Applications	1. conclusions: Estimates of tap water-related cases per year in New York City in non-AIDS subgroups was almost 6-fold less than in AIDS subgroups. 2. authors' extrapolations: Analysis supports recommendations that immunocompromised persons boil tap water if it is to me ingested.
G. Data Gaps and Proposed Solutions	1. data gaps: model data only compared to one years' data from New York, NY 2. proposed solutions: apply method to more datasets in the literature; firm up data underlying the assumptions
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: high 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility: high
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	The data are sparse, but this was recognized by the authors and was an impetus for the approach taken. The ideas are sound and the approach could by applied to other datasets or other pertinent situations.
K. Cross-References	NA

A. Risk Characterization Study Identification (other)	Petterson, S.R., N.J. Ashbolt and A. Sharma. 2001. Microbial risks from wastewater irrigation of salad crops: A screening-level risk assessment. Wat. Environ. Res. 72 (6): 667-672.
B. Objectives and Type of Study	1. purpose: scientific; This paper presents an order-of-magnitude estimate of population infection rates (i.e., screening-level microbial risk assessment). 2. type: RC
C. Publication Attributes	1. sponsors/affiliations: University of New South Wales, Department of Human Services, Melbourne, Australia: Cooperative Research Center for Waste Management and Pollution Control Ltd., Sydney, Australia 2. peer-review mechanism: full peer reviewed scientific journal review
D. Data and Study Design	1. type: occurrence data for enteroviruses in secondary effluent 2. source: published literature 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: Assessed the impact of two factors on the estimated risk of infection; a suitable probability density function of the occurrence of human enteroviruses in irrigation water and appropriate die-off rates for viruses on lettuce crops. Exposure model included components related to number of viruses in secondary treated effluent, number of viruses that will attach to lettuce, and rate of decay of viruses on the lettuce, in the field and with storage. The dose-response model used was that of Ward et al. (1986), developed from data and for rotaviruses (a subgroup of human enteroviruses). 2. specific characteristics: Monte Carlo simulation using a log-normal and a nonparametric kernel estimated probability density function. The kernal density estimator procedure used adopted a simplistic bandwidth choice, the Gaussian reference bandwidth. 3. assumptions: times for storage and removal during household processing were not included; consumption assumed to be 100 grams; dose-response relationship for rotavirus (Ward et al., 1986) assumed to account for all enteroviruses. 4. limitations: parameter input based on available data for any enterovirus. 5. relevance: medium

F. Study Conclusions and Extended Applications	1. conclusions: Estimated viral infection rates (risk) from the model indicted a median and 99 percentile risk of 0.10 and 0.51 per 10,000 lettuce consumers, respectively. 2. authors' extrapolations: estimated risk may not be considered acceptable if compared to EPA's acceptable risk of 0.01 in 10,000 people infected annually for consumption of drinking water.
G. Data Gaps and Proposed Solutions	1. data gaps: more sensitive to virus decay rate 2. proposed solutions: improve infection rate estimates; further development of a risk model through the use of directly enumerated virus data for assessing virus attachment.
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: high 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	Petterson and Ashbolt, 2001; Petterson et al. 2002; Ashbolt and Sharma, 2001

A. Risk Characterization Study Identification (other)	Ross, T. and J. Sumner. 2002. A simple spreadsheet-based food safety risk assessment tool. Int. J. Food Microbiol. 77(1-2): 39-53.
B. Objectives and Type of Study	1. purpose: scientific and potential future regulatory interest; description of a simple food safety risk calculation tool intended as an aid to determine relative risks from different product/pathogen/processing combinations. 2. type: RC
C. Publication Attributes	1. sponsors/affiliations: Centre for Food Safety and Quality, School of Agricultural Science, University of Tasmania, Australia 2. peer-review mechanism: peer-reviewed journal

D. Data and Study Design	1. type: incorporates factors affecting the risk, such as severity of hazard, likelihood of disease-causing dose in the food, probability of exposure 2. source: published literature, Australian-census data, CDC data 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: Microsoft® Excel spreadsheet, using standard mathematical and logical functions. 2. specific characteristics: User is required to answer 11 questions, each with an underlying weighting factor. Weighting loosely based on epidemiologic data. Four measures of risk calculated: 1) probability of disease-causing dose; 2) total predicted illnesses/annum in population of interest; 3) comparative risk; and 4) risk ranking. Tool performance evaluated using actual data or other risk assessments. 3. assumptions: that the input data is of valid design and quality 4. limitations: scenarios available for which model inputs are available (i.e., epidemiologic data). Have not been able to systematically and objectively evaluate the model's performance because there are few detailed data sets describing exposure and food-borne disease incidence. 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions: Model includes all elements required to estimate the risk of illness from foods. It can be modified. Tool is preliminary and requires that users understand the model's limitations 2. authors' extrapolations: Can be used by risk managers and others without extensive experience in risk modeling and as a simple and quick means to develop a first estimate of relative risk. Also can be used as training and risk communication tool.
G. Data Gaps and Proposed Solutions	1. data gaps: inadequacy of data currently available, lack of consideration of variability and uncertainty in the inputs and outputs of the model 2. proposed solutions: better refinement of the model to allow range or distribution of values.
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: high 3. generalizability or external validity: low

	4. soundness of study conclusions or internal validity: low 5. defensibility: high
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	could be a useful tool
K. Cross-References	NA

A. Risk Characterization Study Identification (other)	Rusin, P.A., J.B. Rose, C.N. Haas, et al. 1997. Risk assessment of opportunistic bacterial pathogens in drinking water. Rev. Environ. Contam. Toxicol. 152: 57-83.
B. Objectives and Type of Study	1. purpose: scientific; To rank the importance of opportunistic pathogens as causes of human disease and to perform a risk assessment of human ingestion of these bacteria in drinking water. 2. type: RC
C. Publication Attributes	1. sponsors/affiliations: Water Quality Research Council of the Water Quality Association 2. peer-review mechanism: peer-reviewed journal
D. Data and Study Design	1. type: occurrence, epidemiologic, infective dose, ranking studies for heterotrophic plate count (HPC) bacteria, including *Pseudomonas, Acinetobacter, Xanthomonas, Aeromonas, Moraxella, Mycobacterium avium, Legionella*. 2. source: published literature and surveys from medical centers 3. extent of data: summary of literature search 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: Daily risks based on consumption of 2 liters of water. 2. specific characteristics: Exponential model provided best fit: $P_i=1-e^{(-[1/k]x[N])}$, where P_i is the probability of infection, 1/k is the fraction of ingested microorganisms that survive to initiate infection, and N is the

	number or organisms ingested. Employed dose-response data from experiments conducted at high doses, fit mathematical models to these data sets, and then extrapolated down to doses representative of environmental scenarios. Monte Carlo analysis used to provide distribution of risk. 3. assumptions: ingestion only exposure, only one exposure event considered 4. limitations: dose response data available; infectious doses (as shown with the dose response data) are high 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: No clear evidence that HPC bacteria as a whole pose public health risk. Can use 4-tiered risk assessment approach to estimate probability of infection. 2. authors' extrapolations: none provided
G. Data Gaps and Proposed Solutions	1. data gaps: seasonal concentration of bacteria in water, adequate dose-response data, determining health risks for multiple exposures, evaluating increase in host susceptibility conferred by antibiotic use or immunosuppression 2. proposed solutions: future research to address data gaps
H. Weight of Evidence	1. robustness of method: high 2. representativeness of data: low 3. generalizability or external validity: high 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	Provides simplistic methodology required to conduct MRA, assuming secondary transmission not a concern. Identifies data gaps most likely applicable for agents of concern.
K. Cross-References	NA

A. Risk Characterization Study Identification (other)	Sanaa, M., L. Coroller and O. Cerf. 2004. Risk assessment of listeriosis linked to the consumption of two soft cheeses made from raw milk: Camembert of Normandy and Brie of Meaux. Risk Anal. 24(2): 389-399.
B. Objectives and Type of Study	1. purpose noted by study authors: regulatory; to report an improved and more contemporary risk assessment based on data collected in the years 2000-2001 2. type: RC
C. Publication Attributes	1. sponsors/affiliations: CNIEL, French National Interprofessional Centre of the Dairy Economy 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: data for organism growth in milk (Augustin, 2000), experimental data for organism growth in soft cheese (Back et al., 1993; Maisnier-Patin et al. ,1992; Ryser and Marth, 1987) 2. source: published studies 3. extent of data: NA 4. sampling plan: NA 5. sample size: milk collections from 347 farms for Camembert production and 79 farms for Brie production (total volume collected represents twice the volume needed for production); organism testing performed on 50 mL samples from tanker trucks and 25 mL samples from farm bulk tanks 6. performance characteristics: NA 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: Dose-response relationship to determine probability of illness then estimated number of severe listeriosis for 100 million servings of 27 g. Monte Carlo simulations were run using SAS system for Windows V8 and @RISK V. 4. 2. specific characteristics: Probability of severe illness estimated by P=1-exp® x N), where N is the number of cells at the time of consumption and r is a parameter with values of 1.06×10^{-12} for the more susceptible population and 2.37×10^{-14} for the less susceptible population. The number of listeriosis cases were estimated by drawing 10^8 times the concentration in 2 g servings based on the distribution for *L. monocytogenes* in cheeses, and deriving the expected number of cases by summing the 10^8 Bernouilli. The average of the results from 100 such simulations was calculated which represented the parameter of the Poisson distribution of the number of expected cases per 10^8 servings. 3. assumptions: NA 4. limitations: no animal or human feeding studies used to determine dose response. 5. relevance: low

F. Study Conclusions and Extended Applications	1. conclusions supported by the data: predicted probability of observing at least one case of severe listeriosis from consumption of the cheeses in the study is low 2. extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: no animal or human feeding studies used to determine dose response. 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: low 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	same study in EA

A. Risk Characterization Study Identification (other)	Stewart, C.M., B. Cole and D.W. Shaffner. 2003. Managing the risk of staphylococcal food poisoning from cream-filled baked goods to meet a food safety objective. J. Food Protect. 66(7): 1310-1325.
B. Objectives and Type of Study	1. purpose: a scientific study with regulatory implications for the control of staphylococcal food poisoning. 2. type: RC
C. Publication Attributes	1. sponsors/affiliations: Food Science Australia, New South Wales, Australia 2. peer-review mechanism: peer-reviewed journal
D. Data and Study Design	1. type: epidemiological data on foodborne *Staphylococcus aureus* contamination outbreaks in bakery products; experimental data for thermal destruction of Staphylococcus aureus in pertinent food systems; experimental shelf-life data as influenced by pH, water activity, added humectants and

	preservatives. 2. source: published studies and government data 3. extent of data: a moderate amount of data sufficient to illustrate the risks and approaches that the authors propose is presented. 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: The study presents a simple semi-qualitative analysis of the problem with no modeling or statistical analysis involved. 7. relevance: high
E. Method/Model/Approach	1. general characteristics: The method used is an application of a proposed scheme by The International Commission on Microbiological Specifications for Foods (ICMSF) for the management of microbial hazards for foods during processing. 2. specific characteristics: An illustration of the application of GMP (Good Manufacturing Practices), GHP (Good handling practices), and HACCP (hazard critical control point analysis) to determine reasonable food safety objectives is shown. 3. assumptions: The study assumes 100 cfu/g as the initial load of *S. aureus* cells. Also assumed the maximum permissible level of *S. aureus* contamination at the point of consumption, certain effects of pH and temperature on growth and that generic shelf life estimates are applicable to the foods in question. 4. limitations: none identified 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions: The study illustrates the value of establishing food safety objectives at the point of consumption as an approach for evaluating processing steps and setting reasonable criteria for the microbial load permissible at each step of preparation of the food product of interest. 2. authors' extrapolations: The authors intend that the analysis permits the setting of achievable *S. aureus* loads regardless of the exact process used or the point of origin of the food product.
G. Data Gaps and Proposed Solutions	1. data gaps: not identified 2. proposed solutions: none
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: high 3. generalizability or external validity: low

	4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	The overall scheme of assessing risk may be of use and the information regarding the risks of *Staphylococcus* foodborne is also useful. The study itself seems more like a review with an illustration of how the food safety objective approach could be employed. Focus is definitely on food safety, food processing and regulatory standards.
K. Cross-References	NA

A. Risk Characterization Study Identification (other)	Strachan, N.J., D.R. Fenlon and I.D. Ogden. 2001. Modelling the vector pathway and infection of humans in an environmental outbreak of *Escherichia coli* O157. FEMS Microbiol. Lett. 203(1): 69-73.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific, future regulatory interest - The purpose is to demonstrate a link between environmental dose and the number of cases presented with *E. coli* O157. 2. type: RC
C. Publication Attributes	1. sponsors/affiliations: Scottish *E. coli* O157 Reference Laboratory in Edinburgh. 2. peer-review mechanism: scientific journal review
D. Data and Study Design	1. type: outbreak investigation 2. source: Published studies and government data reports and assumptions 3. extent of data: environmental dose estimates and the number of outbreak cases 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: dose reconstruction, estimating average dose for outbreak population; comparison with 2 published dose-response models

	2. specific characteristics: The average number of organisms shed per animal equates to $8.4x10^3$ g^{-1} in ewes and $1.0x10^5$ g^{-1} in lambs. The model predicted approximately 60 *E. coli* O157 g^{-1} on the field. Three days after the outbreak, the model predicts approximately 5 g^{-1} remaining which corresponds closely to the soil sampled at the time. Utilized the Haas and Crockett models. 3. assumptions: The number of organisms shed by individual sheep and lambs is averaged for the whole flock. The feces (and hence *E. coli* O157) shed by the sheep are uniformly distributed in the top 1cm of soil. There would be no error in the number of scouts affected but there may have been asymptomatic carriers which if identified would give a higher attack rate. Soil ingested at 30 or 200 mg/day. Linear pathogen decline in soil over 4 week period. 4. limitations: lack of validation for dose-response models for *E. coli* O157, doses in this outbreak that caused illness, and doses in this outbreak that did not cause illness 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: Data are insufficient to validate two alternative dose-response models considered by authors 2. authors' extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: high 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	NA

A. Risk Characterization Study Identification (other)	Teunis, P.F.M., G.J. Medema, L. Kruidenier, et al. 1997b. Assessment of the risk of infection by *Cryptosporidium* or *Giardia* in drinking water from a surface water source. Wat. Res. 31(6): 1333-1346.
B. Objectives and Type of Study	1. purpose: scientific, future regulatory interest. This paper focuses on the assessment of the risk of infection by *Cryptosporidium* and *Giardia* via drinking water from a surface water supply. 2. type: RC
C. Publication Attributes	1. sponsors/affiliations: Directorate General for the Environment, Ministry of Housing, Physical Planning and the Environment, The Hague, Netherlands. 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: experimental data for concentration of *Cryptosporidium* and *Giardia* and other relevant parameters were collected at the inlet and outlet of a water storage system (sufficiently large sample volumes have been taken to obtain a considerable proportion of positive (i.e., nonzero) organism counts); published data (by others) for viability of *Cryptosporidium* and *Giardia* (unknown sampling method); unpublished data from another water treatment facility was used to model treatment efficiency (unknown sampling method); published data for water consumption in the Netherlands (unknown sampling method); dose-response data from published studies (unknown sampling method) 2. source: published and unpublished datasets 3. extent of data: large data sets have been collected representing numbers of viable type cysts or oocysts per 1000 liters of water 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: extensive statistical analyses were provided, which includes error structure for analytical data; spiked samples for recovery studies; analytical and statistical methods were adequate 7. relevance: high
E. Method/Model/Approach	1. general characteristics: A statistical model for the probability of *Cryptosporidium* and *Giardia* infection from treated *surface water* is described. 2. specific characteristics: Negative binomial distribution for counts of *Cryptosporidium* and *Giardia*; beta-binomial distribution for recovery, viability and treatment efficiency; exponential distribution for dose-response model. Uncertainty in the dose-response model was modeled by bootstrapping. 5,000 samples were drawn from each distribution to predict probability of risk of infection. Probabilities of infection was calculated separately for summer and winter data (the *Cryptosporidium* and *Giardia* concentration data showed seasonal trends), as well as for the pooled data set. Results indicated the

	seasonal effect was not important source of variability in the predicted risk of infection. The prediction of risk are presented separately for the two protozoa; a combined risk was also calculated as the risk of being infected with either organism or both. 3. assumptions: Risk was calculated assuming the probability distributions for all factors (oocyst concentration, recovery, viability, removal by treatment and daily water consumption) are statistically independent. 4. limitations: Data needed to model treatment efficiency could not be collected because direct detection of the pathogenic organisms in the treated water was not possible; therefore, data on the removal of spores of sulphite reducing clostridia from another drinking water treatment facility were used. 5. relevance: high
F. Study Conclusions and Extended Applications	1. conclusions: The uncertainty in the estimated removal efficiency of the treatment process dominates over uncertainties in other contributing factors. With respect to risk analysis, it seems that the probability of occurrence of episodes of decreased removal efficiency should receive more attention. The frequency of failure of a treatment system to remove protozoans such as *Cryptosporidium* oocysts and *Giardia* may determine health risks, rather than the mean reduction in protozoans. 2. authors' extrapolations: Quantitative analysis should include predicting the probability of failure of the treatment system due to human error and nonhuman error (e.g., equipment failure and excessive load).
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: high 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility: high
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	1. Authors suggests that the work described in the paper should be regarded as a preliminary study, mainly to investigate problem areas and to test the feasibility of the chosen approach. 2. Dose-response template not completed - the authors used dose-response model from literature, and

	assess uncertainty in the model parameters by bootstrapping
K. Cross-References	NA

A. Risk Characterization Study Identification (other)	USDA/FSIS. 2003. Risk assessment for *Listeria monocytogenes* in deli meats. US Department of Agriculture/Food Safety and Inspection Service. www.fsis.usda.gov/OPPDE/rdad/FRPubs/97-013F/ListeriaReport.pdf
B. Objectives and Type of Study	1. purpose: regulatory; to evaluate hypothetical mitigations for contaminated ready-to-eat (RTE) meat 2. type: RC
C. Publication Attributes	1. sponsors/affiliations: USDA, FSIS 2. peer-review mechanism: report mentioned public comment period, but no peer review process
D. Data and Study Design	1. type: retail survey data from National Food Processors Association; experimental results from studies on duration of contamination event, transfer of organisms from food contact surface (FCS) to food, conversion of FCS *Listeria* spp. concentrations to food surface *L. monocytogenes* concentrations 2. source: published scientific studies, government survey 3. extent of data: sparse 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: Monte Carlo simulation in-plant dynamics linked to FDA/USDA retail-to-table exposure assessment and dose-response models (FDA/USDA 2003) 2. specific characteristics: theoretical mass balance approach for in-plant model; 3. assumptions: *Listeria* spp. are evenly distributed across FCSs, and *L. monocytogenes* are evenly distributed within a lot of product; foods encompassed by the food categories account for all cases of foodborne listeriosis; a *Listeria* reservoir exists in the plant and is capable of contaminating FCSs. 4. limitations: model only considers FCS as source of contamination in product; only a generic FCS is

	modeled; variability across FCS or within a lot is not accounted for in model. 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions: combinations of interventions appear more effective than single interventions; proposed minimal frequency of testing and sanitation of FCSs estimated to result in a small reduction in *L. monocytogenes* on deli meats at retail 2. authors' extrapolations: model may also be extended to frankfurters
G. Data Gaps and Proposed Solutions	1. data gaps: amount of *Listeria* spp. on FCS during contamination event; ratio of concentrations of *L. monocytogenes* to *Listeria* spp.; enumeration data for positives to verify theoretical in-plant dynamics 2. proposed solutions: generate data for model calibration and validation
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: low 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	same study in EA; FDA/USDA, 2003

A. Risk Characterization Study Identification (other)	Wein, L.M., D. Craft and E.H. Kaplan. 2003. Emergency response to an anthrax attack. PNAS 100(7): 4346-4351. Supporting Text on www.pnas.org
B. Objectives and Type of Study	1. purpose noted by study authors: scientific, comparison of risk management options 2. type: RC
C. Publication Attributes	1. sponsors/affiliations: Center for Interdisciplinary Research on AIDS (Yale University), National Institutes of Mental Health and Drug Abuse/ Stanford University, Massachusetts Institute of

	Technology, Yale Schools of Management and Medicine 2. peer-review mechanism: full scientific peer-review
D. Data and Study Design	1. type: NA 2. source: assumptions or literature estimates 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: endpoint mortality under 5 emergency response strategies, probit DR model of Glassman (1966), five disease states 2. specific characteristics: system of integropartial differential equations; no characterization of data or probit DR model provided; uncertain if DR was extrapolated from animal species or estimated from human outbreak investigations or inferred from other sources; states modeled were uninfected, incubation, prodromal, fulminant, and death 3. assumptions: lognormal distributions, including disease durations; no secondary exposures; no person-to-person transmission; release 10^{15} anthrax spores (~1 kg) at 100 m altitude ; dispersion for neutral stability in open air for 200 km (downwind, length of plume) and ~36 km (width plume); uniform population age distribution for urban and rural residents release 10^{15} anthrax spores (~1 kg) at 100 m altitude ; dispersion for neutral stability in open air for 200 km (downwind, length of plume) and ~36 km (width plume); uniform population age distribution for urban and rural residents 4. limitations: virulence of available strains dependent on largely uncharacterized host, pathogen, and environmental factors 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: quality of data, and thus rigor of models, uncertain; dispersion may be consistent with theory, but largely unvalidated by controlled scientific studies 2. extrapolations: scenario for dispersion useful for selection of appropriate risk management strategies
G. Data Gaps and Proposed Solutions	1. data gaps: magnitude of intentional releases, form (liquid or dry), actual dispersion dynamics 2. proposed solutions: extend existing model to account for wind, atmospheric influences, time of day for release, stability conditions, form of agent, method of aerosolization

H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: NA
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	authors do not address limitations of data or inconsistencies in body of scientific evidence from animal and human sources; the influence of extensive assumptions of mathematical convenience or opinion is not well documented
K. Cross-References	same study in EA

A. Risk Characterization Study Identification (other)	Westrell, T., O. Bergstedt, T.A. Stenstrom and N.J. Ashbolt. 2003. A theoretical approach to assess microbial risks due to failures in drinking water systems. Int. J. Environ. Health Res. 13: 181-197.
B. Objectives and Type of Study	1. purpose: scientific; To examine the theoretical impact of failures in treatment in the drinking water system on the annual risk of infection in a population served by a large water treatment plant in Sweden. 2. type: RC
C. Publication Attributes	1. sponsors/affiliations: Swedish Foundation for Strategic Environmental Research, the Swedish Water and Wastewater Association and the Recycling Board of Gothenburg, Sweden. 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: Data reflecting the occurrence of three pathogens representing a parasitic protozoan, *Cryptosporidium parvum*, a virus (rotavirus), and a bacterium, *Campylobacter jejuni*, were obtained from national investigations conduced in The United States and several European countries. This data reflected the occurrence of these pathogens in raw water and sewage. 2. source: data from Sweden and other countries

	3. extent of data: Swedish surveillance data from 1980 - 1997 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: high
E. Method/Model/Approach	1. general characteristics: analysis of variance, Monte Carlo simulation 2. specific characteristics: published data and incorporated for hypothetical scenarios 3. assumptions: data from other countries normalized for use in the case study is relevant to the case study area. The dose response functions underestimate the risk of infection for sensitive persons, especially concerning *Cryptosporidium* and *Campylobacter*. 4. limitations: NA 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions: The main risk incidents in water treatment in the case study area of Gothenberg were associated with sub-optimal particle removal or disinfection malfunction. The simulated median annual numbers of infection based on the microbial risk assessment corresponded to the epidemiological situation calculated from Swedish and international data. 2. authors' extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: No quantitative national data from water sources were available regarding the pathogens rotavirus and *Campylobacter*. 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: high 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: UN
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	Westrell, 2002

A. Risk Characterization Study Identification (other)	Whiting, R.C. and R.L. Buchanan. 1997. Development of a quantitative risk assessment model for *Salmonella enteritidis* in pasteurized liquid eggs. Int. J. Food Microbiol. 36: 111-125.
B. Objectives and Type of Study	1. purpose: regulatory, future regulatory interest; to create a quantitative risk assessment model for *Salmonella enteritidis* infection from pasteurized liquid eggs using a 'unit operations' and stochastic simulation approach 2. type: RC
C. Publication Attributes	1. sponsors/affiliations: USDA, Agricultural Research Service 2. peer-review mechanism: peer-reviewed journal
D. Data and Study Design	1. type: experimental data for each step of the liquid whole egg processing and distribution; epidemiological survey data 2. source: published studies and government datasets 3. extent of data: extensive review of published studies 4. sampling plan: factorial design; probability based sampling 5. sample size: distribution of values reported in 27 surveys and experimental trials 6. performance characteristics: NA 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: exposure assessment model simulated 2000 times using @RISK 2. specific characteristics: histogram distribution of log fraction of contaminated eggs; level of *S. enteritidis* in contaminated eggs calculated based on assumptions; thermal death model; binomial distribution of number of contaminated consumer packages; Gompertz growth modeling for growth during storage; *Salmonella* survival model; exponential model for probability of infection 3. assumptions: *S. enteritidis* outbreaks largely a function of transovarian transmission; best estimate of infected flock percentage based on examination of ovaries and oviduct tissue for infection; majority of eggs destined for liquid egg products are refrigerated or processed within 1 wk; washing, shell sanitization, breaking operations are adequate. 4. limitations: risk assessment model not validated due to lack of quantitative knowledge of system

	behavior 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions: dynamic risk assessment models would greatly enhance scientific basis for HACCP programs; thermal processing temperature is particularly important; pasteurization will minimize risk from high contamination in flocks if pathogen is not allowed to grow. 2. authors' extrapolations: none stated
G. Data Gaps and Proposed Solutions	1. data gaps: need additional understanding of lag periods between various growth, pasteurization, and survival steps; need better understanding of virulence mechanisms and infectious doses; didn't consider cellular injury and repair as factors in determining final pathogen populations 2. proposed solutions: conduct studies to fill the data gaps described; rerun model taking into consideration the effects of cellular injury and repair on final pathogen populations
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	This method would be useful for assessing risk in microbial growth and partial inactivation scenarios.
K. Cross-References	NA

A.4 Comprehensive Reference List for Compendium Studies

Adams, M. and R. Mitchel. 2002. Fermentation and pathogen control: A risk assessment approach. Int. J. Food Microbiol. 79(½): 75-83.

Aden, J. and B.R. Scott. 2003. Modeling variability and uncertainty associated with inhaled weapons-grade PuO2. Health Phys 84(6): 726-736.

Ahmed, F., J.D. Clemens, M.R. Rao, et al. 1997. Epidemiology of shigellosis among children exposed to cases of *Shigella* dysentery: A multivariate assessment. Am. J. Trop. Med. Hyg. 56(3): 258-264.

Ashbolt, N.J. 2004. Risk analysis of drinking water microbial contamination versus disinfection by-products (DBPs). Toxicology 198(1-3): 255-262.

Auranen, K., J. Ranta, A.K. Takala and E. Arjas. 1996. A statistical model of transmission of Hib bacteria in a family. Stat. Med. 15: 2235-2252.

Awasthi, S. and S. Moin. 1999. Effectiveness of BCG vaccination against tuberculous meningitis. Indian Pediatrics 36(5): 455-460.

Bachur, R.G. and M.B. Harper. 2001. Predictive model for serious bacterial infections among infants younger than 3 months of age. Pediatrics 108(2): 311-316.

Balbus, J., R. Parkin, A. Makri, et al. 2004. Defining susceptibility for microbial risk assessment: Results of a workshop. Risk Anal. 24(1): 197-208.

Bale, J.F. Jr, B. Zimmerman, J.D. Dawson, et al. 1999. Cytomegalovirus transmission in child care homes. Arch. Pediatr. Adolesc. Med. 153(1): 75-79.

Barker, C.M., W.K. Reisen and V.L. Kramer. 2003. California State Mosquito-Borne Virus Surveillance and Response Plan: A retrospective evaluation using conditional simulations. Am. J. Trop. Med. Hyg. 68(5): 508-518.

Barnes, P.F., Z. Yang, S. Preston-Martin, et al. 1997. Patterns of tuberculosis transmission in central Los Angeles. JAMA 278(14): 1159-1163.

Barnhart, S., L. Sheppard, N. Beaudet, et al. 1997. Tuberculosis in health care settings and the estimated benefits of engineering controls and respiratory protection. J. Occup. Environ. Med. 39(9): 849-854.

Bassett, J., et al. 2002. Project report: Quantitative risk assessment of salmonella in sheep meat produced in New Zealand. New Zealand Food Safety Authority.

Bates, D.W., K. Sands, E. Miller, et al. 1997. Predicting bacteremia in patients with sepsis syndrome. J. Infect. Dis. 176: 1538-1551.

Becker, K.M., C.L. Moe, K.L. Southwick, et al. 2000. Transmission of Norwalk virus during football game. N. Engl. J. Med. 343(17): 1223-1227.

Beggs, C.B., C.J. Noakes, P.A. Sleigh, et al. 2003. The transmission of tuberculosis in confined spaces: An analytical review of alternative epidemiological models. Int. J. Tuberc. Lung Dis. 7(11): 1015-1026.

Bemrah N., M. Sanaa, M.H. Cassin, et al. 1998. Quantitative risk assessment of human listeriosis from consumption of soft cheese made from raw milk. Prev. Vet. Med. 37(1- 4): 129-145.

Bhutta, Z.A., N. Punjwani and B.S. Lindblad. 1996. Concomitant bacteraemia as a risk factor for diarrhoeal disease mortality in Karachi: A case-control study of hospitalized children. Acta Paediatr. 85(7): 809-813.

Blumenthal, U.J., D.D. Mara, A. Peasey, et al. 2000. Guidelines for microbiological quality of treated wastewater used in agriculture: Recommendations for revising WHO guidelines. Bull. World Health Org. 78(9): 1104-1116.

Bowden, K.M. and M.A. McDiarmid. 1994. Occupationally acquired tuberculosis: What's known. J. Occup. Med. 36(3): 320-325.

Bradley, M., R. Shakespeare, A. Ruwende, et al. 1996. Epidemiological features of epidemic cholera (El Tor) in Zimbabwe. Trans. R. Soc. Trop. Med. Hyg. 90(4): 378-382.

Breugelmans, J.G., P. Zucs, K. Porten, et al. 2004. SARS transmission and commercial aircraft. Emerg. Infect. Dis. 10(8): 1502-1503.

Brookmeyer, R., E. Johnson and R. Bollinger. 2003. Modeling the optimum duration of antibiotic prophylaxis in an anthrax outbreak. Proc. Nat. Acad. Sci. U S A 100(17): 10129-10132.

Brown, M.H., K.W. Davies, C.M.-P. Billon, C. Adair and P.J. McClure. 1998. Quantitative microbiological risk assessment: Principles applied to determining the comparative risk of Salmonellosis from chicken products. J. Food Protect. 61(11): 1446-1453.

Buchanan, R. 1998. Principles of risk assessment for illness caused by food-borne biological agents. J. Food Protect. 61(8): 1071-1074.

Buchanan, R.L. W.G. Damert, R.C. Whiting and M. van Schothorst. 1997. Use of epidemiologic and food survey data to estimate a purposefully conservative dose-response relationship for *Listeria monocytogenes* levels and incidence of listeriosis. J. Food Protect. 60(8): 918-922.

Buchanan, R.L., J.L. Smith and W. Long. 2000. Microbial risk assessment: Dose-response relation and risk characterization. Int. J. Food Microbiol. 58: 159-172.

Carlin F., H. Girardin, M.W. Peck, et al. 2000. Research on factors allowing a risk assessment of spore-forming pathogenic bacteria in cooked chilled foods containing vegetables: A FAIR collaborative project. Int. J. Food Microbiol. 60(2/3): 117-135.

Cassin, M.H., A.M. Lammerding, E.C.D. Todd, et al. 1998. Quantitative risk assessment for *Escherichia coli* O157:H7 in ground beef hamburgers. Int. J. Food Microbiol. 41: 21-44.

Cassin, M.H., G.M. Paoli and A.M. Lammerding. 1998. Simulation modeling for microbial risk assessment. J. Food Protect. 61(11): 1560-1566.

Chang, F.Y., N. Singh, T. Gayowski, et al. 1998. Staphylococcus aureus nasal colonization in patients with cirrhosis: Prospective assessment of association with infection. Infect. Control Hosp. Epidemiol. 19(5): 328-332.

Chaulk, C.P., M. Friedman and R. Dunning. 2000. Modeling the epidemiology and economics of directly observed therapy in Baltimore. Int. J. Tuberc. Lung Dis. 4(3): 201-207.

Chen, Y., W.H. Ross, V.N. Scott and D.E. Gombas. 2003. *Listeria monocytogenes*: Low levels equal low risk. J. Food Protect. 66(4): 570-577.

Chick, S.E., J.S. Koopman, S. Soorapanth and M.E. Brown. 2001. Infection transmission system models for microbial risk assessment. Sci. Total Environ. 274: 197-207.

Chowell, G., P.W. Fenimore, M.A. Castillo-Garsow and C. Castillo-Chavez. 2003. SARS outbreaks in Ontario, Hong Kong and Singapore: The role of diagnosis and isolation as a control mechanism. J. Theor. Biol. 224(1): 1-8.

Christensen, B., H. Sommer, H. Rosenquist, et al. 2001. Risk assessment on *Campylobacter jejuni* in chicken products. The Danish Veterinary and Food Administration.

Cifuentes, E., J.E. Hernandez, L. Venczel and M. Hurtado. 1999. Panorama of acute diarrhoeal diseases in Mexico. Health & Place 5: 247-255.

Cody, S.H., S.L. Abbott, A.A. Marfin, et al. 1999. Two outbreaks of multidrug-resistant Salmonella serotype typhimurium DT104 infections linked to raw-milk cheese in Northern California. JAMA 281(19): 1805-1810.

Coleman, M. and H. Marks. 1998. Topics in dose-response modeling. J. Food Protect. 61(11): 1550-1559.

Coleman, M.E. and H.M. Marks. 2000. Mechanistic modeling of salmonellosis. Quantitative Microbiology 2: 227-247.

Coleman, M.E., M.L. Tamplin, J.G. Phillips and B.S. Marmer. 2003. Influence of agitation, inoculum density, pH, and strain on the growth parameters of *Escherichia coli* O157:H7 - relevance of risk assessment. Int. J. Food Microbiol. 83: 147-160.

Coleman, M.E., S. Sandberg and S. Anderson. 2003. Impact of microbial ecology of meat and poultry products on predictions from exposure assessment scenarios for refrigerated storage. Risk Anal. 23(1): 215-28.

Coleman, M.E., H.M. Marks, N.J. Golden, et al. 2004. Discerning strain effects in microbial dose-response data. J. Toxicol. Environ. Health A 67(8-10): 667-685.

Cormack, R.M. 1999. Problems with using capture-recapture in epidemiology: An example of a measles epidemic. J. Clin. Epidemiol. 52(10): 909-914.

Corrigan, E.M. and R.L Clancy. 1999. Is there a role for a mucosal influenza vaccine in the elderly? Drugs Aging 15(3): 169-181.

Crabtree, K.D., C.P. Gerba, J.B. Rose and C.N. Haas. 1997. Waterborne adenovirus: A risk assessment. Wat. Sci. Technol. (35)11-12: 1-6.

Crawford-Brown, D.J. and S. Marquez-Nyarko. 1999. Development of an environmental decision support system (EDSS) for comparing drinking water treatment practices and associated health risks. Report No. 323. Chapel Hill, NC: Water Resources Research Institute of The University of North Carolina.

Crump, J.A., A.C. Sulka, A.J. Langer, et al. 2002. An outbreak of *Escherichia coli* O157:H7 infections among visitors to a dairy farm. N. Engl. J. Med. 347(8): 555-560.

Davidson, V.J. and J. Ryks. 2003. Comparison of Monte Carlo and fuzzy math simulation methods for quantitative microbial risk assessment. J. Food Protect. 66(10): 1900-1910.

Delignette-Muller, M.L. and L. Rosso. 2000. Biological variability and exposure assessment. Int. J. Food Microbiol. 58: 203-212.

den Aantrekker, E.D., R.M. Boom, M.H. Zwietering and M. Van Schothorst. 2003. Quantifying recontamination through factory environments-a review. Int. J. Food Microbiol. 80: 117-130.

Dietz, K. and J.A. Heesterbeek. 2002. Daniel Bernoulli's epidemiological model revisited. Math. Biosci. 180: 1-21.

Douwes, J., P. Thorne, N. Pearce and D. Heederik. 2003. Bioaerosol health effects and exposure assessment: Progress and prospects. Ann. Occup. Hyg. 47(3): 187-200.

Drobniewski, F., I. Eltringham, C. Graham, et al. 2002. A national study of clinical and laboratory factors affecting the survival of patients with multiple drug resistant tuberculosis in the UK. Thorax 57(9): 810-816.

Duffy, S., J. Churey, R.W. Worobo, et al. 2000. Analysis and modeling of the variability associated with UV inactivation of *Escherichia coli* in apple cider. J. Food Protect. 63(11): 1587-1590.

Duffy, S. and D.W. Schaffner DW. 2001. Modeling the survival of *Escherichia coli* O157:H7 in apple cider using probability distribution functions for quantitative risk assessment. J. Food Protect. 64(5): 599-605.

Durham, L.K., I.M. Longini, Jr., M.E. Halloran, et al. 1998. Estimation of vaccine efficacy in the presence of waning: Application to cholera vaccines. Am. J. Epidemiol. 147: 948-59.

Eduard, W. 1996. Measurement methods and strategies for non-infectious microbial components in bioaerosols at the workplace. Analyst 121: 1197-1201.

Eisenberg, J.N., E.Y.W. Seto, A.W. Olivieri and R.C. Spear. 1996. Quantifying water pathogen risk in an epidemiological framework. Risk Anal. 16(4): 549-563.

Eisenberg, J.N., J.A. Soller, J. Scott, et al. 2004. A dynamic model to assess microbial health risks associated with beneficial uses of biosolids. Risk Anal. 24(1): 221-236.

Ejidokun, O.O., D. Killalea, M. Cooper, et al. 2000. Four linked outbreaks of Salmonella enteritidis phage type 4 infection--the continuing egg threat. Commun. Dis. Public Health 3(2): 95-100.

Englehardt, J.D. and J. Swartout. 2004. Predictive population dose-response assessment for *Cryptosporidium parvum*: Infection endpoint. J. Toxicol. Environ. Health, Part A 67(8-10): 651-666.

Falconer, I.R., M.D. Burch, D.A. Steffensen, et al. 1994. Toxicity of the blue-green alga (Cyanobacterium) *Microcystis aeruginosa* in drinking water to growing pigs, as an animal model for human injury and risk assessment. Environ. Toxicol. Wat. Qual. 9: 131-139.

FAO/WHO. 2002a. Risk assessment of *Campylobacter spp*. in broiler chickens and Vibrio spp. in seafood - a joint FAO/WHO consultation. Bangkok, Thailand, 5-9 August 2002. Food and Agriculture Organization/World Health Organization.

FAO/WHO. 2002b. Risk assessments of *Salmonella* in eggs and broiler chickens. Food and Agriculture Organization/World Health Organization.

http://www.who.int/foodsafety/publications/micro/salmonella/en/

FAO/WHO. 2004. Risk assessment of *Listeria monocytogenes* in ready-to-eat foods. Food and Agriculture Organization/World Health Organization.

http://www.who.int/foodsafety/publications/micro/mra_listeria/en/

Farber, J.M., W.H. Ross and J. Harwig. 1996. Health risk assessment of *Listeria monocytogenes* in Canada. Int. J. Food Microbiol. 30(1-2): 145-156.

FDA-CVM. 2001a. The human health impact of fluoroquinolone resistant *Campylobacter* attributed to the consumption of chicken. US Food and Drug Administration Center for Veterinary Medicine. October 18, 2000. Revised: January 5, 2001. http://www.fda.gov/cvm/antimicrobial/Risk_asses.htm

FDA-CVM. 2001b. Risk assessment on the human health impact of fluoroquinolone resistant *Campylobacter* associated with the consumption of chicken. Washington, DC: US Food and Drug Administration Center for Veterinary Medicine.

FDA/USDA. 2003. Quantitative assessment of relative risk to public health from foodborne *Listeria monocytogenes* among selected categories of ready-to-eat foods. http://www.foodsafety.gov/~dms/lmr2-toc.html

Focks, D.A., R.J. Brenner, J. Hayes, et al. 2000. Transmission thresholds for dengue in terms of *Aedes aegypti* pupae per person with discussion of their utility in source reduction efforts. Am. J. Trop. Med. Hyg. 62(1): 11-18.

Gale, P. 1996. Developments in microbiological risk assessment models for drinking water-a short review. J. Appl. Bacteriol. 81: 403-410.

Gale, P., P.A.H. van Dijk and G. Stanfield. 1997. Drinking water treatment increases micro-organism clustering; the implications for microbiological risk assessment. Aqua (Oxford) 46(3): 117-126.

Gale, P. 2001. Developments in microbiological risk assessment for drinking water. J. Appl. Microbiol. 91: 191-205.

Gani, R. and S. Leach. 2004. Epidemiological determinants for modeling pneumonic plague outbreaks. Emerging Infectious Dis. 10: 608-614.

Gerba, C.P. 1996. Risk assessment. Pollution science. San Diego, CA: Academic Press, Inc., p. 345-364.

Gerba, C.P., J.B. Rose, C.N. Haas and K.D. Crabtree. 1996. Waterborne rotavirus: A risk assessment. Wat. Res. 30(12): 2929-2940.

Getoor, L., J.T. Rhee, D. Koller and P. Small. 2004. Understanding tuberculosis epidemiology using structured statistical models. Artificial Intelligence Med. 30(3): 233-256.

Glass, G.E., J.E. Cheek, J.A. Patz, et al. 2000. Using remotely sensed data to identify areas at risk for hantavirus pulmonary syndrome. Emerging Infectious Dis. 6(3): 238-247.

Grasman, J. 1998. Stochastic epidemics: the expected duration of the endemic period in higher dimensional models. Math Biosci. 152(1): 13-27.

Haas, C.N. 2002. Progress and data gaps in quantitative microbial risk assessment (QMRA). Wat. Sci. Technol. 46(11-12): 277-284.

Hajmeer, M.N. and I.A. Basheer. 2003. A hybrid Bayesian-neural network approach for probabilistic modeling of bacterial growth/no-growth interface. Int. J. Food Microbiol. 82(3): 233-243.

Hald T., D. Vose, H.C. Wegener and T. Koupcev. 2004. A Bayesian approach to quantify the contribution of animal-food sources to human salmonellosis. Risk Anal. 24(1): 255-269.

Hardalo, C. and S.C. Edberg. 1997. *Pseudomonas aeruginosa*: Assessment of risk from drinking water. Crit. Rev. Microbiol. 23(1): 47-75.

Harding, I., A.P. MacGowan, L.O. White, et al. 2000. Teicoplanin therapy for *Staphylococcus aureus* septicaemia: Relationship between pre-dose serum concentrations and outcome. J. Antimicrob. Chemother. 45(6): 835-841.

Havelaar, A.H., M.J. Nauta and J.T. Jansen. 2004. Fine tuning food safety objectives and risk assessment. Int. J. Food Microbiol. 93: 11-29.

Hoornstra, E. and S. Notermans. 2001. Quantitative microbiological risk assessment. Int. J. Food Microbiol. 66: 21-29.

Hope, B.K., A.R. Baker, E.D. Edel et al. 2002. An overview of the *Salmonella* enteritidis risk assessment for shell eggs and egg products. Risk Anal. 22(2): 203-218.

Hrudey, S.E., P. Payment, P.M. Huck, et al. 2003. A fatal waterborne disease epidemic in Walkerton, Ontario: Comparison with other waterborne outbreaks in the developed world. Wat. Sci. Technol. 47(3): 7-14.

Humphrey, T.J., K.W. Martin, J. Slader and K. Durham. 2001. *Campylobacter* spp. in the kitchen: Spread and persistence. J. Appl. Microbiol. 90: 115S-120S.

Hurd, H.S., S. Doores, D. Hayes, et al. 2004. Public health consequences of macrolide use in food animals: A deterministic risk assessment. J. Food Protect. (67)5: 980-992.

Huston, T.E., E.B. Farfan, W.E. Bolch and W.E. Bolch. 2003. Influences of parameter uncertainties within the ICRP-66 respiratory tract model: A parameter sensitivity analysis. Health Physics 85(5): 553-566.

Jaakkola, J.J.K. and O.P. Heinonen. 1994. Shared office space and the risk of the common cold. Euro. J. Epidemiol. 11: 213-216.

Jaykus, L.-A. 1996. The application of quantitative risk assessment to microbial food safety risks. Crit. Rev. Microbiol. 22: 279-293.

Jernigan, J.A., A.L. Pullen, C. Partin and W.R. Jarvis. 2003. Prevalence of and risk factors for colonization with methicillin-resistant *Staphylococcus aureus* in an outpatient clinic population. Infect. Control Hosp. Epidemiol. 24(6): 445-450.

Jones, R.C., S.I. Gerber, P.S. Diaz, et al. 2004. Intensive investigation of bacterial foodborne disease outbreaks: Proposed guidelines and tools for the collection of dose-response data by local health departments. J. Food Protect. 67(3): 616-623.

Kistemann, T., S. Zimmer, I. Vagsholm and Y. Andersson. 2004. GIS-supported investigation of human EHEC and cattle VTEC O157 infections in Sweden: Geographical distribution, spatial variation and possible risk factors. Epidemiol. Infect. 132: 495-505.

Klapwijk, P.M., J.-L. Jouve and M.F. Stringer. 2000. Microbial risk assessment in Europe. Int. J. Food Microbiol. 58: 223-230.

Ko, G., K.M. Thompson and E.A. Nardell. 2004. Estimation of tuberculosis risk on a commercial airliner. Risk Anal. 24(2): 379-388.

Koopman, J.S., and I.M. Longini. 1994. The ecological effects of individual exposures and nonlinear disease dynamics in populations. Am. J. Public Health 84(5): 836-842.

Kortepeter, M.G. and M.R. Krauss. 2001. Tuberculosis infection after humanitarian assistance, Guantanamo Bay, 1995. Mil. Med. 166(2): 116-120.

Krewski, D., J. Balbus, D. Butler-Jones, et al. 2002. Managing health risks from drinking water–a report to the Walkerton inquiry. J. Toxicol. Environ. Health, Part A 65: 1635-1823.

Krimsky, S., R.P. Wrubel, I.G. Naess, et al. 1995. Standardized microcosms in microbial risk assessment. Bioscience 45(9): 590-599.

Lammerding, A.M. and A. Fazil. 2000. Hazard identification and exposure assessment for microbial food safety risk assessment. Int. J Food. Microbiol. 58(3): 147-157.

Latimer, H.K., L. Jaykus, R.A. Morales, et al. 2001. A weighted composite dose-response model for human salmonellosis. Risk Anal. 21(2): 295-305.

Li, X. and P.A. Rossignol. 1998. Probability model on the use of sentinel animal monitoring for arbovirus. Epidemiol. 9(4): 446-451.

Lindqvist, R. and A. Westoo. 2000. Quantitative risk assessment for *Listeria monocytogenes* in smoked or gravad salmon and rainbow trout in Sweden. Int. J. Food Microbiol. 58(3): 181-196.

Lui, K.J. 1998. Interval estimation of the risk ratio between a secondary infection, given a primary infection, and the primary infection. Biometrics 54(2): 706-711.

Marks, H. and M. Coleman. 1998. Estimating distributions of numbers of organisms in food products. J. Food Protect. 61(11): 1535-1540.

Marks, H.M., M.E. Coleman, C.-T. J. Lin and T. Roberts. 1998. Topics in microbial risk assessment: Dynamic flow tree process. Risk Anal. 18(3): 309-328.

Martin, S.A., T.S. Walsten and N.D. Beaulieu. 1995. Assessing the risk of microbial pathogens: Application of a judgement-encoding methodology. J. Food Protect. 58(3): 289-295.

Masuda, N., N. Konno and K. Aihara. 2004. Transmission of severe respiratory syndrome in dynamical small-world networks. Physical Review 69(3 Pt 1): 031917.

Matson, D.O. and G. Szucs. 2003. Calicivirus infections in children. Curr. Opin. Infect. Dis. 16(3): 241-246.

Mattick, K.L., F. Jorgensen, J.D. Legan, et al. 2000. Survival and filamentation of *Salmonella enterica* serovar *enteritidis* PT4 and *Salmonella enterica* serovar *typhimurium* DT104 at low water activity. Appl. Environ. Microbiol. 66: 1274-1279.

McKenna, S.A. 2000. Development of a discrete spatial-temporal SEIR simulator for modeling infectious diseases. Albuquerque, NM: Sandia National Laboratories.

McLauchlin, J., R.T. Mitchell, W.J. Smerdon, et al. 2004. *Listeria monocytogenes* and listeriosis: A review of hazard characterisation for use in microbiological risk assessment of foods. Int. J. Food Microbiol. 92(1): 15-33.

McNab, W.B. 1998. A general framework illustrating an approach to quantitative microbial food safety risk assessment. J. Food Protect. 61(9): 1216-1228.

Medema, G.J., P.F.M. Teunis, A.H. Havelaar and C.N. Haas. 1996. Assessment of the dose-relationship of *Campylobacter jejuni*. Int. J. Food Microbiol. 30: 101-111.

Medema, G.J., W. Hoogenboezem, A.J. van der Veer, et al. 2003. Quantitative risk assessment of *Cryptosporidium* in surface water treatment. Wat. Sci. Technol. 47(3): 241-247.

Mossel, D.A.A., G.H. Weenk, G.P. Morris and C.B. Struijk. 1998. Identification, assessment, and management of food-related microbiological hazards: historical, fundamental, and psycho-social essentials. Int. J. Food Microbiol. 39: 19-51.

Mugglin, A.S., N. Cressie and I. Gemmell. 2002. Hierarchical statistical modelling of influenza epidemic dynamics in space and time. Stat. Med. 21: 2703-2721.

Myers, M.F., D.J. Rogers, J. Cox J, et al. 2000. Forecasting disease risk for increased epidemic preparedness in public health. Advances Parasitol. 47: 309-330.

Mylotte, J.M., M.A. Pisano, S. Ram, et al. 1995. Validation of a bacteremia prediction model. Infect. Control Hosp. Epidemiol. 16(4): 203-209.

Nagelkerke, N., S. Heisterkamp, M. Borgdorff, et al. 1999. Semi-parametric estimation of age-time specific infection incidence from serial prevalence data. Stat. Med. 18(3): 307-320.

Nauta, M.J., E.G. Evers, K. Takumi and A.H. Havelaar. 2001. Risk assessment of Shiga-toxin producing *Escherichia coli* O157 in steak tartare in the Netherlands. RIVM report 257851003. http://www.rivm.nl/bibliotheek/rapporten/257851003.html

Nauta, M.J. 2002. Modelling bacterial growth in quantitative microbiological risk assessment: Is it possible? Int. J. Food Microbiol. 73(2-3): 297-304.

Nauta, M.J., S. Litman, G.C. Barker and F. Carlin. 2003. A retail and consumer phase model for exposure assessment of *Bacillus cereus*. Int. J. Food Microbiol. 83(2): 205-218.

Neuman, D.A. and Foran, J.A, 1997. Assessing the risks associated with exposure to waterborne pathogens: An expert panel's report on risk assessment. J. Food Protect. 60: 1426-1431.

Nicas, M. 1994. Modeling respirator penetration values with the beta distribution: An application to occupational tuberculosis transmission. Am. Ind. Hyg. Assoc. J. 55(6): 515-524.

Nicas, M. and E. Seto. 1997. A simulation model for occupational tuberculosis transmission. Risk Anal. 17(5): 609-616.

NIOSH. 2001. Exposure and risk assessment for infectious aerosols. Berkeley, CA: National Institute for Occupational Safety and Health. PB2001101415.

Notermans, S., J. Dufrenne, P. Teunis, et al. 1997. A risk assessment study of *Bacillus cereus* present in pasturized milk. Food Microbiology 14: 143-151.

Notermans, S., J. Dufrenne, P. Teunis and T. Chackraborty. 1998. Studies on the risk assessment of *Listeria monocytogenes*. J. Food Protect. 61(2): 244-248.

Oscar, T. 2004. Dose-response model for 13 strains of *Salmonella*. Risk Anal. 24(1): 41-49.

Oscar, T.P. 1998. The development of a risk assessment model for use in the poultry industry. J. Food Saf. 18: 371-381.

Panisello, P.J. and P.C. Quantick. 1998. Application of food MicroModel predictive software in the development of Hazard Analysis Critical Control Point (HACCP) systems. Food Microbiol. 15(4): 425-439.

Pariza, M.W. and E.A. Johnson. 2001. Evaluating the safety of microbial enzyme preparations used in food processing: Update for a new century. Reg. Toxicol. Pharmacol. 33(2): 173-186.

Parkin, R.T., J.A. Soller and A.W. Olivieri. 2003. Incorporating susceptible subpopulations in microbial risk assessment: Pediatric exposures to enteroviruses in river water. J. Expo. Anal. Environ. Epidemiol. 13(2): 161-168.

Pascual, M., M. J. Bouma and A. P. Dobson. 2002. Cholera and climate: Revisiting the quantitative evidence. Microbes and Infection 4: 237-245.

Perz, J.F., F.K. Ennever and S.M. LeBlancq. 1998. *Cryptosporidium* in tap water. Comparison of predicted risks with observed levels of disease. Am. J. Epidemiol. 147(3): 289-301.

Petterson, S.R., N.J. Ashbolt and A. Sharma. 2001. Microbial risks from wastewater irrigation of salad crops: A screening-level risk assessment. Wat. Environ. Res. 72 (6): 667-672.

Petterson, S.R.. and N.J. Ashbolt. 2001. Viral risks associated with wastewater reuse: Modeling virus persistence on wastewater irrigated salad crops. Wat. Sci. Technol. 43(12): 23-26.

Pouillot, R., I. Albert, M. Cornu, et al. 2003. Estimation of uncertainty and variability in bacterial growth using Bayesian inference Application to Listeria monocytogenes. Int. J. Food Microbiol. 81(2): 87-104.

Powell, M., E. Ebel and W. Schlosser. 2001. Considering uncertainty in comparing the burden of illness due to foodborne microbial pathogens. Int. J. Food Microbiol. 69(3): 209-215.

Powell, S.C. and R. Attwell. 1999. The use of epidemiological data in the control of foodborne viruses. Rev. Environ. Health 14(1): 31-37.

Randolph, S. 2002. Predicting the risk of tick borne diseases. Int. J. Med. Microbiol. 291: 6-10.

Reij, M.W. and E.D. Den Aantrekker. 2004. Recontamination as a source of pathogens in processed foods. Int. J. Food Microbiol. 91(1): 1-11.

Reinders, R.D., R. De Jonge and E.G. Evers. 2003. A statistical method to determine whether micro-organisms are randomly distributed in a food matrix, applied to coliforms and *Escherichia coli* O157 in minced beef. Food Microbiol. 20(3): 297-303.

Rose, J.B. and D.J. Grimes. 2001. Reevaluation of microbial water quality: Powerful new tools for detection and risk assessment. Washington, DC: American Academy of Microbiology.

Ross, T., P. Dalgaard and S. Tienungoon. 2000. Predictive modeling of the growth and survival of *Listeria* in fishery products. Int. J. Food Microbiol. 62(3): 231-245.

Ross, T. and J. Sumner. 2002. A simple spreadsheet-based food safety risk assessment tool. Int. J. Food Microbiol. 77(1-2): 39-53.

Roy, E. and P. Robillard. 1994. Effectiveness of and compliance to preventive measures against the occupational transmission of human immunodeficiency virus. Scand. J. Work Environ. Health 20: 393-400.

Ruef, C. 1998. Noscomial Legionnaires disease-strategies for prevention. J. Microbiol. Methods 33: 81-91.

Rusin, P.A., J.B. Rose, C.N. Haas, et al. 1997. Risk assessment of opportunistic bacterial pathogens in drinking water. Rev. Environ. Contam. Toxicol. 152: 57-83.

Salisbury, J.G., T.J. Nicholls, A.M. Lammerding, et al. 2002. A risk analysis framework for the long-term management of antibiotic resistance in food-producing animals. Int. J. Antimicrob. Agents 20(3): 153-164.

Sanaa, M., L. Coroller and O. Cerf. 2004. Risk assessment of listeriosis linked to the consumption of two soft cheeses made from raw milk: Camembert of Normandy and Brie of Meaux. Risk Anal. 24(2): 389-399.

Schlundt, J. 2000. Comparison of microbiological risk assessment studies published. Int. J. Food Microbiol. 58(3): 197-202.

SDRA. 2003. IRAQ: Environmental and health concerns for Swedish deployed personnel. Hogkvarteret, Stockholm: Swedish Defense Research Agency. PB2004101722.

Sherertz, R.J., S. Bassetti and B. Bassetti-Wyss. 2001. “Cloud” health-care workers. Emerging Infect. Dis. 7(2): 241-244.

Simmons, J.E., L.K. Teuschler, C. Gennings, et al. 2004. Component-based and whole-mixture techniques for addressing the toxicity of drinking water disinfection by product mixtures. J. Toxicol. Environ. Health, Part A 67: 741-754.

Sleator, R.D., G.A. Francis, D. O'Beirne, C.G.M. Gahan and C. Hill. 2003. Betaine and carnitine uptake systems in *Listeria monocytogenes* affect growth and survival in foods and during infection. J. Appl. Microbiol. 95(4): 839-846.

Slifko, T.R., D.E. Huffman, B. Dussert, et al. 2002. Comparison of tissue culture and animal models for assessment of *Cryptosporidium parvum* infection. Exp. Parasitol. 101: 97-106.

Smith, P.J., T.J. Thompson and J.A. Jereb. 1997. A model for interval-censored tuberculosis outbreak data. Stat. Med. 16(5): 485-496.

Springthorpe, V.S., C.L. Loh and S.A. Sattar. 1997. How good is modelling of microbial survival in fluvial systems? Wat. Sci. Technol. 35(11-12): 253-259.

Stewart, C.M., B. Cole and D.W. Shaffner. 2003. Managing the risk of staphylococcal food poisoning from cream-filled baked goods to meet a food safety objective. J. Food Protect. 66(7): 1310-1325.

Strachan, N.J., D.R. Fenlon and I.D. Ogden. 2001. Modelling the vector pathway and infection of humans in an environmental outbreak of *Escherichia coli* O157. FEMS Microbiol. Lett. 203(1): 69-73.

Strachan, N.J., G.M. Dunn and I.D. Ogden. 2002. Quantitative risk assessment of human infection from *Escherichia coli* O157 associated with recreational use of animal pasture. Int. J. Food Microbiol. 75: 39-51.

Tamplin, M.L. 2002. Growth of *Escherichia coli* O157:H7 in raw ground beef stored at 10 C and the influence of competitive bacterial flora, strain variation, and fat level. J. Food Protect. 65(10): 1535-1540.

Teunis, P.F.M., A.H. Havelaar and G.J. Medema. 1995. A literature survey on the assessment of microbiological risk for drinking water. Rijksinstituut Voor Volksgezondheid en Milieuhygiene Bilthoven. Report nr. 734301006.

Teunis, P., A. Havelaar, J. Vliegenthart and G. Roessink. 1997a. Risk assessment of *Campylobacter* species in shellfish: Identifying the unknown. Wat. Sci. Technol. 35(11-12): 29-34.

Teunis, P., K. Takumi and K. Shinagawa. 2004. Dose response for infection by *Escherichia coli* O157:H7 from outbreak data. Risk Anal. 24(2): 401-407.

Teunis, P.F. and A.H. Havelaar. 2000. The Beta Poisson Dose-Response Model is not a single-hit model. Risk Anal. 20(4): 513-520.

Teunis, P.F., C.L. Chappell and P.C. Okhuysen. 2002. *Cryptosporidium* dose-response studies: Variation between hosts. Risk Anal. 22(3): 475-485.

Teunis, P.F.M., O.G. van der Heijden, J.W.B., van der Geissen and A.H. Havelaar. 1996. The dose-response relation in human volunteers for gastro-intestinal pathogens. Report No. 284550002. Leeuwenhoeklaan, The Netherlands: National Institute of Public Health and the Environment.

Teunis, P.F.M., G.J. Medema, L. Kruidenier, et al. 1997b. Assessment of the risk of infection by *Cryptosporidium* or *Giardia* in drinking water from a surface water source. Wat. Res. 31(6): 1333-1346.

Todd, E.C.D. 1996. Risk assessment of use of cracked eggs in Canada. Int. J. Food Microbiol. 30(1-2): 125-143.

Torgerson, P.R. and D.D. Heath. 2003. Transmission dynamics and control options for *Echinococcus granulosus*. Parasitology 127: S123-S158.

Torok, T.J., R.V. Tauxe, R.P. Wise, et al. 1997. A large community outbreak of salmonellosis caused by intentional contamination of restaurant salad bars. JAMA 278(5): 389-395.

Trout, D., T.M. Gomez, B.P. Bernard, et al. 1995. Outbreak of brucellosis at a Unites States pork packing plant. JOEM 37: 697-703.

USDA/FSIS. 2003. Risk assessment for *Listeria monocytogenes* in deli meats. US Department of Agriculture/Food Safety and Inspection Service. www.fsis.usda.gov/OPPDE/rdad/FRPubs/97-013F/ListeriaReport.pdf

van Gerwen, S.J.C. and Zwietering, M.H. 1998. Growth and inactivation models to be used in quantitative risk assessments. J. Food Protect. 61: 1541-1549.

Van Impe, J.F., B.M. Nicolai, M. Schellekens, et al. 1995. Predictive microbiology in a dynamic environment: a system theory approach. Int. J. Food Microbiol. 25(3): 227-249.

van Schothorst, M. 1997. Practical approaches to risk assessment. J. Food Protect. 60(11): 1439-1443.

Vose, D.J. 1998. The application of quantitative risk assessment to microbial food safety. J. Food Protect. 61: 640-648.

Voysey, P.A. and M. Brown. 2000. Microbiological risk assessment: a new approach to food safety control. Int. J. Food Microbiol. 58(3): 173-179.

Wadhwa, S.G., G.H. Khaled and S.C. Edberg. 2002. Comparative microbial character of consumed food and drinking water. Crit. Rev. Microbiol. 28(3): 249-279.

Wallace, C. and D. Clayton. 2003. Estimating the relative recurrence risk ratio using a global cross-ratio model. Genetic Epidemiol. 25(4): 293-302.

Walls, I. and V.N. Scott. 1997. Use of predictive microbiology in microbial food safety risk assessment. Int. J. Food Microbiol. 36: 97-102.

Watson, A. and D. Keir. 1994. Information on which to base assessments of risk from environments contaminated with anthrax spores. Epidemiol. Infect. 113: 479-490.

Webb, G.F. and M.J. Blaser. 2002. Mailborne transmission of anthrax: Modeling and implications. PNAS 99(10): 7027-7032.

Wein, L.M., D. Craft and E.H. Kaplan. 2003. Emergency response to an anthrax attack. PNAS 100(7): 4346-4351. Supporting Text on www.pnas.org

Weis, C.P., A.J. Intrepedo, A.K. Miller, et al. 2002. Secondary aerosolization of viable *Bacillus anthracis* spores in a contaminated US Senate office. JAMA 288(22): 2853-2858.

Westrell, T., O. Bergstedt, T.A. Stenstrom and N.J. Ashbolt. 2003. A theoretical approach to assess microbial risks due to failures in drinking water systems. Int. J. Environ. Health Res. 13: 181-197.

Whiting, R.C. 1995. Microbial modeling in foods. Crit. Rev. Food Sci. Nutr. 35: 467-494.

Whiting, R.C. and R.L. Buchanan. 1997. Development of a quantitative risk assessment model for *Salmonella enteritidis* in pasteurized liquid eggs. Int. J. Food Microbiol. 36: 111-125.

Wolleswinkel-van, B.J., N.J. Nagelkerke, J.F Broekmans , et al. 2002. The impact of immigration on the elimination of tuberculosis in The Netherlands: A model based approach. Int. J. Tuberc. Lung Dis. 6(2): 130-136.

Wyn-Jones, A.P. and J. Sellwood. 2001. Enteric viruses in the aquatic environment. J. Appl. Microbiol. 91: 945-962.

Zitter, J.N., P.D. Mazonson, D.P. Miller, et al. 2002. Aircraft cabin air recirculation and symptoms of the common cold. JAMA 288(4): 483-486.

Zwietering, M.G. and S.J.C. van Gerwen. 2000. Sensitivity analysis in quantitative microbial risk assessment. Int. J. Food Microbiol. 58: 213-221.

A.5 Hazard Identification

Ahmed, F., J.D. Clemens, M.R. Rao, et al. 1997. Epidemiology of shigellosis among children exposed to cases of *Shigella* dysentery: A multivariate assessment. Am. J. Trop. Med. Hyg. 56(3): 258-264. 359

Awasthi, S. and S. Moin. 1999. Effectiveness of BCG vaccination against tuberculous meningitis. Indian Pediatrics 36(5): 455-460. 361

Bale, J.F. Jr, B. Zimmerman, J.D. Dawson, et al. 1999. Cytomegalovirus transmission in child care homes. Arch. Pediatr. Adolesc. Med. 153(1): 75-79. 364

Barnes, P.F., Z. Yang, S. Preston-Martin, et al. 1997. Patterns of tuberculosis transmission in central Los Angeles. JAMA 278(14): 1159-1163. 366

Bassett, J., et al. 2002. Project report: Quantitative risk assessment of salmonella in sheep meat produced in New Zealand. New Zealand Food Safety Authority..... 368

Bates, D.W., K. Sands, E. Miller, et al. 1997. Predicting bacteremia in patients with sepsis syndrome. J. Infect. Dis. 176: 1538-1551. 370

Becker, K.M., C.L. Moe, K.L. Southwick, et al. 2000. Transmission of Norwalk virus during football game. N. Engl. J. Med. 343(17): 1223-1227. 372

Bhutta, Z.A., N. Punjwani and B.S. Lindblad. 1996. Concomitant bacteraemia as a risk factor for diarrhoeal disease mortality in Karachi: A case-control study of hospitalized children. Acta Paediatr. 85(7): 809-813. 374

Bowden, K.M. and M.A. McDiarmid. 1994. Occupationally acquired tuberculosis: What's known. J. Occup. Med. 36(3): 320-325. 376

Bradley, M., R. Shakespeare, A. Ruwende, et al. 1996. Epidemiological features of epidemic cholera (El Tor) in Zimbabwe. Trans. R. Soc. Trop. Med. Hyg. 90(4): 378-382..... 378

Breugelmans, J.G., P. Zucs, K. Porten, et al. 2004. SARS transmission and commercial aircraft. Emerg. Infect. Dis. 10(8): 1502-1503. 380

Chang, F.Y., N. Singh, T. Gayowski, et al. 1998. Staphylococcus aureus nasal colonization in patients with cirrhosis: Prospective assessment of association with infection. Infect. Control Hosp. Epidemiol. 19(5): 328-332. 382

Chaulk, C.P., M. Friedman and R. Dunning. 2000. Modeling the epidemiology and economics of directly observed therapy in Baltimore. Int. J. Tuberc. Lung Dis. 4(3): 201-207. 384

Cifuentes, E., J.E. Hernandez, L. Venczel and M. Hurtado. 1999. Panorama of acute diarrhoeal diseases in Mexico. Health & Place 5: 247-255. 386

Cody, S.H., S.L. Abbott, A.A. Marfin, et al. 1999. Two outbreaks of multidrug-resistant Salmonella serotype typhimurium DT104 infections linked to raw-milk cheese in Northern California. JAMA 281(19): 1805-1810. 388

Crump, J.A., A.C. Sulka, A.J. Langer, et al. 2002. An outbreak of *Escherichia coli* O157:H7 infections among visitors to a dairy farm. N. Engl. J. Med. 347(8): 555-560..... 390

Drobniewski, F., I. Eltringham, C. Graham, et al. 2002. A national study of clinical and laboratory factors affecting the survival of patients with multiple drug resistant tuberculosis in the UK. Thorax 57(9): 810-816. 392

Duffy, S., J. Churey, R.W. Worobo, et al. 2000. Analysis and modeling of the variability associated with UV inactivation of *Escherichia coli* in apple cider. J. Food Protect. 63(11): 1587-1590..... 394

Durham, L.K., I.M. Longini, Jr., M.E. Halloran, et al. 1998. Estimation of vaccine efficacy in the presence of waning: Application to cholera vaccines. Am. J. Epidemiol. 147: 948-59. 396

Ejidokun, O.O., D. Killalea, M. Cooper, et al. 2000. Four linked outbreaks of *Salmonella enteritidis* phage type 4 infection-the continuing egg threat. Commun. Dis. Public Health 3(2): 95-100. 398

Hardalo, C. and S.C. Edberg. 1997. *Pseudomonas aeruginosa*: Assessment of risk from drinking water. Crit. Rev. Microbiol. 23(1): 47-75. 400

Harding, I., A.P. MacGowan, L.O. White, et al. 2000. Teicoplanin therapy for *Staphylococcus aureus* septicaemia: Relationship between pre-dose serum concentrations and outcome. J. Antimicrob. Chemother. 45(6): 835-841. 402

Humphrey, T.J., K.W. Martin, J. Slader and K. Durham. 2001. *Campylobacter* spp. in the kitchen: Spread and persistence. J. Appl. Microbiol. 90: 115S-120S. 404

Jaakkola, J.J.K. and O.P. Heinonen. 1994. Shared office space and the risk of the common cold. Euro. J. Epidemiol. 11: 213-216. 406

Jernigan, J.A., A.L. Pullen, C. Partin and W.R. Jarvis. 2003. Prevalence of and risk factors for colonization with methicillin-resistant *Staphylococcus aureus* in an outpatient clinic population. Infect. Control Hosp. Epidemiol. 24(6): 445-450. 408

Jones, R.C., S.I. Gerber, P.S. Diaz, et al. 2004. Intensive investigation of bacterial foodborne disease outbreaks: Proposed guidelines and tools for the collection of dose-response data by local health departments. J. Food Protect. 67(3): 616-623. 410

Kistemann, T., S. Zimmer, I. Vagsholm and Y. Andersson. 2004. GIS-supported investigation of human EHEC and cattle VTEC O157 infections in Sweden: Geographical distribution, spatial variation and possible risk factors. Epidemiol. Infect. 132: 495-505. 412

Kortepeter, M.G. and M.R. Krauss. 2001. Tuberculosis infection after humanitarian assistance, Guantanamo Bay, 1995. Mil. Med. 166(2): 116-120. 414

Matson, D.O. and G. Szucs. 2003. Calicivirus infections in children. Curr. Opin. Infect. Dis. 16(3): 241-246. 416

Mylotte, J.M., M.A. Pisano, S. Ram, et al. 1995. Validation of a bacteremia prediction model. Infect. Control Hosp. Epidemiol. 16(4): 203-209. 418

Pariza, M.W. and E.A. Johnson. 2001. Evaluating the safety of microbial enzyme preparations used in food processing: Update for a new century. Reg. Toxicol. Pharmacol. 33(2): 173-186. 420

Parkin RT, Soller JA and Olivieri AW. 2003. Incorporating susceptible subpopulations in microbial risk assessment: Pediatric exposures to enteroviruses in river water. J. Expo. Anal. Environ. Epidemiol. 13(2): 161-168. 422

Powell, M., E. Ebel and W. Schlosser. 2001. Considering uncertainty in comparing the burden of illness due to foodborne microbial pathogens. Int. J. Food Microbiol. 69(3): 209-215. 424

Randolph, S. 2002. Predicting the risk of tick borne diseases. Int. J. Med. Microbiol. 291: 6-10. 426

Ruef, C. 1998. Noscomial Legionnaires disease-strategies for prevention. J. Microbiol. Methods 33: 81-91. 428

SDRA. 2003. IRAQ: Environmental and health concerns for Swedish deployed personnel. Hogkvarteret, Stockholm: Swedish Defense Research Agency. PB2004101722. 430

Sherertz R.J., S. Bassetti and B. Bassetti-Wyss. 2001. “Cloud” health-care workers. Emerging Infect. Dis. 7(2): 241-244. 432

Sleator, R.D., G.A. Francis, D. O’Beirne, C.G.M. Gahan and C. Hill. 2003. Betaine and carnitine uptake systems in *Listeria monocytogenes* affect growth and survival in foods and during infection. J. Appl. Microbiol. 95(4): 839-846. 434

Tamplin, M.L. 2002. Growth of *Escherichia coli* O157:H7 in raw ground beef stored at 10 C and the influence of competitive bacterial flora, strain variation, and fat level. J. Food Protect. 65(10): 1535-1540. 436

Torok, T.J., R.V. Tauxe, R.P. Wise, et al. 1997. A large community outbreak of salmonellosis caused by intentional contamination of restaurant salad bars. JAMA 278(5): 389-395. 438

Trout, D., T.M. Gomez, B.P. Bernard, et al. 1995. Outbreak of brucellosis at a Unites States pork packing plant. JOEM 37: 697-703. 440

Wyn-Jones, A.P. and J. Sellwood. 2001. Enteric viruses in the aquatic environment. J. Appl. Microbiol. 91: 945-962. 442

Zitter, J.N., P.D. Mazonson, D.P. Miller, et al. 2002. Aircraft cabin air recirculation and symptoms of the common cold. JAMA 288(4): 483-486. 444

A. Hazard ID Study Identification	Ahmed, F., J.D. Clemens, M.R. Rao, et al. 1997. Epidemiology of shigellosis among children exposed to cases of *Shigella* dysentery: A multivariate assessment. Am. J. Trop. Med. Hyg. 56(3): 258-264.
B. Objectives and Type of Study	1. purpose: survey of *Shigella* diarrhea in Bangladesh communities and identification of risk factors 2. type: HI
C. Publication Attributes	1. sponsors/affiliations: United States Agency for International Development, International Centre for Diarrhoeal Disease Research, Diarrhoeal Diseases Control Program of the World Health Organization 2. peer-review mechanism: scientific journal review
D. Data and Study Design	1. type: surveillance of *Shigella* diarrhea and other types of dysentery in children (<5 years of age) in Bangladesh neighborhoods for one month following the identification of *Shigella* diarrhea cases in their neighborhood 2. source: data were collected (during the period November, 1987 to November, 1989) from neighborhoods of persons ("sentinel patients") presenting with symptoms at 3 diarrheal treatment centers; for each sentinel patient, children living in the immediate neighborhood were identified within 48 hours of presentation at the center 3. extent of data: families of the identified children provided information about diarrhea occurrence, feeding practice, education of family, religion, family size, use of latrine, and other variables; children's age and height were recorded; rectal swabs (and accounts of diarrhea) were collected at onset and at intervals for a period of 1 month for detection of *Shigella* isolates 4. sampling plan: see extent of data 5. sample size: 1756 children 6. performance characteristics (error structure for analytical data; repeatability; reproducibility; adequacy of analytical and statistical methods; completeness of study; etc.): NA 7. relevance of data: medium
E. Method/Model/Approach	1. general characteristics: a surveillance study of cases of shigellosis (*Shigella* diarrhea) and associations with host factors (i.e., breast feeding, age, body height-for-age as an index of stunted growth) 2. specific characteristics: NA 3. assumptions: NA 4. limitations: NA 5. relevance (qualitative judgement of the usefulness of the method to incident-based microbial risk assessment for biothreat agents; high, medium, or low): NA
F. Study Conclusions and Extended Applications	1. conclusions supported by the study: among the 1756 children followed, 12% developed *Shigella* diarrhea and 13% developed dysentery not associated with *Shigella*; risk for *Shigella* diarrhea was associated with age (greater risk in children 1 and 2 years old), stunting (greater risk in children with stunted growth), and breast feeding (less risk in children who were breast fed) 2. authors' extrapolations from the observed data to other populations or conditions: NA

G. Data Gaps and Proposed Solutions	1. identification of data gaps: NA 2. assumptions or source of surrogate data to fill gap: NA
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility (method of uncertain usefulness for incident-based microbial risk assessment of buildings and water systems): NA
I. Criteria for Exclusion from Compendium	1. hazard identification
J. Reviewer Comments	other comments by reviewer: the study shows that the geographical area presents an elevated risk of *Shigella* diarrhea in children less than 5 years old, with the greatest risks in children of 1 and 2 years of age with poor nutritional status
K. Cross-References	NA

A. Hazard ID Study Identification	Awasthi, S. and S. Moin. 1999. Effectiveness of BCG vaccination against tuberculous meningitis. Indian Pediatrics 36(5): 455-460.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific. To assess the protective effectiveness of BCG vaccination against tuberculous meningitis, while controlling for age, nutrition and socio-economic status. 2. type: HI
C. Publication Attributes	1. sponsors/affiliations: King George's Medical College, Lucknow, India and Lucknow (UP) State Council for Science and Technology. 2. peer-review mechanism: full scientific peer review
D. Data and Study Design	1. type: This is a hospital based case-control study. Data was collected on the age, sex, immunization and socio-economic status of each subject. The diagnosis of tuberculous meningitis was based on cerebrospinal fluid examination in 179 cases. For the remaining 13 cases where cerebrospinal examination could not be performed, a CT scan was done. 2. source: Children from King George's Medical College between 1 month to 12 years of age admitted from

	September 1995 through August 1997. 3. extent of data: all available data from 1935 through 1992 was included 4. sampling plan: controls were selected randomly and did not include subjects suffering from central nervous system disorders. Test subjects were selected based on clinical symptoms. 5. sample size (number of observations by treatment, number of treatments, etc.): There were 192 cases and 70 controls. 6. performance characteristics: Crude odd's ratio with 95% confidence interval was calculated and logistic regression was performed using STATA software. 7. relevance: low
E. Method/Model/Approach	1. general characteristics: Univariate analysis was done to study the distribution of various variables as well as to compare them among the cases and the controls. 2. specific characteristics: Univariate association between BCG scar and meningitis was done by calculating the crude odd's ratio with 95% confidence interval. Logistic regression was done to find the association of tuberculous meningitis with BCG scar, while controlling for those variables that were found to have univariate association between the case-control status and were clinically meaningful. 3. assumptions: It was assumed that a BCG scar is a appropriate surrogate marker of immune response to immunization. 4. limitations: Since making the diagnosis of tuberculous meningitis is not always foolproof, there may have been misclassification with other types of meningitis which may have biased the results towards null. 5. relevance: NA
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: It was observed that the association between the presence of BCG scar and tuberculous meningitis is confounded by age and weight, and place of residence (rural) is an independent risk factor. It was found that for children with BCG scar, increased weight for age for both the sexes was associated with a lower risk of tuberculous meningitis. Since an association between BCG vaccination and tuberculous meningitis was found with and without controlling for known confounders, the group concluded that BCG vaccination is preventative against tuberculous meningitis. 2. authors' extrapolations from the observed data to other populations or conditions: This group found a 56.04% protective efficacy of BCG against tuberculous meningitis. This is less than the 80.2% reported from Sao Paulo (Filho, et al. Effectiveness of BCG vaccination against tuberculous meningitis: 2 year case-control study in Sao Paulo Brazil. Bull WHO 1990; 68: 69-74.) But in accordance with unclear protective efficacy reported from India in the past (Indian Medical Research Council Tuberculosis Prevention Trial, Madras. Trial of BCG vaccine in South India. Indian J. Med Res, 1980;72 (Suppl): 1-74.). This group also observed that controlling for confounders, that was not done in the Sao Paulo study, resulted in a reduction in the protective efficacy of the vaccine.
G. Data Gaps and Proposed Solutions	1. data gaps: The influence of ethnicity on the protective efficacy of BCG vaccination against tuberculous meningitis needs to be further studied.

	2. proposed solutions: Evaluate the influence of ethnicity.
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: NA
I. Criteria for Exclusion from Compendium	reported data and methods for Hazard Identification (e.g., risk factors, odds ratios, etc.)
J. Reviewer Comments	1. description of most appropriate uses of method for incident-based microbial risk assessment of buildings and water systems: This general method may be used as a model to determine what specific factors in a given population predispose individuals to preferentially become infected upon exposure. 2. other comments by reviewer: none
K. Cross-References	NA

A. Hazard ID Study Identification	Bale, J.F. Jr, B. Zimmerman, J.D. Dawson, et al. 1999. Cytomegalovirus transmission in child care homes. Arch. Pediatr. Adolesc. Med. 153(1): 75-79.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific; Study of family child care homes to determine if this child care alternative represents a safer haven from cytomegalovirus (CMV) excretion than child care centers. 2. type: HI
C. Publication Attributes	1. sponsors/affiliations: National Institutes of Health 2. peer-review mechanism: peer-reviewed journal
D. Data and Study Design	1. type: experimental data collected to determine rate of CMV acquisition 2. source: women providing home child care in their homes were studied to determine rate of CMV seropositivity at baseline and women who were seronegative for CMV were then sampled prospectively at 6-month intervals to determine annual rate of CMV acquisition, children measured for point-prevalence of CMV excretion in family homes 3. extent of data: small, single-city (Iowa City - Cedar Rapids, Iowa) area 4. sampling plan: random selection of homes for sampling

	5. sample size (number of observations by treatment, number of treatments, etc.): 132 women measured and 106 children from 25 randomly selected homes 6. performance characteristics: repeatable; reproducible; analytical and statistical methods adequate; study complete 7. relevance: low
E. Method/Model/Approach	1. general characteristics: stepwise logistic regression 2. specific characteristics: Wilcoxon rank sum test used to compare CMV-seropositive and -seronegative providers with certain provider characteristics; association of categorical variables with baseline seropositivity tested by Fisher exact test; variables suggesting possible association with provider seropositivity included in stepwise logistic regression analysis 3. assumptions: unknown 4. limitations: unknown 5. relevance: NA
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: the aggregate probability of CMV exposure is lower in child care homes than in child care centers 2. authors' extrapolations from the observed data to other populations or conditions: None
G. Data Gaps and Proposed Solutions	1. data gaps: data do not allow determination of precise pattern of transmission 2. proposed solutions: based on what is known (provider seroconverted during study), most likely event was CMV transmission among children and from a single child or children to provider.
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: NA
I. Criteria for Exclusion from Compendium	Insufficient model documentation to demonstrate viable and credible modeling approaches for microbial risk assessment. Study reports data and methods for Hazard Identification (e.g., risk factors, odds ratios, etc.).
J. Reviewer Comments	Does not provide description of most appropriate uses of method for incident-based microbial risk assessment of buildings and water systems.
K. Cross-References	NA

A. Hazard ID Study Identification	Barnes, P.F., Z. Yang, S. Preston-Martin, et al. 1997. Patterns of tuberculosis transmission in central Los Angeles. JAMA 278(14): 1159-1163.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific; Identification of epidemiological links. 2. type: HI
C. Publication Attributes	1. sponsors/affiliations: National Institutes of Health, Title I Ryan White Comprehensive AIDS Resources Emergency Act, CDC, and Los Angeles County-UCLA Medical Center 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: interviews, “homelessness score”, RFLP analysis 2. source: collected data 3. extent of data: small, urban study 4. sampling plan: prospective evaluation of tuberculosis strain clustering 5. sample size: 191 potential patients identified, 162 culture-proven tuberculosis patients, 96 of whom were in 8 clusters 6. performance characteristics: NA 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: unconditional logistic regression analysis performed to identify independent factors associated with clustering 2. specific characteristics: clustered and nonclustered groups compared with X^2 test, comparisons between groups and location tested with Fisher exact test, maximum likelihood odds ratios and 95% confidence intervals for risk of clustering associated with locations and various demographic variables derived via unconditional logistic regression, stepwise regression using backward elimination method performed to identify best predictor(s) of clustering. 3. assumptions: ability to accurately recall whereabouts for 2 years prior to diagnosis, particularly in a group with known alcohol and drug use; clustering of RFLP strains represents recent disease transmission 4. limitations: accurate recall, extension beyond urban population 5. relevance: NA
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: clustering of RFLP strains 2. authors’ extrapolations from the observed data to other populations or conditions: extrapolation to other population sin question because of disagreement that matching RFLP strains are indicative of recent exposure
G. Data Gaps and Proposed	1. data gaps: NA

Solutions	2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: NA
I. Criteria for Exclusion from Compendium	insufficient data quality or quantity to support rigorous science-based modeling. insufficient model documentation to demonstrate viable and credible modeling approaches. study reports detection only without modeling of likely fate and transport or adverse effects. study reports data and methods for Hazard Identification (e.g., risk factors, odds ratios, etc.).
J. Reviewer Comments	NA
K. Cross-References	NA

A. Hazard ID Study Identification	Bassett, J., et al. 2002. Project report: Quantitative risk assessment of salmonella in sheep meat produced in New Zealand. New Zealand Food Safety Authority.
B. Objectives and Type of Study	1. purpose: identification and control of exposure risks during meat by-product processing 2. Type: HI
C. Publication Attributes	1. sponsors/affiliations: The New Zealand Food Safety Authority 2. peer-review mechanism: Unspecified Government Document
D. Data and Study Design	1. type: The report is a compilation of observational and analytical studies designed to elucidate the existence, prevalence and/or possible cause of transmission of S.brandenburg in human, sheep, and ewe populations. 2. source: The completed studies were carried out on sheep and ewes in New Zealand farms. Cases were taken from the endemic area of the South Island, and controls were taken from the relatively uninfected North Island. 3. extent of data: The researchers identified 3 modules related to the production of sheep and ewe byproducts that they focused on; the farm module, the processing module, and the storage/distribution/retail module. A fourth module, the consumer module, was mentioned but the research was unfinished. Data and samples for sheep and ewe were collected throughout the duration of the modules. 4. sampling plan: NA

	5. sample size: NA 6. performance characteristics: NA 7. relevance: medium, involves the serotype S.brandenburg, a non-typhoid salmonella.
E. Method/Model/Approach	1. general characteristics: an observational and analytical study identifying the potential risk for Salmonellosis 2. specific characteristics: multiple case-control study designs, and a cross-sectional study to determine prevalence. 3. assumptions: none 4. limitations: does not provide a sufficient model of risk characterization 5. relevance: NA
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: S.brandenburg is present in the farm environment, and persists in processing plants, but does not appear to persist at the level of meat retailers. 2. extrapolations: Risk for Salmonellosis infection from handling is possible and likely, but if meat transport and storage by retailers is ideal infection appears unlikely.
G. Data Gaps and Proposed Solutions	1. data gaps: Research focused on the persistence of the bacteria throughout sheep and ewe material production, and only discussed the potential for human infection during handling or consumption. Statistics were absent in identifying the risk for potential human infection. 2. proposed solutions: Finalize the research that is noted as on-going.
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: low 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: low 5. defensibility: NA
I. Criteria for Exclusion from Compendium	The study is reporting detection only without modeling of likely fate and transport or adverse effects
J. Reviewer Comments	1. NA 2. other comments by reviewer: The study sufficiently shows the persistence of S.brandenburg during meat by-product processing.
K. Cross-References	NA

A. Hazard ID Study Identification	Bates, D.W., K. Sands, E. Miller, et al. 1997. Predicting bacteremia in patients with sepsis syndrome. J. Infect. Dis. 176: 1538-1551.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific; to develop and validate clinical prediction rules for bacteremia and subtypes of bacteremia in patients with sepsis syndrome. 2. type: HI
C. Publication Attributes	1. sponsors/affiliations: Academic Medical Center Consortium hospitals 2. peer-review mechanism: full scientific peer review
D. Data and Study Design	1. type: Prospective cohort study including a stratified random sample of sepsis syndrome. 2. source: Patient enrollment from eight academic tertiary care hospitals from January 1993 to April 1994. 3. extent of data: 1,342 episodes of sepsis syndrome. 4. sampling plan: Stratified random sample 5. sample size: 1,342 episodes of sepsis syndrome randomly divided into 881 episodes for the derivation set and 461 episodes for the validation set. 6. performance characteristics: NA 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: Univariate and multivariate analysis 2. specific characteristics: Relationships between variables were first evaluated using univariate analysis, using the weighted chi square statistic for categorical variables, weighted t tests for normally distributed continuous variables, and weighted Wilcoxon rank sum tests for nonparametric comparisons. Univariate correlates of bacteremia were then entered into stepwise logistic regression analysis. 3. assumptions: NA 4. limitations: For patients in the general care unit only those who had blood cultures performed were sampled. Some clinical findings that correlate strongly with bacteremia may occur too rarely to exhibit significance in this data set. Using antibiotic therapy at onset as a predictor may be problematic because it could result in ascertainment bias. All data was collected in academic medical centers and thus not clear how well results generalize to other settings (e.g. community hospitals). 5. relevance: NA
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: A model predicting *S. aureus* bacteremia was developed. 2. extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: Due to the small number of outcomes available for the factors predicting fungal bloodstream infection, P<0.10 was used as the threshold for entering the model.

	2. proposed solutions: None proposed.
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: NA
I. Criteria for Exclusion from Compendium	study reports detection only without modeling of likely fate and transport or adverse effects. study reports data and methods for Hazard Identification (e.g., risk factors, odds ratios, etc.).
J. Reviewer Comments	1. description of most appropriate uses of method for incident-based microbial risk assessment of buildings and water systems: Not applicable to buildings or water systems 2. other comments by reviewer: The clinical utility of the rule has to be determined; clinical prediction rules generally do not get used much.
K. Cross-References	NA

A. Hazard ID Study Identification	Becker, K.M., C.L. Moe, K.L. Southwick, et al. 2000. Transmission of Norwalk virus during football game. N. Engl. J. Med. 343(17): 1223-1227.
B. Objectives and Type of Study	1. purpose: scientific; To determine person to person transmission of Norwalk virus among football players during a football game. 2. type: HI
C. Publication Attributes	1. sponsors/affiliations: Centers for Disease Control and Prevention 2. peer-review mechanism: full scientific review
D. Data and Study Design	1. type: retrospective cohort study 2. source: Interviews of football team members potentially exposed to an agent causing gastrointestinal illness and laboratory data from some of those members. 3. extent of data: Interview of 119 people and laboratory analysis of samples from 6 people. 4. sampling plan: Interview all consenting members 5. sample size: 119 people interviewed; laboratory analysis on six samples.

	6. performance characteristics: NA 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: Chi-square tests for statistical significance and multivariate analysis with use of step-wise, backward logistic regression. 2. specific characteristics: Chi-square tests for statistical significance and multivariate analysis with use of step-wise, backward logistic regression. 3. assumptions: Interview questions were answered truthfully. 4. limitations: Study limited to contact sport (e.g. football). 5. relevance: NA
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: Study documents person to person transmission of Norwalk virus among players during a football game. 2. authors' extrapolations from the observed data to other populations or conditions: Players with acute gastroenteritis should be excluded from competition to avoid transmitting the disease to other players.
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: NA
I. Criteria for Exclusion from Compendium	insufficient model documentation to demonstrate viable and credible modeling approaches. study reports data and methods for Hazard Identification (e.g., risk factors, odds ratios, etc.).
J. Reviewer Comments	NA
K. Cross-References	NA

A. Hazard ID Study Identification	Bhutta, Z.A., N. Punjwani and B.S. Lindblad. 1996. Concomitant bacteraemia as a risk factor for diarrhoeal disease mortality in Karachi: A case-control study of hospitalized children. Acta Paediatr. 85(7): 809-813.

B. Objectives and Type of Study	1. purpose noted by study authors: scientific; to evaluate risk factors for death due to diarrhoea among hospitalized children at the Aga Khan University Hospital. 2. type: HI
C. Publication Attributes	1. sponsors/affiliations: Aga Khan University Medical Center, Karachi, Pakistan 2. peer-review mechanism: full scientific review
D. Data and Study Design	1. type: Retrospective case-control study 2. source: All diarrhoea deaths at Aga Khan University Hospital from 1988 to 1993. 3. extent of data: 42 deaths and 84 matched controls. 4. sampling plan: NA 5. sample size: 126 (includes 84 controls). 6. performance characteristics: Not given 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: Univariate methods and logistic regression analysis. 2. specific characteristics: Data analyzed for differences among continuous variables by analysis of variance and for categorical variables by univariate analysis, computation of respective odds ratios and corresponding 98% confidence intervals using Epi-Info. Risk factors for mortality were further evaluated for significance by multivariate logistic regression using EGRET. 3. assumptions: NA 4. limitations: NA 5. relevance: NA
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: Systemic illnesses and bacteraemia are important complications of diarrhoea in a defined group of hospitalized children. Critically ill children with diarrhoea should be screened and treated for probable bacteraemia. 2. authors' extrapolations from the observed data to other populations or conditions: None.
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: NA

I. Criteria for Exclusion from Compendium	study reports detection only without modeling of likely fate and transport or adverse effects. study reports data and methods for Hazard Identification (e.g., risk factors, odds ratios, etc.).
J. Reviewer Comments	NA
K. Cross-References	NA

A. Hazard ID Study Identification	Bowden, K.M. and M.A. McDiarmid. 1994. Occupationally acquired tuberculosis: What's known. J. Occup. Med. 36(3): 320-325.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific. The study aimed to elucidate the magnitude of risk of occupationally acquired tuberculosis. 2. type: HI
C. Publication Attributes	1. sponsors/affiliations: Branch Clinic White Oak, Naval Surface Warfare Center, Silver Spring, MD 2. peer-review mechanism: full scientific peer review
D. Data and Study Design	1. type: Literature and phone sources were reviewed and employee tuberculosis infection rates were obtained from routine annual monitoring and post-exposure epidemic investigations and incidence rates of employees obtaining tuberculosis occupationally were included. 2. source: Aggressive telephone solicitation and literature review. 3. extent of data: all available data from 1935 through 1992 was included 4. sampling plan: random. All available data in the United States was utilized for this evaluation. 5. sample size: large 6. performance characteristics: only simple statistics were provided (% incident rates of infection). 7. relevance: low
E. Method/Model/Approach	1. general characteristics: Literature and phone sources were reviewed and employee tuberculosis infection rates were obtained from routine annual monitoring and post-exposure epidemic investigations and incidence rates of employees obtaining tuberculosis occupationally was included. 2. specific characteristics: Conversion rates were calculated from the yearly number of new purified protein derivative skin test reactions in the screened population at risk for exposure to tuberculosis. 3. assumptions: the obtained data is representative of all cases 4. limitations: There is a limited amount of information available on occupationally acquired tuberculosis.

	5. relevance: NA
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: The magnitude of tuberculosis infection and disease risk to the health care worker is presently unclear however the implications are distinct. Case finding and isolation of the patient/client population in addition to aggressive worker surveillance are critical elements in resurrecting the public health infrastructure to be enormously successful in managing this disease. 2. authors' extrapolations from the observed data to other populations or conditions: NA
G. Data Gaps and Proposed Solutions	1. data gaps: Limited data were available. 2. proposed solutions: None. The limited data indicate that employer surveillance of employees and employee reporting of occupationally acquired tuberculosis is inadequate.
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: NA
I. Criteria for Exclusion from Compendium	insufficient data quality or quantity to support rigorous science-based modeling. insufficient model documentation to demonstrate viable and credible modeling approaches. study reports data and methods for Hazard Identification (e.g., risk factors, odds ratios, etc.).
J. Reviewer Comments	NA
K. Cross-References	NA

A. Hazard ID Study Identification	Bradley, M., R. Shakespeare, A. Ruwende, et al. 1996. Epidemiological features of epidemic cholera (El Tor) in Zimbabwe. Trans. R. Soc. Trop. Med. Hyg. 90(4): 378-382.
B. Objectives and Type of Study	1. purpose: to study temporal patterns of outbreak of symptomatic cases of cholera in 2 geographical areas 2. type: HI
C. Publication Attributes	1. sponsors/affiliations: World Health Organization 2. peer-review mechanism: scientific journal review
D. Data and Study Design	1. type: surveillance of cholera in 2 geographical areas - Tongogara and Middle Sabi

	2. source: surveys of symptomatic cases, age, and gender 3. extent of data: temporal data for symptomatic cases in the two regions were collected 4. sampling plan: NA 5. sample size: 48,374 subjects in Tongogara and 8209 subjects in Middle Sabi 6. performance characteristics (error structure for analytical data; repeatability; reproducibility; adequacy of analytical and statistical methods; completeness of study; etc.): NA 7. relevance of data: medium

E. Method/Model/Approach	1. general characteristics: the patterns of daily case frequencies as a function of time (days) were distinctly different in the two regions: a fast pattern at Tongogara in which the daily case frequency increased rapidly (initial exponential doubling time of 1.2 days), peaked within the first 10-14 days of the outbreak, showed a second phase of outbreak after 28 days, and the last case was reported at 124 days; and a slow pattern at Middle Sabi in which the daily case frequency increased slowly (initial exponential doubling time of 4.3 days), peaked at 50 days, and the last case was reported at 149 days; the patterns were qualitatively associated with different demographic and spatial characteristics of the two regions 2. specific characteristics: different mathematical models were applied to the Tongogara data in an attempt to theoretically explain the second phase of outbreak 3. assumptions: NA4. limitations: NA 5. relevance (qualitative judgement of the usefulness of the method to incident-based microbial risk assessment for biothreat agents; high, medium, or low): NA
F. Study Conclusions and Extended Applications	1. conclusions supported by the study: statistical analysis suggested that the second phase of outbreak at Tongogara may have been related to differing population densities associated with different water sources within Tongogara. 2. authors' extrapolations from the observed data to other populations or conditions: NA
G. Data Gaps and Proposed Solutions	1. identification of data gaps: NA 2. assumptions or source of surrogate data to fill gap: NA
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility (method of uncertain usefulness for incident-based microbial risk assessment of buildings and water systems): NA
I. Criteria for Exclusion from Compendium	hazard identification
J. Reviewer Comments	NA
K. Cross-References	NA

A. Hazard ID Study Identification	Breugelmans, J.G., P. Zucs, K. Porten, et al. 2004. SARS transmission and commercial aircraft. Emerg. Infect. Dis. 10(8): 1502-1503.
B. Objectives and Type of Study	1. purpose noted by study authors: to document SARS transmission during international flights 2. type: HI
C. Publication Attributes	1. sponsors/affiliations: Robert Koch Institute, Berlin. 2. peer-review mechanism: NA (study results were reported as a letter)
D. Data and Study Design	1. type: observational data 2. source: subject letters 3. extent of data: small data set; 36 of possible 250 passengers 4. sampling plan: none; study included all willing/accessible participants 5. sample size: 36 participants 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: reports study of passengers that were seated in close proximity of a SARS-infected passenger 2. specific characteristics: none of the passengers reported symptoms characteristic of SARS, and all blood samples were negative for SARS-associated coronavirus immunoglobulin G antibodies. 3. assumptions: NA 4. limitations: selection of study participants was not random; nonparticipation rate was very high (214/250) 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: no evidence of SARS transmission was found 2. extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: high nonparticipation rate 2. proposed solutions: authors recommended strengthening the collaboration between national health authorities and the airline industry
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: low 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: low 5. defensibility: NA

I. Criteria for Exclusion from Compendium	reported data and/or methods for hazard identification
J. Reviewer Comments	NA
K. Cross-References	NA

A. Hazard ID Study Identification	Chang, F.Y., N. Singh, T. Gayowski, et al. 1998. Staphylococcus aureus nasal colonization in patients with cirrhosis: Prospective assessment of association with infection. Infect. Control Hosp. Epidemiol. 19(5): 328-332.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific; To determine if *Staphyloccoccus aureus* colonization of the anterior nares was a risk factor for *S. aureus* infection in patients with cirrhosis and to determine the predictors of *S. aureus* infection in colonized patients. 2. type: HI
C. Publication Attributes	1. sponsors/affiliations: University of Pittsburgh, Veterans Affairs Medical Center, Pittsburgh and Houston, Wake Forest University Baptist Medical Center, Winston-Salem, and Erie County Medical Center, Buffalo 2. peer-review mechanism: full scientific peer review
D. Data and Study Design	1. type: clinical data for *Staphyloccoccus aureus* colonization in anterior nares in patients. 2. source: Patients admitted to hospitals 3. extent of data: 84 consecutive patients 4. sampling plan: Random? 5. sample size: 84 consecutive patients 6. performance characteristics: multiple logistic regression model was used to evaluate the effect of several variables on the outcome. 7. relevance: low
E. Method/Model/Approach	1. general characteristics: 84 consecutive patients with cirrhosis admitted to the liver transplant unit. No modeling approach noted. 2. specific characteristics: Child-Pugh score, which combines five different individually weighted clinical and laboratory indices for hepatic dysfunction was used to generate scores. Categorical data analyzed using a chi-square of Fisher test. Continuous variables were compared by using the t test or Mann-Whitney test. A logistic regression model used to examine the effects of multiple risk factors on recurrence. 3. assumptions: none identified

	4. limitations: none identified 5. relevance: NA
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: Colonization of the anterior nares was a significant predictor of *S. aureus* infection in patients with cirrhosis 2. authors' extrapolations from the observed data to other populations or conditions: none reported
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: NA
I. Criteria for Exclusion from Compendium	insufficient data quality or quantity to support rigorous science-based modeling. insufficient model documentation to demonstrate viable and credible modeling approaches. study reports detection only without modeling of likely fate and transport or adverse effects. study reports data and methods for Hazard Identification (e.g., risk factors, odds ratios, etc.).
J. Reviewer Comments	NA
K. Cross-References	NA

A. Hazard ID Study Identification	Chaulk, C.P., M. Friedman and R. Dunning. 2000. Modeling the epidemiology and economics of directly observed therapy in Baltimore. Int. J. Tuberc. Lung Dis. 4(3): 201-207.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific; Modeling was conducted to estimate the range of TB cased prevented by directly observed therapy. 2. type: HI
C. Publication Attributes	1. sponsors/affiliations: City Chest Clinic, Johns Hopkins Schools of Hygiene and Public Health and Medicine, Baltimore City Health Department 2. peer-review mechanism: full scientific peer-review

D. Data and Study Design	1. type: estimated range of TB cases prevented and dollars saved 2. source: tuberculosis estimates based on CDC TB trend data for US and for large US city TB trend and health care expenditure estimates based on cost data from published literature 3. extent of data: TB trends from 1978 through 1992 for Baltimore 4. sampling plan: model estimation 5. sample size: 1577 (US TB trend) or 2233 (large US city TB trend) cases predicted; treatment costs saved estimated at $18.8 million (US TB trend) or $27.1 million (large US city TB trend) 6. performance characteristics: study is complete, highly repeatable and reproducible with adequate employment of analytical methods 7. relevance: NA
E. Method/Model/Approach	1. general characteristics: model estimation of TB cases and dollars saved 2. specific characteristics: used CDC data to estimate cases and costs had DOT not been implemented 3. assumptions: that Baltimore cases would have been a number between the CDC US trend and large state trend for TB; change in # of TB cases and dollars spent impacted only by DOT and no other changes 4. limitations: quality of CDC data used in estimations; estimates based on average values which is possibly conservative estimate, especially since large city average included Baltimore and other city stats in which DOT had been implemented; DOT is truly the only cause for reduction in TB cases; generalizability to other locations 5. relevance: NA
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: DOT was successful in reducing both incidence of TB and associated costs 2. authors' extrapolations from the observed data to other populations or conditions: DOT success may not generalize to other locations
G. Data Gaps and Proposed Solutions	1. data gaps: true expected cases or costs 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: NA
I. Criteria for Exclusion from Compendium	insufficient data quality or quantity to support rigorous science-based modeling. insufficient model documentation to demonstrate viable and credible modeling approaches. study reports detection only without modeling of likely fate and transport or adverse effects.

J. Reviewer Comments	NA
K. Cross-References	NA

A. Hazard ID Study Identification	Cifuentes, E., J.E. Hernandez, L. Venczel and M. Hurtado. 1999. Panorama of acute diarrhoeal diseases in Mexico. Health & Place 5: 247-255.
B. Objectives and Type of Study	1. purpose: future regulatory interest, scientific; examine the recent panorama of ADD-related deaths in Mexico in an effort to assess the overall impact of control measures that may vary in space and time. 2. type: HI
C. Publication Attributes	1. sponsors/affiliations: Center of Human Ecology and Health (ECO) 2. peer-review mechanism: scientific journal review
D. Data and Study Design	1. type: Data were collected from the national mortality registry and national census. Both types of data were incorporated into a vector-based geographic information system. Data ranges from 1985 to 1995. 2. source: national mortality registry and national census; government datasets 3. extent of data: Data ranges from 1985 to 1995 throughout the country of Mexico. 4. sampling plan: Sampling was random. An evaluation was made based on the location of deaths or infection across the country of Mexico. 5. sample size: NA 6. performance characteristics: NA 7. relevance: low.
E. Method/Model/Approach	1. general characteristics: Data were collected from government datasets and analyzed based on linear regression models in order to assess and identify areas and socio-economic populations that are more at risk for acute diarrhoeal disease. 2. specific characteristics: NA 3. assumptions: NA 4. limitations: NA 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions: Higher socio-economic groups had a lower risk of ADD death than those in lower socio-economic groups. Between 1985 and 1990, the highest rates of ADD mortality in children were found in the municipalities of

	the central and southeastern states of Mexico. ADD death was found to decrease in older groups. 2. authors' extrapolations: Substantial improvements in health indicators were noticed among the younger generations during the period of 1991-1992.
G. Data Gaps and Proposed Solutions	1. data gaps: Lack of morbidity data and published epidemiological studies restricted the analysis to computerized data on mortality. 2. proposed solutions: disinfection of water, handwashing, and education
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	This study reports data and methods for Hazard Identification.
J. Reviewer Comments	NA
K. Cross-References	NA

A. Hazard ID Study Identification	Cody, S.H., S.L. Abbott, A.A. Marfin, et al. 1999. Two outbreaks of multidrug-resistant Salmonella serotype typhimurium DT104 infections linked to raw-milk cheese in Northern California. JAMA 281(19): 1805-1810.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific; Provides a determination of an outbreak source. 2. type: HI
C. Publication Attributes	1. sponsors/affiliations: Centers for Disease Control 2. peer-review mechanism: peer-reviewed journal
D. Data and Study Design	1. type: environmental and laboratory data, surveillance data, questionnaire data 2. source: salmonella cultures from reported outbreaks and matched controls, questionnaire responses from cases studies and controls regarding recall exposures for prior week; Outbreak 2 data uncovered under enhanced surveillance 3. extent of data: salmonella isolates found all from persons with Spanish surnames, interviews collected via telephone conducted in Spanish, both outbreaks were cases of *Salmonella* Typhimurium var Copenhagen strain

	4. sampling plan (random, clustered, factorial design, etc.): case-control study 5. sample size (number of observations by treatment, number of treatments, etc.): 16 cases and 25 controls in Outbreak 1; 79 cases in Outbreak 2 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: maximum likelihood estimation of odds ratios and 95% confidence interval 2. specific characteristics: NA 3. assumptions: assume recall for past week's exposures is valid 4. limitations: Outbreak 2 case definition reflected assumption that the cases belonged to Outbreak 1 and that they were simply measuring the magnitude of Outbreak 1, thereby biasing the case findings and precluding identification of another vehicle than cheese. Laboratory constraints at time limited comprehensive subtyping of isolates. It is unknown how many different dairies contributed to the 2 outbreaks or whether outbreaks originated from 1 or more dairies. 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: raw milk Mexican style cheese was the major, if not the only, vehicle causing infections in the outbreaks and pose a risk for multi-drug-resistant *Salmonella typhimurium* DT104 infections 2. authors' extrapolations from the observed data to other populations or conditions: Infections from raw milk products are not limited to the San Francisco Bay Area and the implication of raw milk as a pathogen vehicle are substantial.
G. Data Gaps and Proposed Solutions	1. data gaps: Other vehicles contributing to outbreak not considered. 2. proposed solutions: cannot identify with certainty unless have sample of contaminated product, so sample product.
H. Weight of Evidence	1. robustness of method : NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: NA
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	NA
K. Cross-References	NA

A. Hazard ID Study Identification	Crump, J.A., A.C. Sulka, A.J. Langer, et al. 2002. An outbreak of *Escherichia coli* O157:H7 infections among visitors to a dairy farm. N. Engl. J. Med. 347(8): 555-560.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific; Provides description of an outbreak of *E. coli* as a result of a visit to a farm. 2. type: HI
C. Publication Attributes	1. sponsors/affiliations: Centers for Disease Control and Prevention 2. peer-review mechanism: fully scientific journal review
D. Data and Study Design	1. type: Experimental data for microbial characterization (Swaminathan et al., 2001; Centers for Disease Control and Prevention, 2000; Olsen et al., 1991), Epidemiologic investigation (CDC standard foodborne-illness hypothesis-generating questionnaire, http://www.cdc.gov/ncidod/dbmd/outbreak/stand_qu.htm) and environmental investigations (source of infection). 2. source: Published data and government datasets 3. extent of data: datasets for bacterial characterization and source of infection 4. sampling plan: patients and controls enrolled on the basis of their date of visit to the farm, contact with animals and their environment, hand washing) 5. sample size: 216 cattle, 19,698 telephone numbers contacted and 3497 households contacted,43 animals other than cattle, 37 surface swabs (from the lower railing of the heifer-area fence), 7 Biofilm samples from watering troughs, and 7 water samples. 6. performance characteristics: Collection and transport of samples and culture methods might have affected the rates of *E. coli* O157:H7 colonization in cattle. 7. relevance: low
E. Method/Model/Approach	1. general characteristics: a case-control study and a household survey, multivariate logistic-regression model to identify independent variables (direct contact with animals, environmental exposures, hand-mouth activities, foods and beverages, and hand-washing behavior). 2. specific characteristics: Univariate analysis of risk factors for *E. coli* infection, multivariate analysis of exposures among patients and controls. Analysis stratified according to age, statistical analysis performed (Epi Info, SAS System and LogXact for Windows). 3. assumptions: Among 51 patients, 15 confirmed cases and 36 probable cases of *E. coli* O157:H7 have been identified, 33 of 216 cattle were colonized with *E. coli*, 1 of 7 biofilm samples and 1 of 37 surface swabs were infected and water samples were negative.

	4. limitations: Collection and transport of samples and culture methods might have affected the rates of *E. coli* O157:H7 colonization rates. 5. relevance: NA
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: high rates of carriage of *E. coli* O157:H7 among calves and young cattle, zoonotic transmission. 2. extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: NA
I. Criteria for Exclusion from Compendium	insufficient data quality or quantity to support rigorous science-based modeling: Possibly insufficient model documentation to demonstrate viable and credible modeling approaches. study reports data and methods for Hazard Identification (e.g., risk factors, odds ratios, etc.). Risk factor identification, bacterial characterization
J. Reviewer Comments	NA
K. Cross-References	NA

A. Hazard ID Study Identification	Drobniewski, F., I. Eltringham, C. Graham, et al. 2002. A national study of clinical and laboratory factors affecting the survival of patients with multiple drug resistant tuberculosis in the UK. Thorax 57(9): 810-816.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific; The study aimed to describe the clinical, microbiological, molecular epidemiology and treatment of multi-drug resistant tuberculosis (MDRTB) cases in the UK and to determine factors associated with survival. 2. type: HI
C. Publication Attributes	1. sponsors/affiliations: Public Health Laboratory Service Mycobacterium Reference Unit and Department of Microbiology, King's College Hospital (Dulwich), East Dulwich Grove, London.

	2. peer-review mechanism: full scientific peer review
D. Data and Study Design	1. type: Molecular epidemiology (DNA fingerprinting) was conducted on the samples and clinical and epidemiological factors associated with each case were recorded. 2. source: Ninety multi-drug resistant tuberculosis cases in the UK from the Public Health Laboratory Service, Mycobacterium Reference Laboratory, and Public Health Laboratory Regional Centers for Mycobacterium. 3. extent of data: Patients identified in case centers from January 1, 1996 through June 30, 1997. 4. sampling plan: clustered 5. sample size: 90 patients were used in this evaluation. For each case evaluated tuberculosis drug resistance profiles were determined as well as several clinical, microbiological, and radiological variables. 6. performance characteristics: only simple statistics were provided (means, median ranges, confidence limits on mean values). 7. relevance: low
E. Method/Model/Approach	1. general characteristics: Demographic details for each patient, microbiological and clinical factors including: prior Tuberculosis infection, immunocompromised status, HIV infection status, fever, weight loss, productive cough, haemoptysis, shortness of breath, chest pain, and history of pulmonary disease. Radiology was performed as well as a sputum smear, bacterial culture within 30 days, and a drug resistance screening. 2. specific characteristics: The percentage of each of these variables that were associated with survival of a multi-drug resistant tuberculosis infection were reported. 3. assumptions: this population is representative of individuals with tuberculosis infection in the UK 4. limitations: The sample size was limited to the 90 cases evaluated. 5. relevance: NA
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: Immunocompromised status, failure to culture the bacterium in 30 days or to apply appropriate three drug treatment, and age were significant factors in mortality. An immunocompromised patient was nearly nine times more likely to die while application of treatment reduced risk. Increasing age was associated with increased risk or death. 2. extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: The sample size was limited. 2. proposed solutions: Increase sample size
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: NA

I. Criteria for Exclusion from Compendium	insufficient data quality or quantity to support rigorous science-based modeling. study reports data and methods for Hazard Identification (e.g., risk factors, odds ratios, etc.)
J. Reviewer Comments	NA
K. Cross-References	NA

A. Hazard ID Study Identification	Duffy, S., J. Churey, R.W. Worobo, et al. 2000. Analysis and modeling of the variability associated with UV inactivation of *Escherichia coli* in apple cider. J. Food Protect. 63(11): 1587-1590.
B. Objectives and Type of Study	1. purpose: statistical analysis of a process (UV irradiation in a specially-designed machine called a tube) to reduce levels of *E. coli* in apple cider 2. type: HI
C. Publication Attributes	1. sponsors/affiliations: Rutgers University; Cornell University 2. peer-review mechanism: scientific journal review
D. Data and Study Design	1. type: experimental data on levels of *E. coli* in apple cider with and without UV treatment 2. source: data collected for this study 3. extent of data: characterization of the decrease in *E. coli* numbers in inoculated cider after UV treatment; studied variables were the mean reduction in *E. coli* numbers and the variability around the mean for each apparatus 4. sampling plan: machines (i.e., tubes) which did not reduce *E. coli* number by 10^5 were not included in the analysis 5. sample size: 70 tubes, each tested 12 times for reduction of *E. coli* in a batch of inoculated cider 6. performance characteristics (error structure for analytical data; repeatability; reproducibility; adequacy of analytical and statistical methods; completeness of study; etc.): NA 7. relevance of data: medium; the use of the data to describe variability in the efficacy of the treatment (i.e., the prevalence of *E. coli* in the treated cider) demonstrates the importance of characterizing variability in exposure assessment for food-borne microbial agents
E. Method/Model/Approach	1. general characteristics: application of distribution models to two variables: mean reduction in *E. coli* numbers and variability around the mean reduction 2. specific characteristics: various distribution models were fit to the two variables; a Kolmogorov-Smirnov test was used to assess the best fitting model

	3. assumptions: NA4. limitations: NA 5. relevance (qualitative judgement of the usefulness of the method to incident-based microbial risk assessment for biothreat agents; high, medium, or low): medium; application of the distribution models to the data demonstrates the importance of characterizing variability in exposure assessment for food-borne microbial agents
F. Study Conclusions and Extended Applications	1. conclusions supported by the study: the distribution models predict that if only tubes with higher than $10^{5.5}$ reduction in *E. coli* were marketed, the probability of machine failure would be decreased significantly 2. authors' extrapolations from the observed data to other populations or conditions: NA
G. Data Gaps and Proposed Solutions	1. identification of data gaps: study only assesses prevalence aspect of exposure, does not include aspects of media or host growth 2. assumptions or source of surrogate data to fill gap: NA
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility (method of uncertain usefulness for incident-based microbial risk assessment of buildings and water systems):low - agent not on list of threats, exposure method does not include aspects of growth in media or host
I. Criteria for Exclusion from Compendium	hazard identification - study produced data distributions that could be used in an exposure assessment
J. Reviewer Comments	NA
K. Cross-References	NA

A. Hazard ID Study Identification	Durham, L.K., I.M. Longini, Jr., M.E. Halloran, et al. 1998. Estimation of vaccine efficacy in the presence of waning: Application to cholera vaccines. Am. J. Epidemiol. 147: 948-59.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific; to present a nonparametric method for estimating vaccine efficacy as a smooth function of time from vaccine trials. 2. type: HI, RC

C. Publication Attributes	1. sponsors/affiliations: NIH 2. peer-review mechanism: scientific journal
D. Data and Study Design	1. type: Comparison of confirmed cholera illness cases between vaccinated and unvaccinated study subjects 2. source: Cholera vaccine trial in rural Matlab, Bangladesh 3. extent of data: 89,596 subjects over a 4.5 year study. 4. sampling plan: Randomized double blinded study; only those participants receiving all three doses of vaccine or placebo are included in analysis. 5. sample size: total of 62,285 analyzed; split into 3 groups: placebo (20,837), WC vaccine (20,742), and BS-WC vaccine (20,705). 6. performance characteristics: NA 7. relevance: high
E. Method/Model/Approach	1. general characteristics: Nonparametric method for estimating vaccine efficacy as a smooth function of time from vaccine trials. 2. specific characteristics: A method using smoothing scaled residuals from a proportional hazards model was used. The four steps were: 1. Fit an ordinary proportional hazards model tho the data using the partial likelihood function ; 2. Compute the scaled differences between the actual and expected covariate values at each event time (Schoenfeld residuals); 3. Scale the residuals and add the coefficient from the ordinary proportional hazards model; 4. Recover the time-varying regressions coefficient. 3. assumptions: NA 4. limitations: time dependencies of disease incidence and waning protective effects produce unreliable estimates 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: Differential protection and waning effects for the vaccines as a function of biotype and age were revealed. The estimation procedure allows investigators to assess time-varying changes in vaccine-induced protection. 2. authors' extrapolations: The estimation procedure allows investigators to assess time-varying changes in vaccine-induced protection.
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: high 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: high

	5. defensibility: low
I. Criteria for Exclusion from Compendium	study reports data and methods for hazard identification and vaccine efficacy for limited risk characterization
J. Reviewer Comments	NA
K. Cross-References	NA

A. Hazard ID Study Identification	Ejidokun, O.O., D. Killalea, M. Cooper, et al. 2000. Four linked outbreaks of *Salmonella enteritidis* phage type 4 infection-the continuing egg threat. Commun. Dis. Public Health 3(2): 95-100.
B. Objectives and Type of Study	1. purpose: assess prevalence of gastrointestinal symptoms among subjects attending four catered events associated with *Salmonella enteritidis* phage type 4 infections and examine possible associations with types of foods eaten at the events 2. type: HI
C. Publication Attributes	1. sponsors/affiliations: Dudley Health Authority 2. peer-review mechanism: scientific journal review
D. Data and Study Design	1. type: prevalence of gastrointestinal disease symptoms and application of logistic regression models to assess possible associations with food types 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics (error structure for analytical data; repeatability; reproducibility; adequacy of analytical and statistical methods; completeness of study; etc.): NA 7. relevance of data: NA
E. Method/Model/Approach	1. general characteristics: NA 2. specific characteristics: NA 3. assumptions: NA4. limitations: NA 5. relevance: NA
F. Study Conclusions and Extended Applications	1. conclusions supported by the study: logisitic regression analysis of survey data of foods eaten indicated that egg-containing foods were frequently associated with disease

	2. authors' extrapolations from the observed data to other populations or conditions: NA
G. Data Gaps and Proposed Solutions	1. identification of data gaps: NA 2. assumptions or source of surrogate data to fill gap: NA
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility NA
I. Criteria for Exclusion from Compendium	hazard identification
J. Reviewer Comments	NA
K. Cross-References	NA

A. Hazard ID Study Identification	Hardalo, C. and S.C. Edberg. 1997. *Pseudomonas aeruginosa*: Assessment of risk from drinking water. Crit. Rev. Microbiol. 23(1): 47-75.
B. Objectives and Type of Study	1. purpose: scientific and future regulatory - The article addresses the key health risk factors concerning *P. aeruginosa* and provides a biological framework for its risk assessment, particularly for regulation in food and drinking water. 2. type: HI
C. Publication Attributes	1. sponsors/affiliations: Clinical Microbiology Laboratory, Yale-New Haven and Departments of Laboratory Medicine and Internal Medicine, Yale University School of Medicine, New Haven, CT. 2. peer-review mechanism: peer review journal
D. Data and Study Design	1. type: hazard identification for *P. aeruginosa* 2. source: review of published articles 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA

	6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: NA 2. specific characteristics: NA 3. assumptions: NA 4. limitations: NA 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: *P. aeruginosa* requires very specific host susceptibilities or immune defects in order to cause infections 2. authors' extrapolations: Prevention, early detection, and eradication of colonization are likely to be more effective than attempting to control the number of *P. aeruginosa* ingested.
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: low 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	reviewed data for hazard identification
J. Reviewer Comments	Modeling not performed
K. Cross-References	NA

A. Hazard ID Study Identification	Harding, I., A.P. MacGowan, L.O. White, et al. 2000. Teicoplanin therapy for *Staphylococcus aureus* septicaemia: Relationship between pre-dose serum concentrations and outcome. J. Antimicrob. Chemother. 45(6): 835-841.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific, regulatory, and future regulatory interest - Establish, by logistic regression, what relationship, if any, exists between clinical outcome and factors such as patient demographics,

	dosage regimen, serum concentration and teicoplanin MIC for the infecting organism. 2. type: HI
C. Publication Attributes	1. sponsors/affiliations: Hoechst Marion Roussel 2. peer-review mechanism: scientific journal review
D. Data and Study Design	1. type: Establish which factors account for treatment success. 2. source: A study database held by Hoechst Marion Roussel 3. extent of data: serum concentration data pre- and post dosing with teicoplanin for patients known to have primary *S. aureus* septicaemia. Probability curves and charts 4. sampling plan: 719 patients from a variety of studies. Sampling plan is unknown. 5. sample size: 80 patients formed the basis for the study with 78 being included in the final logistic regression model 6. performance characteristics: calculation of the duration of treatment, mean dose administered, Student's *t*-test, Hosmer and Lemeshow test. 7. relevance: low
E. Method/Model/Approach	1. general characteristics: Logistical regression using SAS© to determine which variables influenced clinical outcome. 2. specific characteristics: Stepwise selection to decrease number of variables influencing outcome: entry set at 0.25, removal set at 0.3. basic statistical calculations (probability and mean). Goodness of fit test assessed by using Hosmer and Lemeshow. 3. assumptions: None found 4. limitations: No preliminary data provided on the patients. Data from multiple studies. Possible variation in definition of clinical cure and timings of serum concentrations 5. relevance: NA
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: More frequent the dosing of teicoplanin may be optional. Transient high peak serum concentrations of teicoplanin are not likely to be os benefit in killing bacteria or curing infection and that sustained concentrations over the MIC will be of benefit in terms of improving extravascular drug penetration and cure rates. For the treatment of septicaemia with teicoplanin, the analysis shows that the two most readily quantifiable factors that influence successful outcome are mean pre-dose serum concentration and age. 2. authors' extrapolations from the observed data to other populations or conditions: The model developed here can be used to predict what trough serum concentrations are needed for efficacy.
G. Data Gaps and Proposed Solutions	1. data gaps: A single model based on only two factors (pre-dose serum concentration and age) leaves much of the variability in outcome unexplained. 2. proposed solutions: NA

H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: NA
I. Criteria for Exclusion from Compendium	reports data and methods for Hazard Identification (e.g., risk factors, odds ratios, etc.)
J. Reviewer Comments	NA
K. Cross-References	NA

A. Hazard ID Study Identification	Humphrey, T.J., K.W. Martin, J. Slader and K. Durham. 2001. *Campylobacter* spp. in the kitchen: Spread and persistence. J. Appl. Microbiol. 90: 115S-120S.
B. Objectives and Type of Study	1. purpose: scientific; to discuss cross-contamination of surfaces and persistence of *Campylobacter* in kitchens; to suggest improvements in sampling and enrichment techniques for recovery of *Campylobacter* from surfaces, dishcloths, and harsh environments 2. type: HI
C. Publication Attributes	1. sponsors/affiliations: Public Health Laboratory Service, Food Microbiology Research Unit, Exeter, UK 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: studies with isolation and persistence data; surface decontamination studies; description of isolation and recovery from surfaces 2. source: published studies; government studies; unpublished government data 3. extent of data: large number of studies for cross-contamination and persistence of organisms; 5 surface decontamination studies 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low

E. Method/Model/Approach	1. general characteristics: NA; no risk assessment models or methods described 2. specific characteristics: NA 3. assumptions: NA 4. limitations: paper dealt only with spread of organism in kitchens when poultry meat is handled 5. relevance: low; potentially useful for exposure assessment
F. Study Conclusions and Extended Applications	1. conclusions: *Campylobacter* spp. are important human pathogens for which cross-contamination is an important contributory factor in a number of outbreaks 2. authors' extrapolations: none stated
G. Data Gaps and Proposed Solutions	1. data gaps: little or no hard scientific evidence on fate of bacteria after contamination of surfaces; source and public health significance of chicken muscle tissue contamination with *C. jejuni* unknown 2. proposed solutions: need to conduct studies in these areas
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: high 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: NA 5. defensibility: low
I. Criteria for Exclusion from Compendium	This study reported detection only without modeling of likely fate and transport or adverse effects. This study reported data and methods for Hazard Identification.
J. Reviewer Comments	This paper provides data that could be used as part of a risk assessment, but it does not describe any risk assessment models or methods.
K. Cross-References	NA

A. Hazard ID Study Identification	Jaakkola, J.J.K. and O.P. Heinonen. 1994. Shared office space and the risk of the common cold. Euro. J. Epidemiol. 11: 213-216.
B. Objectives and Type of Study	1. purpose: scientific; To assess whether the presence of colleagues in the same office increases the risk of the common cold. 2. type: HI

C. Publication Attributes	1. sponsors/affiliations: Department of Epidemiology, National Institute of Public Health, Oslo, Norway. 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: epidemiologic survey (self administered questionnaire about episodes of common cold during the past 12 months, the number of colleagues in the same room, and current diseases and symptoms, and personal, environmental and behavioral [including smoking habits and allergies] factors); airflow, temperature and relative humidity measured in a random sample (33%) of 410 rooms. 2. source: Pasila Office Center, Helsinki. 3. extent of data: 1243 office workers (71%) returned the self-administered questionnaire. One from each room on floors 3-8 were chosen randomly. 4. sampling plan: Random sampling of airflow, temperature and relative humidity were completed. Sampling of individuals (i.e. questionnaire completion) was voluntary however of those that completed the questionnaire one from each office on floors 3-8 were chosen randomly. 5. sample size: The study population, one person from each office on floors 3 to 8, consisted of 893 workers, 493 male and 454 female who were then divided into the exposed (individuals with one or more room colleagues, n=300) or reference (no room colleagues, n=593) groups. 6. performance characteristics: adjusted odds ratios for having experienced more than two bouts of common cold in the exposed vs. reference group and its 95% confidence interval was calculated by logistic regression analysis. 7. relevance: low
E. Method/Model/Approach	1. general characteristics: The distributions of potential determinants of the outcome in the exposed and reference groups were compared to establish the comparability of the two groups. 2. specific characteristics: The adjusted odds ratios for having experienced more than two bouts of common cold in the exposed vs. reference group and its 95% confidence interval was calculated by logistic regression analysis. The following potential confounders were dichotomized and included in the model: gender, allergies, smoking, and children under the age of 8 at home. 3. assumptions: subjects sharing rooms with one or more colleagues exposed to more viable viruses in this setting than those in a single room. 4. limitations: The mode of transmission (airborne, contact with surfaces, person-to-person) could not be assessed with this study design. 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions: sharing office space appears to increase the risk of the common cold 2. authors' extrapolations: The group included in this study is typical of office settings.
G. Data Gaps and Proposed Solutions	1. data gaps: The mode of transmission could not be assessed with this study design. 2. proposed solutions: NA

H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	This study reported data and methods for Hazard Identification (e.g., risk factors, odds ratios, etc.)
J. Reviewer Comments	NA
K. Cross-References	NA

A. Hazard ID Study Identification	Jernigan, J.A., A.L. Pullen, C. Partin and W.R. Jarvis. 2003. Prevalence of and risk factors for colonization with methicillin-resistant *Staphylococcus aureus* in an outpatient clinic population. Infect. Control Hosp. Epidemiol. 24(6): 445-450.
B. Objectives and Type of Study	1. purpose: scientific; to determine the prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) colonization in an outpatient population and to identify risk factors for MRSA colonization 2. type: HI
C. Publication Attributes	1. sponsors/affiliations: Division of Infectious Diseases, Department of Medicine, Emory University School of Medicine, Atlanta, GA and Center for Disease Control and Prevention, Atlanta, GA (primary author has 2 affiliations) 2. peer-review mechanism: peer-reviewed journal
D. Data and Study Design	1. type: biological specimens 2. source: surveillance cultures collected from outpatient visits 3. extent of data: specimens for culture obtained from both anterior nares and cultured in a laboratory 4. sampling plan: case-control study 5. sample size: 500 patients agreed to participate, 122 had *Staphylococcus aureus* (*S. aureus*), 107 of which were methicillin-susceptible and 15 had MRSA 6. performance characteristics: NA 7. relevance: high

E. Method/Model/Approach	1. general characteristics: NA 2. specific characteristics: NA 3. assumptions: NA 4. limitations: NA 5. relevance: NA
F. Study Conclusions and Extended Applications	1. conclusions: found low prevalence of MRSA colonization in adult outpatient population. MRSA carriers most likely acquired organism through contact with health-care facilities rather than community. 2. authors' extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: NA
I. Criteria for Exclusion from Compendium	hazard identification with no model development
J. Reviewer Comments	NA
K. Cross-References	NA

A. Hazard ID Study Identification	Jones, R.C., S.I. Gerber, P.S. Diaz, et al. 2004. Intensive investigation of bacterial foodborne disease outbreaks: Proposed guidelines and tools for the collection of dose-response data by local health departments. J. Food Protect. 67(3): 616-623.
B. Objectives and Type of Study	1. purpose: regulatory, future regulatory interest; to design and develop a survey instrument to collect and organize dose-response data in the context of an outbreak investigation. 2. type: HI
C. Publication Attributes	1. sponsors/affiliations: US Food and Drug Administration, National Center for Food Safety and Technology

	2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: survey data 2. source: data collected by authors 3. extent of data: interviews of all surviving ill guests from one salmonellosis outbreak 4. sampling plan: NA 5. sample size: 40 guests who ate contaminated food 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: survey instrument used to collect dose-response data from an investigation of an outbreak of salmonellosis caused by *Salmonella* serotype Enteritidis at a catered party 2. specific characteristics: data collected on adverse health outcomes and severity, amount of contaminated food consumed, and host susceptibility factors 3. assumptions: number of exposed persons is >20; retrospective cohort study design is feasible; epidemiologic and environmental data implicates a single food vehicle; bacterial pathogen confirmed as etiologic agent based on epidemiological, microbiological, and clinical criteria 4. limitations: NA 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions: the authors' survey instrument can be successfully used to collect dose-response data from foodborne disease outbreak investigations that meet the four criteria 2. authors' extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: survey instrument only applied to one outbreak 2. proposed solutions: survey instrument should be applied to more outbreaks to confirm usefulness.
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	reported data/methods for hazard identification and extensions for dose-response research
J. Reviewer Comments	The survey instrument would be useful in more intensive outbreak investigations to generate additional data for dose-response

K. Cross-References	NA

A. Hazard ID Study Identification	Kistemann, T., S. Zimmer, I. Vagsholm and Y. Andersson. 2004. GIS-supported investigation of human EHEC and cattle VTEC O157 infections in Sweden: Geographical distribution, spatial variation and possible risk factors. Epidemiol. Infect. 132: 495-505.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific, future regulatory interest; Describes the spatial and temporal distribution of verotoxin-producing *Escherichia coli* among humans (EHEC) and cattle (VTEC) in Sweden in order to evaluate relationships between the incidence of EHEC in humans, prevalence of VTEC O157 in livestock and agricultural structure by an ecological study in Sweden. 2. type: HI
C. Publication Attributes	1. sponsors/affiliations: University of Bonn, National Veterinary Institute, and Swedish Institute for Infections Disease Control 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: Ecological study concerning the frequency and spatial patterns of human EHEC infections in Sweden and the relation to agricultural structure and VTEC O157 prevalence in livestock. 2. source: government datasets and published journals 3. extent of data: Spatial analysis of all reported findings of EHEC in humans and VTEC O157 in cattle in Sweden 4. sampling plan: Clustered 5. sample size: 525 human infections (1995-1999), 5602 samples were taken from an abattoir monitoring program, and 249 dairy farms were included in this study 6. performance characteristics: Mean annual incidence rates were calculated, a X^2 test was used to test for spatial heterogeneity of incidence beyond random, Moran's I test and joint count statistics were used for spatial autocorrelation, spatial patterns were exhibited by dot maps, choropleth maps, and probability maps 7. relevance: medium - includes the correlation between livestock population and human proximity to livestock as it relates to the infection rate of EHEC.
E. Method/Model/Approach	1. general characteristics: A spatial analysis of EHEC in humans and VTEC O157 in cattle 2. specific characteristics: multiple linear regression model applying the ordinary least squares procedure 3. assumptions: Instability of the regression model was assumed if *t* values changed rapidly and regression coefficients changed their sign. Factors, which were spatially differentiated, were assumed to influence the

	obvious spatial variation. 4. limitations: No controls were mentioned in the article. No leisure activity (e.g., visits to farms, petting zoos, picnics, etc.) of the human population was taken into account during the study. 5. relevance: NA
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: The temporal distribution showed a seasonal peak of human cases in late summer and autumn. The spatial comparison of human and cattle infection patterns showed that in areas with more human EHEC infections a higher prevalence of VTEC O157 was detected in cattle also. A correlation between cattle prevalence and human incidence. Incidence of human infection was higher in municipalities where more animals tested positive. 2. authors' extrapolations from the observed data to other populations or conditions: The vicinity of cases indicated a positive association between human and cattle infection. Cattle VTEC O157 prevalence and farm density contributed to further insight in the disease ecology of human EHEC infections in Sweden.
G. Data Gaps and Proposed Solutions	1. data gaps: No controls were mentioned in the article. The lifestyle of the human population was not included in the article. 2. proposed solutions: Prevent cattle from grazing close to waterways in order to prevent water contamination from cattle feces.
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: NA
I. Criteria for Exclusion from Compendium	reports data and methods for Hazard Identification (e.g., risk factors, odds ratios, etc.)
J. Reviewer Comments	NA
K. Cross-References	NA

A. Hazard ID Study Identification	Kortepeter, M.G. and M.R. Krauss. 2001. Tuberculosis infection after humanitarian assistance, Guantanamo Bay, 1995. Mil. Med. 166(2): 116-120.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific. To document the number of soldiers who PPD converted (became

	positive for a purified protein derivative test) and identify risk factors among the soldiers for purified protein derivative conversion while they were in Cuba. 2. type: HI
C. Publication Attributes	1. sponsors/affiliations: Operational Medicine Division, US Army Medical Research Institute of Infectious Diseases, Fort Detrick, MD 21702-5011. Preventive Medicine Division, Walter Reed Army Institute of Research, Washington, DC 20307-5100. 2. peer-review mechanism: full scientific peer review
D. Data and Study Design	1. type: A case-control study was conducted to identify risk factors for purified protein derivative conversion during Operation Sea Signal, that was conducted in Guantanamo Bay, Cuba from early January to mid June 1995. Soldiers that participated completed a extensive survey prior to their inclusion. 2. source: Soldiers that were deployed to Guantanamo Bay, Cuba from early January to mid June 1995 from the First Brigade, 25th Infantry Division. 3. extent of data: Attempts were made to contact all of the soldiers for the survey. Forty-four converters, 21 reactors, and 84 controls were included. 4. sampling plan: Soldiers included in the same Battalion were considered for inclusion in the analysis. 5. sample size: 44 converters, 21 reactors, and 84 controls were included in the survey. 6. performance characteristics: Odds ratios with 95% confidence intervals were calculated with Epi-Info, version 6. Logistic regression analysis was performed using SAS, version 7. 7. relevance: low
E. Method/Model/Approach	1. general characteristics: A case-control study was conducted to identify risk factors for purified protein derivative conversion during Operation Sea Signal, that was conducted in Guantanamo Bay, Cuba from early January to mid June 1995. Available records of nurse and physician interviews from the tuberculosis clinic were reviewed to classify soldiers as either converters (cases) or reactors. A group of controls was also included that were selected from the same Battalion as the infected soldiers. 2. specific characteristics: Cases were defined as soldiers with a negative purified protein derivative skin test in the 2 years prior to deployment who were found to be positive for this test upon return from Cuba. Reactors were soldiers with a history of a positive skin test prior to deployment to Cuba. Controls served in the same deployment as cases, had documented negative tests at least 3 months after returning from Cuba. A self administered questionnaire was used to verify pre-deployment skin test status, previous travel history and birthplace. It also contained questions regarding previous duties and exposures to migrants while in Cuba. Among the risk factors evaluated from the questionnaire were exposure to psychiatric hospital, coughed on directly by migrant, enclosed area with coughing migrant, around coughing migrants, contact with migrants with tuberculosis and birthplace outside the United States. 3. assumptions: Other factors not related to deployment also could have influenced the result and were not included as variables in the analysis.

	4. limitations: The prevalence of active tuberculosis among the Cubans in the camps during 1995 is unknown. 5. relevance: NA
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: Only upon exposure to coughing migrants statically increased the risk of conversion to a purified protein derivative skin test. 2. extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: NA
I. Criteria for Exclusion from Compendium	study reports data and methods for Hazard Identification (e.g., risk factors, odds ratios, etc.)
J. Reviewer Comments	NA
K. Cross-References	NA

A. Hazard ID Study Identification	Matson, D.O. and G. Szucs. 2003. Calicivirus infections in children. Curr. Opin. Infect. Dis. 16(3): 241-246.
B. Objectives and Type of Study	1. purpose: Scientific; to review calicivirus biology to include its diversity, outbreaks, and viral diversity due to recombination events. 2. type: HI
C. Publication Attributes	1. sponsors/affiliations: Center for Pediatric Research, Eastern Virginia Medical School. 2. peer-review mechanism: Journal article.
D. Data and Study Design	1. type: NA 2. source: NA 3. extent of data: NA 4. sampling plan: NA

	5. sample size: NA 6. performance characteristics: NA 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: NA 2. specific characteristics: NA 3. assumptions: NA 4. limitations: NA 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions: Caliciviruses are important human pathogens. 2. authors' extrapolations: The properties of Norovirus are reminiscent of those of *Salmonella*, a framework that may be useful for predicting which interventions will succeed for prevention and control of Norovirus infection.
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: NA
I. Criteria for Exclusion from Compendium	No models presented. Pathogen characteristics provided.
J. Reviewer Comments	Provided information about the pathogen, not modeling of infection.
K. Cross-References	NA

A. Hazard ID Study Identification	Mylotte, J.M., M.A. Pisano, S. Ram, et al. 1995. Validation of a bacteremia prediction model. Infect. Control Hosp. Epidemiol. 16(4): 203-209.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific; to validate a previously published model for predicting bacteremia in hospitalized patients.

	2. type: HI
C. Publication Attributes	1. sponsors/affiliations: State University of New York, Buffalo; Erie County Medical Services 2. peer-review mechanism: scientific journal
D. Data and Study Design	1. type: Prospective validation using a patient cohort 2. source: Blood cultures from patients at the Erie County Medical Center, Buffalo, New York 3. extent of data: 559 blood culture episodes between October 14, 1992 and December 5, 1992. 4. sampling plan: epidemiologic study with defined cohort 5. sample size: 559 blood culture episodes from 342 patients. 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: Student's t test for continuous variables and Pearson's chi square for test for categorical variables. 2. specific characteristics: Article refers reader to Bates et al, 1990 Ann Intern Med 113:495-500 for details. 3. assumptions: Classification of samples by human evaluators as being positive due to bacteremia or contamination is correct. 4. limitations: Model may be hospital/population specific. 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: Model able to identify two extreme risk groups–those with low risk and those with high risk. 2. authors' extrapolations: Model for other hospital/patient groups may need to be modified or may not be applicable.
G. Data Gaps and Proposed Solutions	1. data gaps: Only performed in one hospital. 2. proposed solutions: additional studies in other hospital populations are needed to verify the validity of the bacteremia prediction model.
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: low 5. defensibility: low
I. Criteria for Exclusion from Compendium	Study reported detection only without modeling of likely fate and transport or adverse effects. Study reported data and methods for Hazard Identification.

J. Reviewer Comments	NA
K. Cross-References	NA

A. Hazard ID Study Identification	Pariza, M.W. and E.A. Johnson. 2001. Evaluating the safety of microbial enzyme preparations used in food processing: Update for a new century. Reg. Toxicol. Pharmacol. 33(2): 173-186.
B. Objectives and Type of Study	1. purpose noted by study authors: Regulatory; Future regulatory interest - The purpose of this report is to present guidelines that can be used to evaluate the safety of metabolites of the production strain that are also present in the enzyme preparation, including, but not limited to, the desired enzyme activity itself. 2. type: HI
C. Publication Attributes	1. sponsors/affiliations: Enzyme Technical Association 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: This article was an update to previous articles. It addresses the new molecular techniques for this century and how this new techniques impact the evaluation of microbial enzyme preparations used in food processing. 2. source: published studies 3. extent of data: Report builds on previous reports (Pariza and Foster, 1983; IFBC, 1990; Kessler et al., 1992) 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: Addressing the impact of new molecular techniques on safe enzyme preparations for use in food processing, specifically engineering enzymes. Presenting guidelines that can be used to evaluate the safety of metabolites present in the enzyme preparations. Introduced a decision tree mechanism that updates previous enzyme safety evaluation mechanisms. 2. specific characteristics: NA 3. assumptions: NA 4. limitations: NA 5. relevance: low

F. Study Conclusions and Extended Applications	1. conclusions supported by the data: The safety of the production strain should remain as the primary consideration in evaluating enzyme safety (toxigenic potential and pathogenic potential). Thoroughly characterized nonpathogenic, nontoxigenic microbial strains are logical candidates for generating a safe strain lineage, through which improved strains may be derived via genetic modification either by using traditional/classical or rDNA strain improvement strategies (IFBC, 1990). 2. authors' extrapolations from the observed data to other populations or conditions: NA
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: NA
I. Criteria for Exclusion from Compendium	insufficient data quality or quantity to support rigorous science-based modeling insufficient model documentation to demonstrate viable and credible modeling approaches
J. Reviewer Comments	NA
K. Cross-References	NA

A. Hazard ID Study Identification	Parkin RT, Soller JA and Olivieri AW. 2003. Incorporating susceptible subpopulations in microbial risk assessment: Pediatric exposures to enteroviruses in river water. J. Expo. Anal. Environ. Epidemiol. 13(2): 161-168.
B. Objectives and Type of Study	1. purpose: scientific; To report the results of a comprehensive, risk assessment-oriented evaluation of the literature on sensitive subpopulations' exposures and responses to enteroviruses in recreational water. 2. type: HI, evaluation of available hazard identification, exposure assessment, and dose-response for subpopulations with special susceptibility to enteroviruses
C. Publication Attributes	1. sponsors/affiliations: City of Stockton (California), Municipal Utilities Department 2. peer-review mechanism: peer-reviewed journal
D. Data and Study Design	1. type: Epidemiological studies for enterovirus occurrence and/or health-related information

	2. source: published literature and outbreak surveillance data from CDC 3. extent of data: all available literature, dated prior to 1966 through 2003 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: This paper describes an evaluation of published literature on sensitive populations' exposures and adverse health responses to enteroviruses in recreational waters. The data were evaluated to determine if they could be used to improve a disease transmission model (i.e., exposure model), which is described and applied for risk characterization purposes in a companion paper (Soller et al. 2003). 2. specific characteristics: Information/data found for occurrence of viruses in recreational waters, epidemiology, sensitive subpopulations, nature of illnesses, extent of illnesses, and other risk-related factors. Some quantitative data available for severity and extent of illness. No dose-response data reported. 3. assumptions: All recreational settings are equal with respect to exposure. 4. limitations: Not all recreational settings relevant to the risk assessment being studied here, so had to incorporate a broader context. 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions: Qualitative data offer limited insights for improving the disease transmission model for susceptible populations. 2. authors' extrapolations: Limitations identified are likely to be relevant to other microbial pathogens and susceptible populations.
G. Data Gaps and Proposed Solutions	1. data gaps: prevalence data for enteroviruses in recreational waters is sparse, dose-response data lacking, quantitative occurrence data, other factors relating to variation among human populations in disease transmission (i.e., physiological development, nutritional states) 2. proposed solutions: enhanced virus monitoring in recreational water, report health and exposure data separately for child and adult, more complete ascertainment of the numbers at risk
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: NA
I. Criteria for Exclusion from Compendium	study excluded because the report does not describe the model

J. Reviewer Comments	Companion paper (Soller et al. 2003) describes the exposure models, disease transmission models, dose-response models, and the estimated risks for adverse health effects in populations who recreationally use the San Joaquin River under various flow and treatment scenarios
K. Cross-References	Soller et al., 2003

A. Hazard ID Study Identification	Powell, M., E. Ebel and W. Schlosser. 2001. Considering uncertainty in comparing the burden of illness due to foodborne microbial pathogens. Int. J. Food Microbiol. 69(3): 209-215.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific, future regulatory interest; To motivate the importance in a decision-theoretic framework of taking uncertainty into account in comparing the public health impact of different food borne pathogens. 2. type: HI
C. Publication Attributes	1. sponsors/affiliations: USDA 2. peer-review mechanism: full scientific peer review
D. Data and Study Design	1. type: Experimental data and Monte-Carlo simulation 2. source: published studies and FoodNet surveys 3. extent of data: large datasets 4. sampling plan: NA 5. sample size: Large number of annual reported cases of *E. coli O157* taken into consideration. 6. performance characteristics: NA 7. relevance: high
E. Method/Model/Approach	1. general characteristics: The case of *E. coli O157*:H7 is developed to provide an example of how to characterize and analyze the uncertainty attendant to pathogen specific estimates of food-borne illness. 2. specific characteristics: Probabilistic risk assessment methods are used to characterize the uncertainty regarding the burden of illness due to *E. coli O157*:H7. The magnitude of uncertainty is substantial, ranging from less than 50,000 to more than 120,000 cases/year. 3. assumptions: A negative binomial distribution is employed in a stepwise fashion to add the number of cases that are missed by the surveillance system due to test insensitivity, laboratories not culturing stool samples for *E. coli O157*:H7, physicians not obtaining stool samples from patients and ill patients not seeking medical care. This procedure assumes independence among cases, which may not be the case.

	4. limitations: NA 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: The importance of considering the uncertainty attendant to burden-of-illness estimates in comparing the public health impacts of different pathogens. 2. authors' extrapolations from the observed data to other populations or conditions: None reported
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: high 2. representativeness of data: high 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	reported data and/or methods for Hazard Identification
J. Reviewer Comments	NA
K. Cross-References	NA

A. Hazard ID Study Identification	Randolph, S. 2002. Predicting the risk of tick borne diseases. Int. J. Med. Microbiol. 291: 6-10.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific; Value of predictive risk mapping and test predictions of the spatial and temporal variation in risk of tick borne disease, specifically caused by tick borne encephalitis virus (TBEv) are discussed. 2. type: HI
C. Publication Attributes	1. sponsors/affiliations: Wellcome Trust 2. peer-review mechanism: full scientific peer review
D. Data and Study Design	1. type: review of disease dynamics for tick-borne diseases 2. source: satellite imagery data of vector tick *Ixodes ricinus*; climactic variables 3. extent of data: NA

	4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: Predictions of the present distribution of TBEv, driven by satellite data, match the mapped records of TBE cases with 90% accuracy in the Baltic region and 81% accuracy in central Europe. 2. specific characteristics: After digitizing the TBEv map (from meteorological satellites) and incorporating it into a geographical information system, logistic regression analysis was used to predict the probability of TBEv presence or absence in a 8x8km pixel depending on remotely sensing environmental conditions. Multivariate climactic descriptions analyzed by General Circulation Model. 3. assumptions: NA 4. limitations: some parameters unvalidated by data 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: Current model predicts vector seasonal dynamics, linking powerful models using satellite imagery and cellular mechanism of virus transmission 2. authors' extrapolations: prototype biological process based models will be applicable to many pathogens transmitted by tick vector
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: low 5. defensibility: low
I. Criteria for Exclusion from Compendium	Reported data and methods for Hazard Identification and risk factors influencing disease dynamics; unclear if sufficient data quality or quantity exist to support rigorous science-based modeling that would be need to predict biothreat tick-borne transmission dynamics
J. Reviewer Comments	Authors point out complexity of life cycles, with temporal, spatial, and climactic interactions and rates of contact of virus, tick vector (larval and nymph life stages), secondary rodent host, and human host; only when basic reproduction number R_0 exceeds 1 would virus circulate. Public health controls, agricultural activities, and leisure activities could be influential in viral transmission dynamic models
K. Cross-References	NA

A. Hazard ID Study Identification	Ruef, C. 1998. Noscomial Legionnaires disease-strategies for prevention. J. Microbiol. Methods 33: 81-91.
B. Objectives and Type of Study	1. purpose: scientific review of literature; Summarizes current state-of-the-art regarding detection and quantification of *Legionella spp*. 2. type: HI
C. Publication Attributes	1. sponsors/affiliations: Hospital Epidemiology Unit, Division of Infectious Diseases and Hospital Epidemiology, University Hospital of Zurich, Zurich Switzerland 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: epidemiological data for hospital acquired *Legionella*-caused pneumonia. 2. source: government and scientific literature 3. extent of data: minimal 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: NA 2. specific characteristics: NA 3. assumptions: NA 4. limitations: NA 5. relevance: medium; Article does provide general risk assessment for noscomial occurrences of the disease.
F. Study Conclusions and Extended Applications	1. conclusions: Methodological and technical aspects of surveillance and prevention of noscomial Legionnaires disease are not standardized. 2. authors' extrapolations: They point out that detection methods need better standardization and that the relationship between microbial load and infection incidence needs to be better understood.
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: low

	3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	1. Insufficient data quantity to support rigorous science-based modeling 2. Study reviews data and methods for Hazard Identification (e.g., risk factors, odds ratios, etc.)
J. Reviewer Comments	1. Good for background information, but not directly applicable for incident-base risk assessment of building and water systems. 2. A review with information on Legionella detection, surveillance, and hospital water supply sanitation.
K. Cross-References	NA

A. Hazard ID Study Identification	SDRA. 2003. IRAQ: Environmental and health concerns for Swedish deployed personnel. Hogkvarteret, Stockholm: Swedish Defense Research Agency. PB2004101722.
B. Objectives and Type of Study	1. purpose: user report; To provide a preliminary situation report concerning potential health risks and environmental risks for personnel deployed to Iraq. 2. type: HI
C. Publication Attributes	1. sponsors/affiliations: Swedish Defense Research Agency 2. peer-review mechanism: NA
D. Data and Study Design	1. type: compilation of information for Swedish military personnel to review prior to deployment to Iraq. 3. extent of data: Data reviews cultural customs expected to be encountered, condition of the manufacturing infrastructure in Iraq, and potential for exposure to biological or chemical weapons or unexploded ordinance. 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: NA 2. specific characteristics: NA 3. assumptions: NA

	4. limitations: NA 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions: NA 2. authors' extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: Summary is limited to information available at the time of preparation of the report. 2. proposed solutions: unknown
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: NA
I. Criteria for Exclusion from Compendium	report data and/or methods for Hazard Identification
J. Reviewer Comments	NA
K. Cross-References	NA

A. Hazard ID Study Identification	Sherertz R.J., S. Bassetti and B. Bassetti-Wyss. 2001. "Cloud" health-care workers. Emerging Infect. Dis. 7(2): 241-244.
B. Objectives and Type of Study	1. purpose: scientific; a review of outbreaks of disease in healthcare workers associated with airborne exposures to *Bordetella pertusis*, Group A *Streptococcus pyogenes*, and *Staphylococcus aureus*. 2. type: HI review
C. Publication Attributes	1. sponsors/affiliations: report supported in part by RO1 AI-46558 (no further info provided) 2. peer-review mechanism: peer-reviewed journal
D. Data and Study Design	1. type: no new data presented, historical data from past studies 2. source: numerous past studies 3. extent of data: wide variety of results from past studies discussed, but not actual data itself 4. sampling plan: review

	5. sample size: NA 6. performance characteristics: NA 7. relevance: low (1 of 3 agents mentioned in review are on list)
E. Method/Model/Approach	1. general characteristics: review, methodology employed in various studies not discussed 2. specific characteristics: NA 3. assumptions: NA 4. limitations: NA 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions: Data support the existence of airborne transmission of disease from healthcare workers to patients. 2. authors' extrapolations: none
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: NA
I. Criteria for Exclusion from Compendium	A review of hazard identification information
J. Reviewer Comments	NA
K. Cross-References	NA

A. Hazard ID Study Identification	Sleator, R.D., G.A. Francis, D. O'Beirne, C.G.M. Gahan and C. Hill. 2003. Betaine and carnitine uptake systems in *Listeria monocytogenes* affect growth and survival in foods and during infection. J. Appl. Microbiol. 95(4): 839-846.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific; To establish the relative importance of the osmo- and cryoprotective

	compounds betaine and carnitine, and their transporters, for listerial growth and survival in foods and during infection 2. type: HI
C. Publication Attributes	1. sponsors/affiliations: Irish Government National Development Plan 2000-2006 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: experimental data for microbial growth in plant-based and animal-based processed foods at room and refrigeration temperatures 2. source: authors' experimental data 3. extent of data: data sets for growth of wild type and created mutant strains in defined minimal medium, dry coleslaw mix, and ready-to-eat hotdogs; data sets for virulence of wild type and created mutant strains in BALB/c mice. 4. sampling plan: factorial design for growth studies 5. sample size: in the strain characterization study, reported populations represent the mean of at least 3 values for each of 11 timepoints at 37ºC and 6 timepoints at 4ºC; in the food experiments, reported populations represent the mean of four values at each of 5 timepoints for each of two temperatures in dry coleslaw mix and ready-to-eat hotdogs; in the virulence assays, reported populations represented the mean of four animals for each of 6 strains tested. 6. performance characteristics: NA 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: research article, no risk assessment methods or models were presented 2. specific characteristics: NA 3. assumptions: NA 4. limitations: NA 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: betaine uptake systems play the dominant role in bacterial growth and survival in foods; carnitine uptake system plays the dominant role in bacterial growth and survival in the animal host during infection; multiple osmolyte uptake systems allow the organism to overcome temperature and osmotic stresses to grow in diverse environments.
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: high 2. representativeness of data: low

	3. generalizability or external validity: high 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	insufficient data quality or quantity to support rigorous science-based modeling insufficient model documentation to demonstrate viable and credible modeling approaches study reports detection only without modeling of likely fate and transport or adverse effects studies reporting data and methods for Hazard Identification (e.g., risk factors, odds ratios, etc.)
J. Reviewer Comments	NA
K. Cross-References	NA

A. Hazard ID Study Identification	Tamplin, M.L. 2002. Growth of *Escherichia coli* O157:H7 in raw ground beef stored at 10 C and the influence of competitive bacterial flora, strain variation, and fat level. J. Food Protect. 65(10): 1535-1540.
B. Objectives and Type of Study	1. purpose: scientific, future regulatory interest 2. type: HI
C. Publication Attributes	1. USDA 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: generated experimental data for strain variation influence, ground beef fat content and native bacterial population density for comparison with *E. coli* O157:H7 growth densities 2. source: published studies 3. extent of data: 9 strains of *E. coli* O157:H7 isolated from meats (provided by USDA Food Safety Inspection Service; strain 933 isolated from meat implicated in human illness (obtained from ARS Microbial Food Safety Research Unit); native bacterial strains were isolated from retail ground beef 4. sampling plan: four-strain cocktails were manipulated for growth studies under various *E. coli* strain concentrations, pH, native bacterial flora population densities; 5. sample size: samples were taken at predetermined time intervals 6. performance characteristics: only simple statistics provided (e.g., student t's, confidence limits on the mean, pairwise least significance of the mean) 7. relevance (qualitative judgement of the usefulness of the data to incident-based microbial risk assessment for

	biothreat agents): medium, includes data for biothreat agent of concern that could grow under certain threat conditions (*E. coli* O157:H7) but no model generated.
E. Method/Model/Approach	1. general characteristics: developed experimental manipulations to examine strength of microbial growth models determined with pure-culture pathogen 2. specific characteristics: no model generated 3. assumptions: NA 4. relevance (qualitative judgement of the usefulness of the method to incident-based microbial risk assessment for biothreat agents): NA
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: observed low levels of variation in growth among strains; EGR and MPD increased with decreasing fat levels in ground beef; two isolated strains of native flora found to inhibit pathogen growth; population density of native flora found to significantly influence EGR and MPD of *E. coli* O157:H7; fat content does significantly influence growth and establishment of *E. coli* O157:H7. 2. authors' extrapolations from the observed data to other populations or conditions: competition experiments designed for broth may not translate to ground beef growth; methods of isolation, storage and different strain use may account for variance among studies; studies using BHI broth may not be relevant for comparison to typical contamination scenarios due to lack of lag phase
G. Data Gaps and Proposed Solutions	1. identification of data gaps: broth based models relevance to food studies 2. assumptions or source of surrogate data to fill gap: new studies incorporating strain variation, competition with native flora and influence of food matrix on pathogen growth and establishment.
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: high 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: medium 5. defensibility (scientific judgement of appropriateness of method to incident-based microbial risk assessment of buildings and water systems)low, does not permit modeling for threat scenarios that support bacterial growth, instead provides important parameters than influence bacterial colonization
I. Criteria for Exclusion from Compendium	1. Insufficient model documentation to demonstrate viable and credible modeling approaches 2. studies reporting detection only without modeling of likely fate and transport or adverse effects
J. Reviewer Comments	describes important conditions influencing establishment of pathogen in ground beef but does not indicate model useful for incident-based microbial risk assessment of buildings and water systems
K. Cross-References	NA

A. Hazard ID Study Identification	Torok, T.J., R.V. Tauxe, R.P. Wise, et al. 1997. A large community outbreak of salmonellosis caused by intentional contamination of restaurant salad bars. JAMA 278(5): 389-395.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific; To investigate a large community outbreak of *Salmonella*. 2. type: HI
C. Publication Attributes	1. sponsors/affiliations: Wasco-Sherman Public Health Department, Oregon Health Division, CDC, USFDA, Oregon State Police, Wasco County Sheriff, FBI 2. peer-review mechanism: peer-reviewed journal
D. Data and Study Design	1. type: interview data, environmental samples, laboratory samples 2. source: interview data (case patients/customers, restaurant employees, managers), stool specimens, restaurant inspections, tap water samples, salad bar temperatures 3. extent of data: comprehensive collection of all possible contributors to salmonella outbreak 4. sampling plan: factorial design 5. sample size: 751 patients identified, 674 with known date of onset, 692 restaurant-associated cases 6. performance characteristics: NA 7. relevance: high
E. Method/Model/Approach	1. general characteristics: Univariate analyses; odds rations; stepwise logistic regression; relative risks 2. specific characteristics: food exposure analyzed separately by restaurant and date of onset by univariate analysis using Epi Info computer program, odds ratios calculated; foods found to be associated with illness in univariate analysis were analyzed using stepwise regression model. Univariate analyses of employee survey data were performed and relative risks calculated using Epi Info. Laboratory analyses compared outbreak strain with available human and animal isolates from national surveys. 3. assumptions: NA 4. limitations: NA 5. relevance: high
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: contamination came from salad bars at multiple restaurants, epidemic exposure curves indicated that salad bars were contaminated multiple times during a several-week period suggesting necessity of a sustained source, a few employees had onset of illness before recognized patron exposure but in general did not precede exposure among customers; laboratory analysis of outbreak strain demonstrated a single outbreak strain exclusive of independent, simultaneous outbreaks and one that was not common before outbreaks; waterborne contamination excluded as cause.

G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: high 2. representativeness of data: low 3. generalizability or external validity: high 4. soundness of study conclusions or internal validity: high 5. defensibility: high
I. Criteria for Exclusion from Compendium	study reports data and methods for Hazard Identification (e.g., risk factors, odds ratios, etc.)
J. Reviewer Comments	NA
K. Cross-References	NA

A. Hazard ID Study Identification	Trout, D., T.M. Gomez, B.P. Bernard, et al. 1995. Outbreak of brucellosis at a Unites States pork packing plant. JOEM 37: 697-703.
B. Objectives and Type of Study	1. purpose noted by study authors: future regulatory interest - An evaluation of an outbreak of brucellosis among employees of a pork slaughter and processing plant. 2. type: HI
C. Publication Attributes	1. sponsors/affiliations: National Institute for Occupational Safety and Health; NC Department of Environment, Health, and Natural Resources; USDA/Animal Plant Health Inspection Service; Centers for Disease Control and Prevention 2. peer-review mechanism: regulatory article
D. Data and Study Design	1. type: The evaluation was conduced as part of the NIOSH health hazard evaluation program. The evaluation was limited to the kill floor workers at the pork packing plant. 2. source: government datasets 3. extent of data: 154 of the 156 kill floor employees participated in the study. 4. sampling plan: factorial design 5. sample size: 154 samples

	6. performance characteristics: NA 7. relevance: high
E. Method/Model/Approach	1. general characteristics: 154 participants in study. Blood samples were drawn from each participant and split so that two identical samples were obtained from each participant. These samples were sent to Laboratory A and B for analysis of brucellosis. 2. specific characteristics: A case of brucellosis was defined by an STA titer of ≥160 and either two or more symptoms consistent with brucellosis (fever, chills, sweats, headache, weakness, malaise, anorexia, weight loss, or myalgia) or a positive 2-ME test. 3. assumptions: NA 4. limitations: Because of poor reproducibility present in the results from Laboratory A, the results from Laboratory B was used for all data analysis. Did not account for people that may have been previously exposed to brucellosis or those who had recently been exposed and had not yet developed an immune response. 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: There was no statistically significant association in prevalence rates among employees by the number of years employed at the plant or age. High rates of infection were found among workers who had a high level of contact with lymph tissue and liver. It appears that skin contact with infectious tissue or body fluids has been the primary route of exposure in the outbreak occurring at this plant. 2. extrapolations: Screening a population at risk of brucellosis increases the detection rate and that ongoing surveillance of such population is warranted.
G. Data Gaps and Proposed Solutions	NA
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: high 3. generalizability or external validity: high 4. soundness of study conclusions or internal validity: high 5. defensibility: high
I. Criteria for Exclusion from Compendium	studies reports data and methods for Hazard Identification (e.g., risk factors, odds ratios, etc.). insufficient model documentation to demonstrate viable and credible modeling approaches.
J. Reviewer Comments	This article may be applied to worker exposure. A history of being cut or scratched while working was identified as a risk factor of becoming infected. This agrees with the evidence suggesting that skin contact is the primary route of infection. Not washing hands before work breaks was related to an increased risk of infection.
K. Cross-References	NA

A. Hazard ID Study Identification	Wyn-Jones, A.P. and J. Sellwood. 2001. Enteric viruses in the aquatic environment. J. Appl. Microbiol. 91: 945-962.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific; Review article of enteric viruses found in aquatic environments. 2. type: HI
C. Publication Attributes	1. sponsors/affiliations: UK Water Industry Research, plc 2. peer-review mechanism: full scientific peer review
D. Data and Study Design	1. type: Descriptions of various enteric viruses that have been detected in water, concentrations detected and detection methods utilized. 2. source: numerous published literature 3. extent of data: Information pertaining to pathogen characteristics and concentration are provided for enteroviruses, NLV, astroviruses, rotavirus, adenovirus, and Hepatitis A and E virus. Various detection methodology is discussed. 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: NA 2. specific characteristics: NA 3. assumptions: NA 4. limitations: NA 5. relevance: NA
F. Study Conclusions and Extended Applications	NA
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA

	4. soundness of study conclusions or internal validity: NA 5. defensibility: NA
I. Criteria for Exclusion from Compendium	insufficient data quality or quantity to support rigorous science-based modeling insufficient model documentation to demonstrate viable and credible modeling approaches study reports detection only without modeling of likely fate and transport or adverse effects study reports data and methods for Hazard Identification (e.g., risk factors, odds ratios, etc.)
J. Reviewer Comments	NA
K. Cross-References	NA

A. Hazard ID Study Identification	Zitter, J.N., P.D. Mazonson, D.P. Miller, et al. 2002. Aircraft cabin air recirculation and symptoms of the common cold. JAMA 288(4): 483-486.
B. Objectives and Type of Study	1. purpose noted by study authors: to scientifically evaluate role of air recirculation as a predictor of postflight upper respiratory tract infections (URI) 2. type: HI
C. Publication Attributes	1. sponsors/affiliations: National Institutes of Health and the Lewin Group 2. peer-review mechanism: full scientific peer review
D. Data and Study Design	1. type: questionnaire data, including self-reporting of URI symptoms 2. source: pre-boarding questionnaire and follow-up telephone questionnaire 3. extent of data: restricted to passengers departing San Francisco Bay area in California and traveling to Denver, Colorado, during January through early April 1999 4. sampling plan: epidemiological survey 5. sample size: 1,501 participants enrolled with 1,000 providing follow-up responses, 516 traveled on fresh air ventilation planes and 584 on re-circulated air ventilated planes 6. performance characteristics: NA 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: generalized estimating equations used to examine interpassenger within-flight correlation; logistic regression models 2. specific characteristics: generalized estimating equations analysis estimated an interpassenger within-flight

	correlation of .02.; univariate analyses performed on a variety of risk factors; odds ratios and confidence intervals computed for 3 outcomes according to multiple logistic regression analysis that included recirculation as a risk factor 3. assumptions: self-reporting os URI symptoms was accurate measure of possible infection; URI symptoms would reveal themselves with one week‘s time 4. limitations: limited study size, potential for a missed modest effect, intergroup differences in some baseline variables greater than expected, possibility of dose-dependant effect of air recirculation that would become evident on flights longer than 2 hours 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: cabin air recirculation was not a risk factor for developing the symptoms of a cold during a week after flight
G. Data Gaps and Proposed Solutions	NA
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: medium 5. defensibility: low
I. Criteria for Exclusion from Compendium	study reports data/methods for Hazard Identification
J. Reviewer Comments	NA
K. Cross-References	NA

A.6 Other Exclusions

Adams, M. and R. Mitchel. 2002. Fermentation and pathogen control: A risk assessment approach. Int. J. Food Microbiol. 79(½): 75-83. 450

Ashbolt, N.J. 2004. Risk analysis of drinking water microbial contamination versus disinfection by-products (DBPs). Toxicology 198(1-3): 255-262. 452

Ashbolt, N.J. 2004. Risk analysis of drinking water microbial contamination versus disinfection by-products (DBPs). Toxicology 198(1-3): 255-262. 454

Balbus, J., R. Parkin, A. Makri, et al. 2004. Defining susceptibility for microbial risk assessment: Results of a workshop. Risk Anal. 24(1): 197-208. 456

Blumenthal, U.J., D.D. Mara, A. Peasey, et al. 2000. Guidelines for microbiological quality of treated wastewater used in agriculture: recommendations for revising WHO guidelines. Bull. World Health Org. 78(9): 1104-1116. 458

Buchanan, R. 1998. Principles of risk assessment for illness caused by food-borne biological agents. J. Food Protect. 61(8): 1071-1074. 460

Carlin F., H. Girardin, M.W. Peck, et al. 2000. Research on factors allowing a risk assessment of spore-forming pathogenic bacteria in cooked chilled foods containing vegetables: A FAIR collaborative project. Int. J. Food Microbiol. 60(2/3): 117-135. 462

Carlin F., H. Girardin, M.W. Peck, et al. 2000. Research on factors allowing a risk assessment of spore-forming pathogenic bacteria in cooked chilled foods containing vegetables: A FAIR collaborative project. Int. J. Food Microbiol. 60(2/3): 117-135. 464

Carlin F., H. Girardin, M.W. Peck, et al. 2000. Research on factors allowing a risk assessment of spore-forming pathogenic bacteria in cooked chilled foods containing vegetables: A FAIR collaborative project. Int. J. Food Microbiol. 60(2/3): 117-135. 466

Cassin, M.H., A.M. Lammerding, E.C.D. Todd, et al. 1998. Quantitative risk assessment for *Escherichia coli* O157:H7 in ground beef hamburgers. Int. J. Food Microbiol. 41: 21-44. 468

Cormack, R.M. 1999. Problems with using capture-recapture in epidemiology: An example of a measles epidemic. J. Clin. Epidemiol. 52(10): 909-914. 471

Corrigan, E.M. and R.L Clancy. 1999. Is there a role for a mucosal influenza vaccine in the elderly? Drugs Aging 15(3): 169-181. 473

Crabtree, K.D., C.P. Gerba, J.B. Rose and C.N. Haas. 1997. Waterborne adenovirus: A risk assessment. Wat. Sci. Technol. (35)11-12: 1-6. 474

den Aantrekker, E.D., R.M. Boom, M.H. Zwietering and M. Van Schothorst. 2003. Quantifying recontamination through factory environments-a review. Int. J. Food Microbiol. 80: 117-130. 476

Douwes, J., P. Thorne, N. Pearce and D. Heederik. 2003. Bioaerosol health effects and exposure assessment: Progress and prospects. Ann. Occup. Hyg. 47(3): 187-200. 478

Eduard, W. 1996. Measurement methods and strategies for non-infectious microbial components in bioaerosols at the workplace. Analyst 121: 1197-1201. 480

FAO/WHO. 2002a. Risk assessment of *Campylobacter spp.* in broiler chickens and *Vibrio spp.* in seafood. Report of a Joint FAO/WHO Consultation; Bangkok, Thailand; 5-9 August 2002. 482

Gale, P. 1996. Developments in microbiological risk assessment models for drinking water-a short review. J. Appl. Bacteriol. 81: 403-410. 484

Gerba, C.P. 1996. Risk assessment. Pollution science. San Diego, CA: Academic Press, Inc., p. 345-364. 486

Gerba, C.P., J.B. Rose, C.N. Haas and K.D. Crabtree. 1996. Waterborne rotavirus: A risk assessment. Wat. Res. 30(12): 2929-2940. 488

Haas, C.N. 2002. Progress and data gaps in quantitative microbial risk assessment (QMRA). Wat. Sci. Technol. 46(11-12): 277-284. 490

Hoornstra, E. and S. Notermans. 2001. Quantitative microbiological risk assessment. Int. J. Food Microbiol. 66: 21-29. 492

Hrudey, S.E., P. Payment, P.M. Huck, et al. 2003. A fatal waterborne disease epidemic in Walkerton, Ontario: Comparison with other waterborne outbreaks in the developed world. Wat. Sci. Technol. 47(3): 7-14. 494

Jaykus, L.-A. 1996. The application of quantitative risk assessment to microbial food safety risks. Crit. Rev. Microbiol. 22: 279-293. 496

Klapwijk, P.M., J.-L. Jouve and M.F. Stringer. 2000. Microbial risk assessment in Europe. Int. J. Food Microbiol. 58: 223-230. 498

Koopman J.S., and I.M. Longini. 1994. The ecological effects of individual exposures and nonlinear disease dynamics in populations. Am. J. Public Health 84(5): 836-842. 500

Krewski, D., J. Balbus, D. Butler-Jones, et al. 2002. Managing health risks from drinking water– a report to the Walkerton inquiry. J. Toxicol. Environ. Health, Part A 65: 1635-1823. 502

Krimsky, S., R.P. Wrubel, I.G. Naess, et al. 1995. Standardized microcosms in microbial risk assessment. Bioscience 45(9): 590-599. 504

Lammerding, A.M. and A. Fazil. 2000. Hazard identification and exposure assessment for microbial food safety risk assessment. Int. J Food. Microbiol. 58(3): 147-157. 507

McLauchlin, J., R.T. Mitchell, W.J. Smerdon, et al. 2004. *Listeria monocytogenes* and listeriosis: A review of hazard characterisation for use in microbiological risk assessment of foods. Int. J. Food Microbiol. 92(1): 15-33. 509

McNab, W.B. 1998. A general framework illustrating an approach to quantitative microbial food safety risk assessment. J. Food Protect. 61(9): 1216-1228. 511

Mossel, D.A.A., G.H. Weenk, G.P. Morris and C.B. Struijk. 1998. Identification, assessment, and management of food-related microbiological hazards: historical, fundamental, and psycho-social essentials. Int. J. Food Microbiol. 39: 19-51. 513

Myers M.F., D.J. Rogers, J. Cox J, et al. 2000. Forecasting disease risk for increased epidemic preparedness in public health. Advances Parasitol. 47: 309-330. 515

Neuman, D.A. and Foran, J.A, 1997. Assessing the risks associated with exposure to waterborne pathogens: An expert panel's report on risk assessment. J. Food Protect. 60: 1426-1431. 517

Nicas, M. 1994. Modeling respirator penetration values with the beta distribution: An application to occupational tuberculosis transmission. Am. Ind. Hyg. Assoc. J. 55(6): 515-524. 519

Powell, S.C. and R. Attwell. 1999. The use of epidemiological data in the control of foodborne viruses. Rev. Environ. Health 14(1): 31-37. 521

Reij, M.W. and E.D. Den Aantrekker. 2004. Recontamination as a source of pathogens in processed foods. Int. J. Food Microbiol. 91(1): 1-11. 523

Rose, J.B. and D.J. Grimes. 2001. Reevaluation of microbial water quality: Powerful new tools for detection and risk assessment. Washington, DC: American Academy of Microbiology. 525

Roy E. and P. Robillard. 1994. Effectiveness of and compliance to preventive measures against the occupational transmission of human immunodeficiency virus. Scand. J. Work Environ. Health 20: 393-400. 527

Salisbury, J.G., T.J. Nicholls, A.M. Lammerding, et al. 2002. A risk analysis framework for the long-term management of antibiotic resistance in food-producing animals. Int. J. Antimicrob. Agents 20(3): 153-164. 529

Schlundt, J. 2000. Comparison of microbiological risk assessment studies published. Int. J. Food Microbiol. 58(3): 197-202. 531

Simmons, J.E., L.K. Teuschler, C. Gennings, et al. 2004. Component-based and whole-mixture techniques for addressing the toxicity of drinking water disinfection by product mixtures. J. Toxicol. Environ. Health, Part A 67: 741-754. 533

Springthorpe, V.S., C.L. Loh and S.A. Sattar. 1997. How good is modelling of microbial survival in fluvial systems? Wat. Sci. Technol. 35(11-12): 253-259. 535

Teunis, P.F.M., A.H. Havelaar and G.J. Medema. 1995. A literature survey on the assessment of microbiological risk for drinking water. Rijksinstituut Voor Volksgezondheid en Milieuhygiene Bilthoven. Report nr. 734301006. 537

Teunis, P., A. Havelaar, J. Vliegenthart and G. Roessink. 1997a. Risk assessment of *Campylobacter* species in shellfish: Identifying the unknown. Wat. Sci. Technol. 35(11-12): 29-34. 539

Teunis, P., A. Havelaar, J. Vliegenthart and G. Roessink. 1997a. Risk assessment of *Campylobacter* species in shellfish: Identifying the unknown. Wat. Sci. Technol. 35(11-12): 29-34. 541

Teunis, P., A. Havelaar, J. Vliegenthart and G. Roessink. 1997a. Risk assessment of *Campylobacter* species in shellfish: Identifying the unknown. Wat. Sci. Technol. 35(11-12): 29-34. 543

Todd, E.C.D. 1996. Risk assessment of use of cracked eggs in Canada. Int. J. Food Microbiol. 30(1-2): 125-143. 545

van Schothorst, M. 1997. Practical approaches to risk assessment. J. Food Protect. 60(11): 1439-1443. 547

Vose, D.J. 1998. The application of quantitative risk assessment to microbial food safety. J. Food Protect. 61: 640-648. 549

Voysey, P.A. and M. Brown. 2000. Microbiological risk assessment: a new approach to food safety control. Int. J. Food Microbiol. 58(3): 173-179. 551

Wadhwa, S.G., G.H. Khaled and S.C. Edberg. 2002. Comparative microbial character of consumed food and drinking water. Crit. Rev. Microbiol. 28(3): 249-279. 553

Wallace, C. and D. Clayton. 2003. Estimating the relative recurrence risk ratio using a global cross-ratio model. Genetic Epidemiol. 25(4): 293-302. 555

Walls, I. and V.N. Scott. 1997. Use of predictive microbiology in microbial food safety risk assessment. Int. J. Food Microbiol. 36: 97-102. 557

Watson, A. and D. Keir. 1994. Information on which to base assessments of risk from environments contaminated with anthrax spores. Epidemiol. Infect. 113: 479-490. 559

Weis, C.P., A.J. Intrepedo, A.K. Miller, et al. 2002. Secondary aerosolization of viable *Bacillus anthracis* spores in a contaminated US Senate office. JAMA 288(22): 2853-2858. 561

A. Other Exclusions Study Identification (review)	Adams, M. and R. Mitchel. 2002. Fermentation and pathogen control: A risk assessment approach. Int. J. Food Microbiol. 79(½): 75-83.
B. Objectives and Type of Study	1. purpose: future regulatory interest; the paper discusses aspects of processes used in the production, storage, preparation, and consumption of fermented food products in the framework of identification of hazards presented by bacterial contamination of fermented food products (e.g., fermented sausages and cheeses), exposure to bacteria which cause illness (e.g., diarrhea associated with "food poisoning") associated with consumption of fermented food products, and characterization of risk for illness from bacteria in fermented foods 2. type: review
C. Publication Attributes	1. sponsors/affiliations: University of Surrey, UK 2. peer-review mechanism: scientific journal review
D. Data and Study Design	1. type: discussed published data of various types related to hazard identification, exposure assessment, and risk characterization for pathogens in fermented food products 2. source: published studies 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics (error structure for analytical data; repeatability; reproducibility; adequacy of analytical and statistical methods; completeness of study; etc.): NA 7. relevance of data: NA
E. Method/Model/Approach	1. general characteristics: provides a review of information related to risks of illness from pathogens in fermented foods 2. specific characteristics: NA 3. assumptions: NA4. limitations: NA 5. relevance (qualitative judgement of the usefulness of the method to incident-based microbial risk assessment for biothreat agents; high, medium, or low): NA
F. Study Conclusions and Extended Applications	1. conclusions supported by the review: because of the diversity of fermented foods, quantitative risk assessments of illness from consuming fermented foods as a group cannot be presented; assessments of risks for specific illnesses from consumption of specific fermented foods can be accomplished with limited quantitation (e.g., the risk of human listeriosis from consumption of raw milk soft cheeses) 2. authors' extrapolations from the observed data to other populations or conditions: NA
G. Data Gaps and Proposed Solutions	1. identification of data gaps: NA 2. assumptions or source of surrogate data to fill gap: NA

H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility (method of uncertain usefulness for incident-based microbial risk assessment of buildings and water systems): NA
I. Criteria for Exclusion from Compendium	study included no unique data and/or modeling of likely fate and transport or adverse effects of microbial agents
J. Reviewer Comments	other comments by reviewer: NA
K. Cross-References	additional data from the same study or same secondary data source summarized elsewhere in the compendium: NA

A. Other Exclusions Study Identification (dose-response)	Ashbolt, N.J. 2004. Risk analysis of drinking water microbial contamination versus disinfection by-products (DBPs). Toxicology 198(1-3): 255-262.
B. Objectives and Type of Study	1. purpose noted by study authors: future regulatory interest; Illustrates a case example, covering the health benefits of ozonation for *Cryptosporidium* inactivation versus potential cancers. 2. type: DR
C. Publication Attributes	1. sponsors/affiliations: none 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: NA 2. source: Published literature (Teunis and Havelaar, 1999; WHO, 1999; and Bartram et al., 2001) 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: NA
E. Method/Model/Approach	1. general characteristics: Dose response equations for assessing health outcomes.

	2. specific characteristics: Exponential model for probability of infection is P=1-exp(-rD), where D is pathogen dose, r is the fraction of pathogens that survives to produce infection. Beta-Poisson model for probability of infection is $P=1-(1+(D/\beta))^{-\alpha}$, where D is the pathogen dose, alpha and beta are parameters of the beta distribution used to describe variability in infectivity. 3. assumptions: NA 4. limitations: Probability outcomes limited by pathogen virulence characteristics, distribution in the environment, secondary transmission, and host/pathogen interaction. 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: NA 2. authors' extrapolations from the observed data to other populations or conditions: NA
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: NA
I. Criteria for Exclusion from Compendium	insufficient model documentation to demonstrate viable and credible modeling approaches
J. Reviewer Comments	NA
K. Cross-References	NA

A. Other Exclusions Study Identification (risk character.)	Ashbolt, N.J. 2004. Risk analysis of drinking water microbial contamination versus disinfection by-products (DBPs). Toxicology 198(1-3): 255-262.
B. Objectives and Type of Study	1. purpose noted by study authors: future regulatory interest; Illustrates a case example, covering the health benefits of ozonation for *Cryptosporidium* inactivation versus potential cancers. 2. type: RC
C. Publication Attributes	1. sponsors/affiliations: none

	2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: NA 2. source: Published literature (Havelaar, 2000; Teunis 1996; WHO, 1996) 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: NA
E. Method/Model/Approach	1. general characteristics: Probabilistic approach to model exposure to *Cryptosporidium* in drinking water. 2. specific characteristics: Monte Carlo sampling of oocyst distributions provided a probability density function of oocyst in water. Assumed 800 ml ingestion rate. An exponential dose response function used with bootstrapping for the parameter, r. 3. assumptions: 71% of population infected would become ill and 100% of AIDS population exposed would become ill. 4. limitations: Only includes drinking water 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: Median risk of infection was 10^{-3} per person per year. 2. authors' extrapolations from the observed data to other populations or conditions: NA
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: NA
I. Criteria for Exclusion from Compendium	insufficient model documentation to demonstrate viable and credible modeling approaches
J. Reviewer Comments	NA
K. Cross-References	NA

A. Other Exclusions Study Identification (review)	Balbus, J., R. Parkin, A. Makri, et al. 2004. Defining susceptibility for microbial risk assessment: Results of a workshop. Risk Anal. 24(1): 197-208.
B. Objectives and Type of Study	1. purpose: scientific; summary from an interdisciplinary workshop convened to discuss how to incorporate new knowledge about susceptibility to microbial pathogens into risk assessment and management strategies 2. type: review
C. Publication Attributes	1. sponsors/affiliations: US EPA, Office of Water, Health and Ecological Criteria Division 2. peer-review mechanism: scientific journal review
D. Data and Study Design	1. type: no new data; review/discussion 2. source: NA 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: NA
E. Method/Model/Approach	1. general characteristics: no new analyses; review/discussion 2. specific characteristics: NA 3. assumptions: NA 4. limitations: NA 5. relevance: NA
F. Study Conclusions and Extended Applications	1. conclusions: NA 2. authors' extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA

	5. defensibility: NA
I. Criteria for Exclusion from Compendium	review/discussion
J. Reviewer Comments	NA
K. Cross-References	original sources cited may be of relevance

A. Other Exclusions Study Identification (review)	Blumenthal, U.J., D.D. Mara, A. Peasey, et al. 2000. Guidelines for microbiological quality of treated wastewater used in agriculture: recommendations for revising WHO guidelines. Bull. World Health Org. 78(9): 1104-1116.
B. Objectives and Type of Study	1. purpose: future regulatory interest; Three different approaches for establishing guidelines for the microbiological quality of treated wastewater that is reused for agriculture are reviewed. 2. type: review of applying different approaches to setting acceptable levels of microbial agents in wastewater
C. Publication Attributes	1. sponsors/affiliations: Department for International Development, United Kingdom; and Water and Sanitation in Developing Countries, Switzerland 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: A review and assessment of the three main approaches used for establishing microbiological quality guidelines and standards for the reuse of treated wastewater in agriculture. 2. source: published scientific studies and government documents, including those from US guidelines, 1989 WHO guidelines. 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: a qualitative assessment of three approaches 2. specific characteristics: The three approaches reviewed for setting microbiological quality guidelines and standards are: (1) use of fecal coliforms as indicators of possible pathogen presence, (2) use of epidemiological studies to determine risks, and (3) quantitative microbial risk assessments using modeling approaches. 3. assumptions: For (1), it is assumed that need for expensive and time-consuming monitoring is eliminated; For

	(2), changes in exposure variable are assumed that might affect outcome. For (3), values for exposure variables are often assessed (i.e., various exposure parameters, pathogen characteristics). 4. limitations: For (1), strict guidelines and state-specific standards. For (2), results are specific to specific time and place of study. For (3), data availability for exposure and pathogen occurrence and dose response. 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions: The authors recommend new guidelines based on a mixture of the epidemiological approach and the microbial risk assessment modeling approach. 2. authors' extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: dose response (use of healthy individuals, previous exposure, high-dose/low dose extrapolation); definition of risk itself. 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: low
I. Criteria for Exclusion from Compendium	Insufficient data quantity to support rigorous science-based modeling. The review deals more with how one approaches the setting of microbiological quality guidelines and standards for the reuse of treated wastewater in agriculture.
J. Reviewer Comments	A useful review that gives insight on the advantages and disadvantages of all of the three approaches to setting guidelines and standards. The framework of the guidelines might be of use in assessing how to make water supplies, food supplies and buildings safer from biothreats.
K. Cross-References	NA

A. Other Exclusions Study Identification (review)	Buchanan, R. 1998. Principles of risk assessment for illness caused by food-borne biological agents. J. Food Protect. 61(8): 1071-1074.
B. Objectives and Type of Study	1. purpose: future regulatory interest 2. type: review

C. Publication Attributes	1. sponsors/affiliations: requested by the NACMCF 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: Describes the 3 major components of a risk assessment (exposure assessment, dose response, and risk characterization), describes basic principles for each component. 2. source: NA 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: NA 2. specific characteristics: NA 3. assumptions: NA 4. limitations: NA 5. relevance: low. No data is used to demonstrate how the components described are integrated into a model.
F. Study Conclusions and Extended Applications	1. conclusions: NA 2. authors' extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: low 5. defensibility: low
I. Criteria for Exclusion from Compendium	The model provided no data or models to show how the components are integrated to demonstrate a defensible modeling approach.
J. Reviewer Comments	framework for setting up and identifying data for a food-borne risk assessment
K. Cross-References	NA

A. Other Exclusions Study Identification (dose-response)	Carlin F., H. Girardin, M.W. Peck, et al. 2000. Research on factors allowing a risk assessment of spore-forming pathogenic bacteria in cooked chilled foods containing vegetables: A FAIR collaborative project. Int. J. Food Microbiol. 60(2/3): 117-135.
B. Objectives and Type of Study	1. purpose: scientific; To evaluate the risk due to spore-forming bacteria (SFB) in cooked chilled foods through a formal quantitative risk assessment. 2. type: DR
C. Publication Attributes	1. sponsors/affiliations: Commission of the European Communities, Agriculture and Fisheries (FAIR) specific RTD programme, CT97-3159; additional funding from the strategic grant of the BBSRC. 2. peer-review mechanism: peer reviewed journal
D. Data and Study Design	1. type: literature review for SFB with the potential to cause foodborne disease. 2. source: electronic databases (e.g., Medline, Toxline, Current Contents) housing citations for published literature from 1969 to 1998. 3. extent of data: foodborne outbreaks associated with six SFBs: *B. cereus, B. subtilis, B. licheniformis, B. pumilus*, and proteolytic and non-proteolytic *C. botulinum*. Data gathered included incidents of SFBs on food products, fatality rates, number of outbreaks per year, relation to vegetables and vegetable-based foods, growth temperatures. Also reviewed limited dose-response information for some of the pathogens. 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: toxicity data provided for *C. botulinum* neurotoxin (BoNT) and toxin description for *B. cereus*. 2. specific characteristics: LD_{50} for BoNT is about 1 ng toxin/kg body weight for mice, guinea pigs, rabbits, monkeys, and humans. Injected dose for medical applications of BoNT is 0.33 to 0.66 ng. Local injections of higher doses close to 5 ng results in a spreading of the paralysis and other effects. Safe dose for BoNT is 0.004-0.008 ng/kg body weight. Dose of 0.06 ng/kg body weight results in adverse health effects. For B. cereus, epidemiological data suggests 10^5 spores have to be consumed for food poisoning to occur. 3. assumptions: NA 4. limitations: lack of data concerning DR relation of the toxins of *B. cereus* and *C. botulinum*; lack of a clear relation between numbers of organisms in the food and the amount of toxin produced; lack of methods to detect different complexes of toxins. 5. relevance: low

F. Study Conclusions and Extended Applications	1. conclusions: The poor quality of DR assessments will limit quality of risk assessment. An understanding of the mechanism of virulence of pathogenic bacteria or toxin production is still needed. 2. authors' extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: see E4 2. proposed solutions: research in the area of uncertainty (e.g., DR assessment, toxin production, growth and inactivation, etc).
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: high 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: low 5. defensibility: low
I. Criteria for Exclusion from Compendium	This study had insufficient data quality or quantity to support rigorous science-based modeling and insufficient model documentation to demonstrate viable and credible modeling approaches.
J. Reviewer Comments	Lack of quantitative DR assessment; no attempt to provide a DR relation with the specific pathogens or use of surrogates.
K. Cross-References	NA

A. Other Exclusions Study Identification (exposure assessment)	Carlin F., H. Girardin, M.W. Peck, et al. 2000. Research on factors allowing a risk assessment of spore-forming pathogenic bacteria in cooked chilled foods containing vegetables: A FAIR collaborative project. Int. J. Food Microbiol. 60(2/3): 117-135.
B. Objectives and Type of Study	1. purpose: scientific; To evaluate the risk due to spore-forming bacteria (SFB) in cooked chilled foods through a formal quantitative risk assessment. 2. type: EA
C. Publication Attributes	1. sponsors/affiliations: Commission of the European Communities, Agriculture and Fisheries (FAIR) specific RTD programme, CT97-3159; additional funding from the strategic grant of the BBSRC. 2. peer-review mechanism: peer reviewed journal
D. Data and Study Design	1. type: literature review for SFB with the potential to cause foodborne disease. 2. source: electronic databases (e.g., Medline, Toxline, Current Contents) housing citations for published

	literature from 1969 to 1998. 3. extent of data: foodborne outbreaks associated with six SFBs: *B. cereus, B. subtilis, B. licheniformis, B. pumilus*, and proteolytic and non-proteolytic *C. botulinum*. Data gathered included incidents of SFBs on food products, fatality rates, number of outbreaks per year, relation to vegetables and vegetable-based foods, growth temperatures. Also reviewed limited dose-response information for some of the pathogens. 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: literature reviewed for the number of or amount of toxin produced by the SFB, mainly *C. botulinum* and *B. cereus*. 2. specific characteristics: Number of cells depends on initial contamination of foods, effect of heat-processing, and growth of SFB during storage. Information regarding each of these factors were compiled from the literature reviews and summarized in this paper. 3. assumptions: NA 4. limitations: NA 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions: NA 2. authors' extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: high 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: low 5. defensibility: low
I. Criteria for Exclusion from Compendium	This study had insufficient data quality or quantity to support rigorous science-based modeling and insufficient model documentation to demonstrate viable and credible modeling approaches.
J. Reviewer Comments	Information summarized for C. botulinum would be of use for exposure assessment under a foodborne threat scenario.
K. Cross-References	Data from same study summarized elsewhere in the compendium for dose response and risk characterization.

A. Other Exclusions Study Identification (risk character.)	Carlin F., H. Girardin, M.W. Peck, et al. 2000. Research on factors allowing a risk assessment of spore-forming pathogenic bacteria in cooked chilled foods containing vegetables: A FAIR collaborative project. Int. J. Food Microbiol. 60(2/3): 117-135.
B. Objectives and Type of Study	1. purpose: scientific; To evaluate the risk due to spore-forming bacteria (SFB) in cooked chilled foods through a formal quantitative risk assessment. 2. type: RC
C. Publication Attributes	1. sponsors/affiliations: Commission of the European Communities, Agriculture and Fisheries (FAIR) specific RTD programme, CT97-3159; additional funding from the strategic grant of the BBSRC. 2. peer-review mechanism: peer reviewed journal
D. Data and Study Design	1. type: literature review for SFB with the potential to cause foodborne disease. 2. source: electronic databases (e.g., Medline, Toxline, Current Contents) housing citations for published literature from 1969 to 1998. 3. extent of data: foodborne outbreaks associated with six SFBs: *B. cereus, B. subtilis, B. licheniformis, B. pumilus*, and proteolytic and non-proteolytic *C. botulinum*. Data gathered included incidents of SFBs on food products, fatality rates, number of outbreaks per year, relation to vegetables and vegetable-based foods, growth temperatures. Also reviewed limited dose-response information for some of the pathogens. 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: Probability of food poisonings not calculated, but rather an estimation of the number of bacteria identified as hazardous, B. cereus and C. botulinum, at different times during the shelf life of the product. 2. specific characteristics: Two approaches used: a Monte Carlo simulation and a Bayesian belief network approach. For both approaches, parameters associated with variability were incorporated into the model. Uncertainties were represented by probability distributions. Parameter estimates were either from experimental data or from expert opinion. The spread of the associated parameters were established by estimating the minimum, most likely and maximum values and represented by a BetaPert distribution. 3. assumptions: NA 4. limitations: poor quality DR assessments and limited knowledge of the virulence of the pathogens. 5. relevance: medium

F. Study Conclusions and Extended Applications	1. conclusions: Project demonstrated how microbial risk assessment may be used to determine which elements have the highest contribution to overall risk and where effort must be applied for improvement of food safety. 2. authors' extrapolations: Predictive microbiology models may be used to describe the developments of populations of microorganisms throughout the manufacturing process.
G. Data Gaps and Proposed Solutions	1. data gaps: often data results from experimental measurements which may not directly reflect the process of interest. 2. proposed solutions: develop research in areas of uncertainty, continue to develop analytical tools, reinforce collaboration between food microbiologists and risk assessors.
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: high 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: low 5. defensibility: low
I. Criteria for Exclusion from Compendium	This study had insufficient data quality or quantity to support rigorous science-based modeling and insufficient model documentation to demonstrate viable and credible modeling approaches.
J. Reviewer Comments	There were no conclusive results provided, nor were there comparisons between the two methods used.
K. Cross-References	Data from same study summarized elsewhere in the compendium for dose response and risk characterization.

A. Other Exclusions Study Identification (RC, EA, DR)	Cassin, M.H., A.M. Lammerding, E.C.D. Todd, et al. 1998. Quantitative risk assessment for *Escherichia coli* O157:H7 in ground beef hamburgers. Int. J. Food Microbiol. 41: 21-44.
B. Objectives and Type of Study	1. purpose noted by study authors: regulatory, future regulatory interest; to describe the behavior of the pathogen from the production of food through processing, handling, and consumption to predict human exposure. 2. type: limited RC, EA, DR
C. Publication Attributes	1. sponsors/affiliations: International Life Sciences Institute North America Technical Committee on Food Microbiology 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: data from three human feeding studies of two *Shigella* species; studies of pathogen detection in cattle, data on beef carcass surface sampling, data on pathogen growth parameters from Food MicroModel, data from

	cooking experiments measuring log survivors of *E. coli* O157:H7 in hamburgers. 2. source: published studies, government datasets, expert opinion 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: 25,000 iteration Monte Carlo simulation using Latin Hypercube sampling with @Risk software; model predictions used to evaluate risk mitigation strategies 2. specific characteristics: Process Risk Model built on two submodels representing the stages in the farm-to-table continuum for hamburger and a dose-response model; Beta-Binomial model of infection used to estimate probability of illness from a particular dose including variability in this probability; Spearman rank correlation coefficient used in importance analysis to quantitatively determine most important factors affecting risk to human health from *E. coli* O157:H7; model used to analyze three hypothetical risk mitigation strategies. 3. assumptions: one cell is capable of causing illness, and each cell is equally infective; susceptible population has a similar vulnerability to illness following pathogen ingestion but an increased propensity for severe outcomes such as HUS; organism prevalence can be characterized with a beta distribution, and outcome of a detection study was a binomial random variable; original source of pathogen considered to be feces of an animal shedding the pathogen; microbial profile of a production lot of beef trimmings is independent of previous lots processed at abattoir; risk of contamination of carcasses during evisceration is negligible; prevalence of pathogen on carcasses is proportional to prevalence of animals shedding the pathogen; retail grinder randomly mixes pathogen throughout 5 kg lot of ground beef; ratio of contaminated carcasses to uncontaminated carcasses is 2-3 times the ratio of pathogen-shedding animals to non-shedding animals (unsupported assumption); aggregate effect of all decontamination treatments was assumed to be 1-2.5 log reduction in pathogen counts; pathogen growth under control until delivery to retail outlet; temperature determining factor in magnitude of pathogen growth with pH, % NaCl, and water activity held constant. 4. limitations: many assumptions, some unsupported, made in construction of model; applicability of model limited by uncertainty and ignorance of hygienic effects of individual operations during production, processing, and handling of ground beef. 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions supported by the data given assumptions: risk for most scenarios was <1 in 10,000 chance of illness; probability of illness per hamburger meal in the US estimated to be 5.7e-7 to 1.2e-6; carcass contamination, storage time and temperature during retail display were significant risk factors; microbial growth during processing was also a risk factor; model indicated that supposed higher level of compliance in retail storage temperature control versus level of consumer compliance in end-product cooking would produce greatest reduction in risk.

	2. authors' extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: seasonality, geographical effects, feeding practices not incorporated into model; possibility of reduced infectivity of pathogen after cooking not incorporated into model; lack of empirical data forced several assumptions; dose-response relationship likely to be inaccurate because it was based on feeding studies with *Shigella spp*. using healthy adults. 2. proposed solutions: need to refine model to take into account more factors that may influence pathogen presence and fate in the farm-to-table continuum for hamburger; need data for dose-response relationships
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: some high 3. generalizability or external validity: high 4. soundness of study conclusions or internal validity: low 5. defensibility: low
I. Criteria for Exclusion from Compendium	insufficient data quality to support rigorous science-based modeling
J. Reviewer Comments	Method of uncertain usefulness due to large number of data gaps and assumptions.
K. Cross-References	NA

A. Other Exclusions Study Identification (risk character.)	Cormack, R.M. 1999. Problems with using capture-recapture in epidemiology: An example of a measles epidemic. J. Clin. Epidemiol. 52(10): 909-914.
B. Objectives and Type of Study	1. purpose: To draw attention to the use of capture-recapture methodology in estimating disease prevalence or sizes of population at risk. 2. type: RC
C. Publication Attributes	1. sponsors/affiliations: University of St Andrews, Scotland 2. peer-review mechanism: peer-review journal
D. Data and Study Design	1. type: epidemiologic data and asyptotic statistical theory 2. source: measles epidemic in Sydney Australia (McGilchrist et al., 1996) 3. extent of data: reported cases of measles stratified by age 4. sampling plan: capture/recapture of measles cases with 4 source categories: doctors, hospitals, laboratories,

	others 5. sample size: 503 cases reported, 11 of which reported by 2 sources; 100 simulations of each of the five multinomial distributions 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: capture-recapture methodology; simulation using loglinear models; goodness of fit 2. specific characteristics: test of capture-recapture methodology used to estimate size of population; parametric bootstrap including loglinear models examined for best fitting model; acceptability of model assessed by comparing residual deviance with $\chi 2$ goodness of fit. 3. assumptions: population size estimate is sensitive to selected model, statistical independence between lists. 4. limitations: problems with sparse data, problem with heterogeneity; uncertainty of matching individuals between lists, derivation of a formal interval estimate for the population size which allows of the effect of data exploration and model selection. 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions: authors judge available data insufficient to support modeling or estimation of measles prevalences and populations at risk 2. authors' extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: sparse data, uncertainty of matched cases between lists, variability between individuals 2. proposed solutions: better data, but not usually possible in population estimation
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: low 5. defensibility: low
I. Criteria for Exclusion from Compendium	insufficient data quality to support rigorous science-based modeling
J. Reviewer Comments	NA
K. Cross-References	NA

A. Other Exclusions Study Identification (review)	Corrigan, E.M. and R.L Clancy. 1999. Is there a role for a mucosal influenza vaccine in the elderly? Drugs Aging 15(3): 169-181.
B. Objectives and Type of Study	1. purpose: this review of mechanisms of mucosal immunity to influenza supports the opinion that serum levels of antibody response are inappropriate markers of efficacy of vaccines and that alternative markers of efficacy should be developed for use in developing vaccines 2. type: review
C. Publication Attributes	1. sponsors/affiliations: Royal Newcastle Hospital 2. peer-review mechanism: scientific journal review
D. Data and Study Design	1. type: NA 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance of data: NA
E. Method/Model/Approach	1. general characteristics: NA 2. specific characteristics: NA 3. assumptions: NA4. limitations: NA 5. relevance: NA
F. Study Conclusions and Extended Applications	1. conclusions supported by the study: NA 2. authors' extrapolations from the observed data to other populations or conditions: NA
G. Data Gaps and Proposed Solutions	1. identification of data gaps: NA 2. assumptions or source of surrogate data to fill gap: NA
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: NA
I. Criteria for Exclusion from Compendium	review is of mucosal immunity and markers to assess efficacies of mucosal vaccination; no information is provided on microbial risk assessment methods

J. Reviewer Comments	NA
K. Cross-References	NA

A. Other Exclusions Study Identification (risk character.)	Crabtree, K.D., C.P. Gerba, J.B. Rose and C.N. Haas. 1997. Waterborne adenovirus: A risk assessment. Wat. Sci. Technol. (35)11-12: 1-6.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific; to assess the risk of obtaining an adenovirus infection from exposure to contaminated drinking or recreational water. 2. type: RC
C. Publication Attributes	1. sponsors/affiliations: University of Arizona Tucson, University South Florida, Drexel University 2. peer-review mechanism: full scientific peer review
D. Data and Study Design	1. type: theoretical study using two assumed adenovirus concentrations and published DR model 2. source: previous published literature to obtain assumed virus concentrations, water exposure, morbity rate, and probability of mortality from an infection (Rose et al. 1996) 3. extent of data: Two assumed concentrations of virus with risk reported for two different exposure times. 4. sampling plan: NA 5. sample size: For risks associated with drinking water: four risks (infection, illness, death–general population, and death elderly population) reported for two different virus levels and two different exposure levels. For risks associated with swimming in contaminated freshwater: three risks (infection, illness, death) reported for two different virus levels and two different exposure levels. 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: deterministic exponential model 2. specific characteristics: Model used was P=1-exp(-rN), where P represents the probability of infection, N represents the number of organisms ingested or inhaled and r=0.4172. 3. assumptions: The range of adenovirus concentration in water is the same as for other enteric viruses in water. 4. limitations: NA 5. relevance: medium
F. Study Conclusions and Extended	1. conclusions supported by the data: Annual risks of infection in drinking water for adenovirus at average levels

Applications	of 1 per 1,000L to 1 per 100L ranged from 8.3/10,000 to 8.3/1000. 2. authors' extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: Limited data available as to actual concentration/occurrence of adenovirus in water 2. proposed solutions: Additional investigations on adenovirus prevalence and survivability in water as well as susceptibility to water treatments are needed.
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: low 5. defensibility: low
I. Criteria for Exclusion from Compendium	insufficient data quality and quantity to support rigorous science-based modeling
J. Reviewer Comments	estimated illnesses due to adenovirus in drinking water or recreational water; sensitive to assumptions for exposure assessment and dose-response assessment
K. Cross-References	NA

A. Other Exclusions Study Identification (exposure assessment)	den Aantrekker, E.D., R.M. Boom, M.H. Zwietering and M. Van Schothorst. 2003. Quantifying recontamination through factory environments-a review. Int. J. Food Microbiol. 80: 117-130.
B. Objectives and Type of Study	1. purpose: scientific; future regulatory application 2. type: EA
C. Publication Attributes	1. sponsors/affiliations: Laboratory of Food Microbiology and Bioprocess Engineering Group, Wageningen University; Danone Vitapole, France 2. peer-review mechanism: full scientific review
D. Data and Study Design	1. type: EA 2. source: published studies 3. extent of data: some data on transfer and growth rates for different recontamination routes.

	4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA. 7. relevance: low
E. Method/Model/Approach	1. general characteristics: Extensive, well-documented overview of modeling approaches available to quantify recontamination of food products in factory environments. Development of a general framework for including recontamination models in predictive models of microbial growth in food products 2. specific characteristics: recontamination via air, processing equipment, and hand contact was considered - processing equipment models: biofilm formation in reactors and pipelines; differential equations describing attachment, growth, and detachment of cells (Wanner, 1995); Monad kinetics models (Stewart, 1993); detachment models including shear stress (De Jong et al., 1999) and adhesion variables (Dickinson and Cooper, 1995); two-dimensional biofilm formation (Lu et al., 1995); recontamination of drinking water (Dahi and Thogerson, 1996) air models: food contamination via air; quadratic relationship between the number of bacteria found in air vs contaminated products (Randmore et al., 1998); settling velocity models (Whyte, 1986); spore contamination (Pielaat and van den Bosch, 1998) hands models: quantify hand contamination; handling infected laundry (Gibson et al., 1999); transfer from hands to cloth (Mackintosh and Hoffman, 1984); transfer of *Enterobacter aerogenes* from chickens, via hands, to lettuce (Chen et al., 2001); effect of wearing gloves (Montville et al., 2001) 3. assumptions: NA 4. limitations: NA 5. relevance: NA
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: the entire biofilm process should be taken into account; 2. extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: data for the number of bacteria on the floor and air; validation of recontamination via air using experimental data; better data needed for transfer rates for the different recontamination routes. 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: NA
I. Criteria for Exclusion from	review paper that does not present the result of an original study or unique modeling effort

Compendium	
J. Reviewer Comments	Although this paper does not provide data that may be used directly in exposure assessment, it is considerably valuable for identifying models for performing exposure assessments. The paper lists a large variety of models that can be used to model air contamination, contamination from equipment surfaces, and contamination via hand contact. The paper also lists some areas where further empirical data are required (i.e., bacteria on floors). Numerous equations are presented that can aid the risk assessor in quantifying recontamination routes.
K. Cross-References	NA

A. Other Exclusions Study Identification (exposure assessment)	Douwes, J., P. Thorne, N. Pearce and D. Heederik. 2003. Bioaerosol health effects and exposure assessment: Progress and prospects. Ann. Occup. Hyg. 47(3): 187-200.
B. Objectives and Type of Study	1. purpose: scientific; Provides an overview of health effects associated with bioaerosol exposure in occupational environment (e.g., infectious diseases, biological and nonbiological agents causing respiratory diseases, agents causing cancer), review exposure assessment methods, discuss potential for standard setting and identify relevant future research areas. 2. type: review, EA
C. Publication Attributes	1. sponsors/affiliations: Netherlands Organization for Scientific Research; NIEHS P30 ES05605; New Zealand Health Research Council 2. peer-review mechanism: peer-reviewed journal
D. Data and Study Design	1. type: No data are presented, reviews a large number of existing studies 2. source: NA 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: high
E. Method/Model/Approach	1. general characteristics: Various methods are presented in review from past studies, but no new methods are presented in detail. 2. specific characteristics: NA

	3. assumptions: NA 4. limitations: NA 5. relevance: NA
F. Study Conclusions and Extended Applications	1. conclusions: More research is needed to establish better exposure assessment tools and to validate newly developed methods. 2. authors' extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: no data presented 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: NA
I. Criteria for Exclusion from Compendium	A review paper covering various past studies with no original data presented in a new analysis. Original sources should be cited if needed.
J. Reviewer Comments	good review
K. Cross-References	NA

A. Other Exclusions Study Identification (risk character.)	Eduard, W. 1996. Measurement methods and strategies for non-infectious microbial components in bioaerosols at the workplace. Analyst 121: 1197-1201.
B. Objectives and Type of Study	1. purpose: scientific; Gives an overview of measurement methods for microbial bioaerosol components and some of their properties that may serve as an aid for selecting methods in future studies and to make suggestions on strategies for risk assessments. 2. type: RC
C. Publication Attributes	1. sponsors/affiliations: National Institute of Occupational Health 2. peer-review mechanism: peer-reviewed journal
D. Data and Study Design	1. type: no data analyzed, various types of bioaerosol agents outlined

	2. source: literature 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: There are various possible bioaerosol methods outlined in overview, but none are analyzed. 2. specific characteristics: Different approaches and methods are recommended dependent on bioaerosol of interest. 3. assumptions: NA 4. limitations: NA 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions: filter sampling and analysis by non-viable methods are recommended for the measurement of exposure to non-infectious microbial bioaerosol components in the work environment. 2. authors' extrapolations: Further studies are needed to clarify which microbial components are most relevant for health effects from non-infectious bioaerosol exposure in the work environment.
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: NA
I. Criteria for Exclusion from Compendium	overview, analytical methods described but not used
J. Reviewer Comments	NA
K. Cross-References	NA

A. Other Exclusions Study Identification (prelim. review)	FAO/WHO. 2002a. Risk assessment of *Campylobacter spp.* in broiler chickens and *Vibrio spp.* in seafood. Report of a Joint FAO/WHO Consultation; Bangkok, Thailand; 5-9 August 2002.
B. Objectives and Type of Study	1. purpose: scientific; To document the results of an approach to quantify illnesses caused by *Vibrio spp.* in different countries following the consumption of a range of seafood. 2. type: preliminary review
C. Publication Attributes	1. sponsors/affiliations: Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO) 2. peer-review mechanism: summary of meeting
D. Data and Study Design	1. type: surveillance, monthly or seasonally or ad hoc, from waters and seafood (Japan, Australia, New Zealand, Canada, US); human clinical studies for *Campylobacter jejuni*, *V. parahaemolyticus*, and *V. cholerae* O1 2. source: published literature and government data 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: various preliminary models briefly described, including some with Monte Carlo simulation linking estimated exposure in poultry and seafoods with the dose-response models 2. specific characteristics: NA 3. assumptions: NA. 4. limitations: NA 5. relevance: NA
F. Study Conclusions and Extended Applications	1. conclusions: draft quantitative risk assessments not finalized to date 2. authors' extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: lack of systematic data and fundamental knowledge for modeling foodborne exposures of both pathogens leading to human illness 2. proposed solutions: conduct targeted research
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: some high 3. generalizability or external validity: NA

	4. soundness of study conclusions or internal validity: NA 5. defensibility: NA
I. Criteria for Exclusion from Compendium	meeting participants determined that draft risk assessments presented were preliminary due to limitations of data and theory
J. Reviewer Comments	NA
K. Cross-References	NA

A. Other Exclusions Study Identification (review)	Gale, P. 1996. Developments in microbiological risk assessment models for drinking water-a short review. J. Appl. Bacteriol. 81: 403-410.
B. Objectives and Type of Study	1. purpose: scientific 2. type: review
C. Publication Attributes	1. sponsors/affiliations: Department of Environment, Drinking Water Inspectorate, UK 2. peer-review mechanism: scientific journal review
D. Data and Study Design	1. type: NA 2. source: NA 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: NA
E. Method/Model/Approach	1. general characteristics: NA 2. specific characteristics: NA 3. assumptions: NA 4. limitations: NA 5. relevance: NA
F. Study Conclusions and Extended Applications	1. conclusions: in contrast to assumptions of current models, pathogens are clustered (not randomly dispersed), even within small volumes of drinking water; by assuming that pathogens are randomly distributed, current

	models overestimate the risk from more infectious agents (e.g., rotovirus) and underestimate risk from less infectious pathogens (e.g., *C. parvum*) 2. authors' extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: NA
I. Criteria for Exclusion from Compendium	review article
J. Reviewer Comments	NA
K. Cross-References	NA

A. Other Exclusions Study Identification (overview)	Gerba, C.P. 1996. Risk assessment. Pollution science. San Diego, CA: Academic Press, Inc., p. 345-364.
B. Objectives and Type of Study	1. purpose: future regulatory interest; 2. type: overview of risk assessment framework or processes only
C. Publication Attributes	1. sponsors/affiliations: unknown 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: discusses the components used in developing models and equation used for MRA 2. source: published studies 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics (error structure for analytical data; repeatability; reproducibility; adequacy of

	analytical and statistical methods; completeness of study; etc.): NA 7. relevance of data: NA
E. Method/Model/Approach	1. general characteristics: review of components used in different types of risk assessment models (chemical and microbiological) 2. specific characteristics: NA 3. assumptions: NA4. limitations: NA 5. relevance (qualitative judgement of the usefulness of the method to incident-based microbial risk assessment for biothreat agents; high, medium, or low): NA
F. Study Conclusions and Extended Applications	1. conclusions supported by the review: discusses the process of developing RA models and the components of each step (Hazard ID, Exposure Assessment, Dose Response); describes use of uncertainty analyses (i.e Monte Carlo simulation); lists case fatality rates for some Biothreat agents of concern found elsewhere 2. authors' extrapolations from the observed data to other populations or conditions: NA
G. Data Gaps and Proposed Solutions	1. identification of data gaps: NA 2. assumptions or source of surrogate data to fill gap: NA
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: NA
I. Criteria for Exclusion from Compendium	study included no unique data and/or modeling of likely fate and transport or adverse effects of microbial agents
J. Reviewer Comments	other comments by reviewer: this "article" is actually a chapter from a text book that seeks to introduce the concepts behind risk assessment and the process of developing models for human health use. It does not, however, provide specific models for biothreat agents of interest as potential contaminants of food and water
K. Cross-References	NA

A. Other Exclusions Study Identification (risk character.)	Gerba, C.P., J.B. Rose, C.N. Haas and K.D. Crabtree. 1996. Waterborne rotavirus: A risk assessment. Wat. Res. 30(12): 2929-2940.

B. Objectives and Type of Study	1. purpose: scientific; to present an approach that assesses the risks associated with waterborne rotavirus. 2. type: RC
C. Publication Attributes	1. sponsors/affiliations: American Water Works Research Foundation 2. peer-review mechanism: scientific journal
D. Data and Study Design	1. type: Theoretical study 2. source: small targeted surveys from published literature 3. extent of data: Two assumed concentrations of virus with risk reported for two different exposure times. 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: assumptions for exposure linked with published dose-response models (Haas 1983; Haas et al. 1993; Regei et al. 1993) 2. specific characteristics: Probability of infection calculated on the beta-Poisson model (parameters beta=0.42 and alpha=0.26). Probability of clinical illness was determined by multiplying B by 0.5 and mortality by multiplying the this number by case fatality rates of 0.01% for the general population and 1.0% for the elderly. 3. assumptions: exposure in drinking water equals 4/1,000 L □ day or 100/L □ day for 21 or 41 days 4. limitations: Lack of data on rotavirus in drinking water and the potential for human exposure. 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions: risk of disease could be associated with drinking and recreational waters contaminated with rotavirus 2. authors' extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: Lack of quantitative data of rotavirus in water, particularly in developed countries. 2. proposed solutions: Additional study of exposure and dose-response relationships
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: low 5. defensibility: low
I. Criteria for Exclusion from Compendium	insufficient data quality and quantity to support rigorous science-based modeling

J. Reviewer Comments	Gives a first approximation of estimating illness due to rotavirus in drinking water or recreational water. Assumptions used in generating risks associated with rotavirus may incorrectly characterize the frequency and magnitude of illness
K. Cross-References	NA

A. Other Exclusions Study Identification (review)	Haas, C.N. 2002. Progress and data gaps in quantitative microbial risk assessment (QMRA). Wat. Sci. Technol. 46(11-12): 277-284.
B. Objectives and Type of Study	1. purpose: scientific; This paper reviews the development of QMRA and outlines the nature of additional data that would be useful for its development. 2. type: review
C. Publication Attributes	1. sponsors/affiliations: Department of Civil, Architectural and Environmental Engineering, Drexel University 2. peer-review mechanism: peer-reviewed journal
D. Data and Study Design	1. type: Four case studies using QMRA: one for risk of pathogen in food (*E. coli* in hamburger [Cassin et al., 1998]), the other three involve drinking water (*Giardia* [Regli et al., 1991; and Rose et al., 1991] and *Cryptosporidium* [Teunis et al., 1997; and NRC, 2000; Haas et al., 2000]) 2. source: published literature 3. extent of data: summarizes the risk results of the QMRA for each of the four case studies. Depending on the case study, “risk” given as attack rates, median annual risk of infection, estimated risk to consumers, and potential impact of controls. 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: In the case studies, dose-response relationships and exposure assumptions were used to derive risk, but details of the models were not included. 2. specific characteristics: For *Giardia*, risk estimates were used compared to attack rates from outbreaks to derive an acceptable finished water concentration. For *C. parvum*, derived an annual risk of infection based on the dose response relationship. 3. assumptions: NA

	4. limitations: NA 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions: Author offers general overviews on data gaps in QMRA 2. authors' extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: Elements of dose response, such as extrapolation of high dose to low dose; relationship between ingested dose and severity of consequences, strain differences, use of animal models. Elements of exposure assessment include differences in exposure via variability in concentrations or in consumption patterns; also, detection methods are less than adequate for some pathogens. Population level dynamics are not well known. 2. proposed solutions: Use of exponential and beta Poisson are successful at extrapolation of high to low dose; derivation of dose response-severity relationships. For exposure assessment, need to adequately characterize the distribution of risks, focusing on temporal and spatial relations; need to determine better detection methods.
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: high 3. generalizability or external validity: high 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	NA
J. Reviewer Comments	The data gaps identified here are very useful to the MRA itself for any pathogen.
K. Cross-References	Primary reports of the 4 QMRA case studies include Regli et al. 1991; Rose et al. 1991; Teunis et al. 1997; NRC 2000; and Haas et al. 2000. The primary reports are likely to contain more specific information on the exposure and dose-response models used in the risk assessments.

A. Other Exclusions Study Identification (review)	Hoornstra, E. and S. Notermans. 2001. Quantitative microbiological risk assessment. Int. J. Food Microbiol. 66: 21-29.
B. Objectives and Type of Study	1. purpose noted by study authors: future regulatory interest 2. type: review article
C. Publication Attributes	1. sponsors/affiliations: TNO Nutrition and Food Research Institute, the Netherlands

	2. peer-review mechanism: peer-reviewed journal
D. Data and Study Design	1. type: the article addressed the risks presented by *E. coli* O157:H7-contaminated sausages, but data were compiled from several reports for generating data for different aspects of the sausage production process. 2. source: Riordan et al. (2000), Cassin et al. (1998), Juneja et al. (1997) 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: this paper provides a crude description of the influence of uncertainty analysis (i.e., the application of probability distribution functions) on modeling contamination of sausages. The data and models reported were used as a means of illustration and are not sufficient for application 2. specific characteristics: the report used Monte Carlo sampling analysis to estimate different distributional effects of the levels of the initial contamination, the heat treatment (both duration and D-value) on *E. coli* O157:H7 surviving a 2 second treatment at 70 °C. 3. assumptions: worst case concentration of 10^3 *E. coli* O157:H7 per gram of sausage material 4. limitations: model not fully developed to address all aspects of meat contamination. Authors noted the need to gather more information about the probability of pathogen occurring in and reduction in different types of raw fermented sausages. 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: authors demonstrate some improvement in determining the bacterial contamination of sausages when uncertainty analysis was used instead of data derived from worst case scenarios. 2. extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: high 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: low 5. defensibility: low
I. Criteria for Exclusion from	1. insufficient data quality or quantity to support rigorous science-based modeling

Compendium	2. insufficient model documentation to demonstrate viable and credible modeling approaches
J. Reviewer Comments	The report communicates that incorporation of probability distributions in to the risk analysis of sausages provides a better estimate of the potential risk of contamination. The suggestions are not novel and better approaches (explicit model descriptions; wider application of models to other data) have been provided elsewhere in the compendium.
K. Cross-References	NA

A. Other Exclusions Study Identification (exposure assessment)	Hrudey, S.E., P. Payment, P.M. Huck, et al. 2003. A fatal waterborne disease epidemic in Walkerton, Ontario: Comparison with other waterborne outbreaks in the developed world. Wat. Sci. Technol. 47(3): 7-14.
B. Objectives and Type of Study	1. purpose: scientific; to compare causes of a waterborne outbreak to those occurring elsewhere in the developed world in order to identify common themes relating to water supply safety 2. type: EA
C. Publication Attributes	1. sponsors/affiliations: Government of Ontario, Canada. 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: selected waterborne disease outbreak epidemiological data 2. source: published scientific studies and official government inquiries 3. extent of data: 16 outbreaks of waterborne disease over a 30-year period were compared. 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: Analysis appears to be qualitative, although in actuality the results could be a summary of statistically analyzed data. 7. relevance: medium; the study analyzes waterborne outbreaks caused by several of the agents on the EPA list
E. Method/Model/Approach	1. general characteristics: a narrative presentation 2. specific characteristics: The authors compared the Walkerton outbreak to 15 other outbreaks for similarities in factors contributing to incidences of increased waterborne microbial-induced disease. Five factors were discussed: 1) source (e.g., increased sewage input with high rainfall); 2) treatment; 3) distribution; 4) monitoring; and 5) response. 3. assumptions: NA

	4. limitations: The article is simply descriptive, no real analysis or modeling is shown. 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions: Failures in water supplies that occur in developed countries mainly because of multiple failures in the systems, not the least of which is human error and a lack of commitment to properly treat water supplies. 2. authors' extrapolations: The authors show that proper chlorination and multiple treatment steps are needed to protect water supplies from contamination.
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: Better regulation and training of personnel operating water treatment plants; and a better understanding of how weather events, placement, and geology effect water supply contamination would be useful.
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: high 3. generalizability or external validity: high 4. soundness of study conclusions or internal validity: high 5. defensibility: high
I. Criteria for Exclusion from Compendium	The article of summarizes factors contributing to microbial-induced outbreaks of disease associated with drinking water contamination. No data, statistics, or modeling are presented.
J. Reviewer Comments	The insights provided by the authors are valuable and the investigation associated with it probably has a fair amount of good epidemiological analysis.
K. Cross-References	NA

A. Other Exclusions Study Identification (review)	Jaykus, L.-A. 1996. The application of quantitative risk assessment to microbial food safety risks. Crit. Rev. Microbiol. 22: 279-293.
B. Objectives and Type of Study	1. purpose noted by study authors: future regulatory interest 2. type: review article
C. Publication Attributes	1. sponsors/affiliations: Department of Food Science, North Carolina State University, North Carolina 2. peer-review mechanism: peer reviewed journal

D. Data and Study Design	1. type: NA 2. source: NA 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: NA
E. Method/Model/Approach	1. general characteristics: this article is a review of risk assessment approach issues that are related to food safety 2. specific characteristics: this article does not provide any specific data, models, or incidence based information that can be used for predicting infection arising from EPA agents of concern. It reviews the issues of risk assessment that are related to food microbiology. 3. assumptions: NA 4. limitations: NA 5. relevance: NA
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: the strongest conclusions from this paper are that it is important to consider uncertainty analysis in estimating the pathogen loadings in foods and in subsequent risks 2. extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: NA
I. Criteria for Exclusion from Compendium	1. insufficient data quality or quantity to support rigorous science-based modeling 2. insufficient model documentation to demonstrate viable and credible modeling approaches 3. studies reporting detection only without modeling of likely fate and transport or adverse effects
J. Reviewer Comments	There is no direct use of this report for incident-based microbial risk assessment. The report may be of use for background reading for risk assessors interested in a review of data relevant to microbial risk assessment.
K. Cross-References	NA

A. Other Exclusions Study Identification (review)	Klapwijk, P.M., J.-L. Jouve and M.F. Stringer. 2000. Microbial risk assessment in Europe. Int. J. Food Microbiol. 58: 223-230.
B. Objectives and Type of Study	1. purpose noted by study authors: regulatory. 2. type: review only
C. Publication Attributes	1. sponsors/affiliations: Unilever, the Netherlands, DGXXIV-Health and Consumer Protection, Belgium, Division of Food Technology, Campden and Chorleywood Food RA, Goucestershire, UK. 2. peer-review mechanism: peer reviewed journal
D. Data and Study Design	1. type: food safety review - the article provides an inventory of developments in the microbial risk assessment arena.- no data or models are provided 2. source: NA 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: NA
E. Method/Model/Approach	1. general characteristics: NA 2. specific characteristics: NA 3. assumptions: NA 4. limitations: NA 5. relevance: NA
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: No conclusions can be inferred from the publication that relate to pathogens, modeling exposures, risks or hazards. 2. extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA

	3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: NA
I. Criteria for Exclusion from Compendium	1. insufficient data quality or quantity to support rigorous science-based modeling 2. insufficient model documentation to demonstrate viable and credible modeling approaches 3. studies reporting detection only without modeling of likely fate and transport or adverse effects
J. Reviewer Comments	There is no method described in this report that can be used for incidence based microbial risk assessment in either buildings or in water systems. The contents of this article describe the results of a literature survey for microbial risk assessment.
K. Cross-References	NA

A. Other Exclusions Study Identification (risk character-ization, disease transmission)	Koopman J.S., and I.M. Longini. 1994. The ecological effects of individual exposures and nonlinear disease dynamics in populations. Am. J. Public Health 84(5): 836-842.
B. Objectives and Type of Study	1. purpose: scientific; Comparison of individual exposure v. ecological exposure and transmission model of vector of dengue fever in Mexico 2. type: RC, disease transmission
C. Publication Attributes	1. sponsors/affiliations: University of Michigan School of Public Health 2. peer-review mechanism: peer reviewed journal
D. Data and Study Design	1. type: comparison of two design and regression methods 2. source: Dengue fever in 70 villages in Mexico 3. extent of data: 50 individuals under 29 in period after five years of epidemic following 25 years of no epidemic 4. sampling plan: subjects chosen with respect to dengue antibody levels and dengue risk factors. 5. sample size: 50 subjects, only one per household 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: Compare ecological and individual models 2. specific characteristics: linear regression for exposure and disease; ecological regression coefficient is divided

	into three components: individual's effects, confounding, and effect modification. 3. assumptions: Assumed limited exposure misclassification 4. limitations: Exposure misclassification can be significant during inter-epidemic years 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusion: for ecological model, odds ratio was a 0% larva v. a 100% larva level was 12.7 (95% CI 8.3,17.8); regressions for individual transmission were non-linear 2. authors' extrapolations: models of transmissions effects do not necessarily relate to exposures measured in the individuals at risk, but rather to characteristics of individuals to which contagions have contact.
G. Data Gaps and Proposed Solutions	1. data gaps: Some real data, but somewhat limited and paper is primarily a comparison of statistical models. 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: high 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	The study is primarily a comparison of statistical models for disease transmission.
J. Reviewer Comments	Very strong methodologically, although not necessarily applicable to the pathogens of interest here. Identifies important epidemiologic issue about the ecologic fallacy and the conditions under which may not apply; addresses potentially important differences in results based on likelihood of misclassification errors.
K. Cross-References	NA

A. Other Exclusions Study Identification (review)	Krewski, D., J. Balbus, D. Butler-Jones, et al. 2002. Managing health risks from drinking water–a report to the Walkerton inquiry. J. Toxicol. Environ. Health, Part A 65: 1635-1823.
B. Objectives and Type of Study	1. purpose noted by study authors: regulatory 2. type: review article
C. Publication Attributes	1. sponsors/affiliations: McLaughlin Centre for Population Health Risk Assessment, University of Ottawa, George Washington University School of Public Health and Health Services, University of Saskatchewan, Drexel

	University, University of British Columbia, Monash University 2. peer-review mechanism: peer reviewed journal
D. Data and Study Design	1. type: NA 2. source: NA 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: NA
E. Method/Model/Approach	1. general characteristics: review of issues related to water safety 2. specific characteristics: this article touches on many issues related to water safety, but no specific information is supplied that can be used in incidence based risk assessment 3. assumptions: NA 4. limitations: NA 5. relevance: NA
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: NA 2. extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: NA
I. Criteria for Exclusion from Compendium	1. insufficient data quality or quantity to support rigorous science-based modeling 2. insufficient model documentation to demonstrate viable and credible modeling approaches
J. Reviewer Comments	This review does not supply any description of a method for incident-based microbial risk assessment of buildings and water systems. It is a relatively complete issue paper that addresses almost all components related to safe water supplies. It does not provide data-based modeling approaches.
K. Cross-References	NA

A. Other Exclusions Study Identification (risk character.)	Krimsky, S., R.P. Wrubel, I.G. Naess, et al. 1995. Standardized microcosms in microbial risk assessment. Bioscience 45(9): 590-599.
B. Objectives and Type of Study	1. purpose: scientific, regulatory, and future regulatory interest; describes uses and limitations of using microcosms for prerelease assessment of genetically engineered microorganisms into natural soil environments 2. type: risk characterization
C. Publication Attributes	1. sponsors/affiliations: EPA's Center for Environmental Management 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: compared design of microcosm studies used to examine the risks involved when introducing genetically engineered microorganisms into natural environments. 2. source: published studies 3. adequate experimental studies employing different variations of the microcosm technique; no consistencies on data or detailed experimental designs 4. sampling plan: NA 5. sample size: NA 6. performance characteristics (error structure for analytical data; repeatability; reproducibility; adequacy of analytical and statistical methods; completeness of study; etc.):no statistical results reported by these authors in their review 7. relevance of data: NA
E. Method/Model/Approach	1. general characteristics: soil samples or cores extracted from natural ecosystem in attempts to mimic environmental parameters influencing the behavior of genetically engineered microorganisms as they would in the environment; thereby providing a pre-release assessment of the microorganism and the risks involved with the original microbial community dynamics and ecosystem functioning. 2. specific characteristics: Didn't actually test microcosm with specified bacterium; merely a review paper 3. assumptions: microcosms are more likely to exhibit the natural behaviors of the genetically microorganism in the field environment than in synthetic (i.e., culture- and enrichment-based) studies. Intact soil cores with minimal disturbance should accurately reflect the natural microbial communities. This approach may also be used to compare the interaction of the microorganism and some environmental parameter. 4. limitations: microcosms can't fully replicate ecosystem dynamics because they are closed systems with static parameters and therefore neglect to examine true environmental conditions; lack the ability to examine vector-mediated movement due to many unknown vectors for bacteria or vectors are too large (i.e. insects or

	vertebrates) for scale of microcosm study; since majority of soil microbes are unculturable DNA-based assays are often employed to evaluate changes in soil microbial communities which are often laborious or expensive techniques; furthermore lack of standardized parameters and protocols for microcosm design make it impractical and inappropriate to compare results across studies. 5. relevance (qualitative judgement of the usefulness of the method to incident-based microbial risk assessment for biothreat agents; high, medium, or low): low, methods for development and use of microcosms for genetically engineered microorganisms may not be very useful for incident-based microbial risk assessment of buildings and water systems due to the time obligation and extensive assays for assessment.
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: There is a need to calibrate microcosms to field studies to provide more reliable data; one study comparing microcosms to field plots and growth chambers found *Pseudomonas sp.* populations were more significantly influenced by plant age than duration/time point of experimental sample. 2. authors' extrapolations from the observed data to other populations or conditions: these authors were not able to extrapolate conclusions from the observed data to other populations due to the inconsistensies in microcosm design and experimental parameters examined.
G. Data Gaps and Proposed Solutions	1. identification of data gaps: many studies were unable to correlate microcosm results to field studies; inability to compare influences of genetically engineered microorganisms across field sites or among different genetically engineered microorganisms. 2. assumptions or source of surrogate data to fill gap: if defined parameters for microcosm design are established and calibrations can be made to field data, this approach could be used to compare the genetically engineered microorganism behaviors across sites or for environmental studies.
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: low 5. defensibility: low, acknowledges limitations of the available data and offers insights for risk management
I. Criteria for Exclusion from Compendium	1. Insufficient data quality to support rigorous science-based modeling 2. Insufficient model documentation to demonstrate viable and credible modeling approaches
J. Reviewer Comments	description of most appropriate uses of microcosm studies for evaluation of the microbial risks involved in introducing genetically engineered microorganisms into natural ecosystems not buildings or water systems; other comments: useful for screening genetically engineered microorganisms and their impact on the indigenous populations and whether they should be deemed harmful or not.
K. Cross-References	NA

A. Other Exclusions Study Identification (overview)	Lammerding, A.M. and A. Fazil. 2000. Hazard identification and exposure assessment for microbial food safety risk assessment. Int. J Food. Microbiol. 58(3): 147-157.
B. Objectives and Type of Study	1. purpose: future regulatory interest 2. type: overview of risk assessment framework or processes only
C. Publication Attributes	1. sponsors/affiliations: not specified 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: discussed basic components of risk assessment involving microbial food safety 2. source: published studies and governmental surveys 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance of data: NA
E. Method/Model/Approach	1. general characteristics: described necessary tools for hazard identification and exposure assessment for microbial food safety 2. specific characteristics: NA 3. assumptions: NA4. limitations: NA 5. relevance: NA
F. Study Conclusions and Extended Applications	1. conclusions supported by the review: quantitative risk assessment is preferred choice; can be subdivided into two categories: point-estimate (single value used for analysis to produce single risk value) and probabilistic (uses all data for analysis and produces a range of risk values); recognizing uncertainty and variability have different ramifications on results of risk assessment; scope of risk assessment should be carefully considered (farm-to-fork versus processing only) 2. authors' extrapolations from the observed data to other populations or conditions: NA
G. Data Gaps and Proposed Solutions	1. identification of data gaps: variability and uncertainty are often ignored in point estimate models; substantial loss of information 2. assumptions or source of surrogate data to fill gap: probabilistic models are more representative of significant occurrences or events likely to cause human health problems
H. Weight of Evidence	1. robustness of method: NA

	2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: NA
I. Criteria for Exclusion from Compendium	study included no unique data and/or modeling of likely fate and transport or adverse effects of microbial agents
J. Reviewer Comments	other comments by reviewer: this paper is not useful for constructing models of fate or transport, rather it is a simple review and explanation of what microbial risk assessment involves
K. Cross-References	NA

A. Other Exclusions Study Identification (dose-response)	McLauchlin, J., R.T. Mitchell, W.J. Smerdon, et al. 2004. *Listeria monocytogenes* and listeriosis: A review of hazard characterisation for use in microbiological risk assessment of foods. Int. J. Food Microbiol. 92(1): 15-33.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific; Reviews aspects of *Listeria* and human listeriosis from a public health perspective and provides hazard characterization data consisting of the qualitative/quantitative evaluation of adverse health effects associated with the hazard. 2. type: DR
C. Publication Attributes	1. sponsors/affiliations: Food Standards Agency of the United Kingdom project B01020 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: Clinical and epidemiological data review. 2. source: Numerous published sources used in this review. 3. extent of data: LD_{50} for mice after intraperitoneal or intravenous inoculation ranges from 10^2 to 10^7 bacteria. Oesophageal inoculation of juvenile rates with 10^6 cfu *L. monocytogenes* showed 50% infection rate in the spleen and the liver. Infection of mice via aerosol route resulted in LD_{50}s of 10^3 - 10^5. Oral challenge of Cynomologous monkeys with 10^9 bacteria developed symptoms of infection. Monkey fed 10^5 and 10^7 bacteria shed the organism in their faeces. In chick embryos, the LD_{50} is about 100 organisms. 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: NA

E. Method/Model/Approach	1. general characteristics: Briefly points out various mathematical forms to represent dose-response data. 2. specific characteristics: Models mentioned included the Beta-Poisson, Weibull, Weibull-Gamma, Gompertz models. However, no one model singled out for *L. monocytogenes*. 3. assumptions: Extrapolation from population used to develop is the same as that under consideration. 4. limitations: The models are empirical in that their principal justification is that they fit the data. Uncertainties place great limitations on use of quantitative dose response models. 5. relevance: NA
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: different models may fit the data equally, but give widely differing predictions in the dose region corresponding to levels of the organism in food. Recommend using more than one model to encompass uncertainty. 2. use animal data proposed
G. Data Gaps and Proposed Solutions	1. data gaps: little success in incorporating the food matrix component of the dose response into mathematical models 2. proposed solutions: Adopted from the USDA FSIS Study (Anonymous, 2001) and endorsed by Buchanan and Lindqvist (2000) whereby number of plausible functional forms are parameterized on appropriate data; resulting models adjusted to accord with available epidemiologic information on population of interest; and the uncertainty resulting from this procedure is explicitly considered and presented with the dose response model.
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: NA
I. Criteria for Exclusion from Compendium	insufficient data quality or quantity to support rigorous science-based modeling (no specific data contained in here, but references to sources of data are available)
J. Reviewer Comments	NA
K. Cross-References	NA

A. Other Exclusions Study Identification (review)	McNab, W.B. 1998. A general framework illustrating an approach to quantitative microbial food safety risk assessment. J. Food Protect. 61(9): 1216-1228.

B. Objectives and Type of Study	1. purpose: regulatory, future regulatory interest; to present a framework to illustrate one potential approach to quantitative risk assessment for microbial food safety 2. type: review of MRA framework
C. Publication Attributes	1. sponsors/affiliations: Ontario Ministry of Agriculture, Food and Rural Affairs 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: not applicable; no data used 2. source: NA 3. extent of data: no data used 4. sampling plan: random selection from distribution 5. sample size: NA 6. performance characteristics: method was very complete, but not specific to an organism; no data used 7. relevance: low; none of the criteria were met
E. Method/Model/Approach	1. general characteristics: 10,000 iteration Monte Carlo simulation using @Risk for each of four scenarios 2. specific characteristics: Gompertz equation represented microbial growth; beta-Poisson model used to characterize dose-response relationships; curved betaPERT distributions created to use in the simulations 3. assumptions: NA 4. limitations: framework presented as an illustration only; requires specific models with specific parameters based on large realistic data sets for application to specific risk scenarios 5. relevance: medium; describes aspects needed for incident-based scenario modeling even though no data were used or presented
F. Study Conclusions and Extended Applications	1. conclusions: Framework illustrated a method for risk assessment that could be applied to many different situations if the appropriate models and data were input in the framework. 2. authors' extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: no data was presented 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: low; no data used 2. representativeness of data: low; no organisms named 3. generalizability or external validity: low; no data used 4. soundness of study conclusions or internal validity: high; method was very complete 5. defensibility: high; method applicable to incident-based microbial risk assessment
I. Criteria for Exclusion from	presented an illustration of the framework

Compendium	
J. Reviewer Comments	NA
K. Cross-References	NA

A. Other Exclusions Study Identification (review)	Mossel, D.A.A., G.H. Weenk, G.P. Morris and C.B. Struijk. 1998. Identification, assessment, and management of food-related microbiological hazards: historical, fundamental, and psycho-social essentials. Int. J. Food Microbiol. 39: 19-51.
B. Objectives and Type of Study	1. purpose: regulatory; review concerning microbiological risk assessment and impacts on the regulatory environment, food processors, and consumers. 2. type: review
C. Publication Attributes	1. sponsors/affiliations: Eijkman Foundation, Utrecht University, Utrecht, Netherlands 2. peer-review mechanism: scientific journal review
D. Data and Study Design	1. type: NA 2. source: NA 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: NA
E. Method/Model/Approach	1. general characteristics: NA 2. specific characteristics: NA 3. assumptions: NA 4. limitations: NA 5. relevance: NA
F. Study Conclusions and Extended Applications	1. conclusions: NA 2. authors' extrapolations: NA
G. Data Gaps and Proposed	1. data gaps: NA

Solutions	2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: NA
I. Criteria for Exclusion from Compendium	review article
J. Reviewer Comments	a general presentation of steps and ideas involved in microbiological risk assessment as it functions in society
K. Cross-References	some studies cited in the review may be suitable for inclusion in the compendium

A. Other Exclusions Study Identification (review)	Myers M.F., D.J. Rogers, J. Cox J, et al. 2000. Forecasting disease risk for increased epidemic preparedness in public health. Advances Parasitol. 47: 309-330.
B. Objectives and Type of Study	1. purpose: scientific; review in a book chapter examining the potential for epidemic forecasting and a discussion of the issues associated with the development of global networks for surveillance and prediction 2. type: review
C. Publication Attributes	1. sponsors/affiliations: NASA Earth Science Enterprise Environmental and Health Initiative and the Innovation Fund of the National Performance Review 2. peer-review mechanism: NA; book chapter that has presumably been reviewed in some manner before publication, but process is not described
D. Data and Study Design	1. type: no new data presented; historical data from past studies 2. source: numerous past studies 3. extent of data: wide variety of results from past studies discussed, but not actual data itself 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: NA

E. Method/Model/Approach	1. general characteristics: review; methodology employed in various studies not discussed 2. specific characteristics: NA 3. assumptions: NA 4. limitations: NA 5. relevance: NA
F. Study Conclusions and Extended Applications	1. conclusions: NA 2. authors' extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: NA
I. Criteria for Exclusion from Compendium	review article, presented as a chapter in a book
J. Reviewer Comments	NA
K. Cross-References	some studies cited in the review may be suitable for inclusion in the compendium

A. Other Exclusions Study Identification (review)	Neuman, D.A. and Foran, J.A, 1997. Assessing the risks associated with exposure to waterborne pathogens: An expert panel's report on risk assessment. J. Food Protect. 60: 1426-1431.
B. Objectives and Type of Study	1. purpose noted by study authors: future regulatory interest. Overview of the charge to the ILSI working group. 2. type: review
C. Publication Attributes	1. sponsors/affiliations: US EPA, Office of Water, American Water Works Association Research Foundation, ILSI Risk Science Institute 2. peer-review mechanism: Full Scientific Peer Review

D. Data and Study Design	1. type: Expert panel report 2. source: NA 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: expert panel report on assessing the risks associated with exposure to waterborne pathogens. 2. specific characteristics: The panel was charged with developing a conceptual framework for assessing human health risks associated with waterborne pathogens. Such a framework would provide a model for organizing and characterizing information for performing pathogen risk assessments. 3. assumptions: NA 4. limitations: waterborne only 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: none reported 2. authors' extrapolations from the observed data to other populations or conditions: none reported
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: high 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: low 5. defensibility: low
I. Criteria for Exclusion from Compendium	review not developing case study or model
J. Reviewer Comments	No methods for incident-based microbial risk assessment of buildings and water systems reported. Maybe future regulatory interest, but not of use for this compendium.
K. Cross-References	NA

A. Other Exclusions Study Identification (risk character.)	Nicas, M. 1994. Modeling respirator penetration values with the beta distribution: An application to occupational tuberculosis transmission. Am. Ind. Hyg. Assoc. J. 55(6): 515-524.
B. Objectives and Type of Study	1. purpose: scientific; To determine whether respirator penetration of airborne tuberculosis can be modeled better by the beta distribution than the lognormal 2. type: RC
C. Publication Attributes	1. sponsors/affiliations: Center for Occupational and Environmental Health, Univ of California School of Public Health 2. peer-review mechanism: peer reviewed journal
D. Data and Study Design	1. type: Theoretical occupational health study 2. source: NA 3. extent of data: hypothetical data only 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: This paper is limited to a hypothetical analysis of statistical models to evaluate devices to protect health care workers exposed to infectious TB patients. 2. specific characteristics: NA 3. assumptions: NA 4. limitations: NA 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusion: NA 2. authors' extrapolations: Application for NIOSH testing and certification protocols
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: low 5. defensibility: low

I. Criteria for Exclusion from Compendium	not relevant for the compendium
J. Reviewer Comments	This is an interesting and reasonably well done modeling exercise for a hospital based occupational health problem. It does not, however, fit with the general questions or analysis for microbial risk assessment.
K. Cross-References	NA

A. Other Exclusions Study Identification (overview)	Powell, S.C. and R. Attwell. 1999. The use of epidemiological data in the control of foodborne viruses. Rev. Environ. Health 14(1): 31-37.
B. Objectives and Type of Study	1. purpose: future regulatory interest 2. type: overview of risk assessment framework or processes only
C. Publication Attributes	1. sponsors/affiliations: not specified 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: discussed basic RA design as specified by HACCP and how it can be applied to small, round-structured virus (SRSV) 2. source: published studies and governmental surveys 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics (error structure for analytical data; repeatability; reproducibility; adequacy of analytical and statistical methods; completeness of study; etc.): NA 7. relevance of data: NA
E. Method/Model/Approach	1. general characteristics: short review of approaches to food safety control involving HAACP, RA, foodborne viruses and prevention and control of SRSV infections 2. specific characteristics: NA 3. assumptions: NA4. limitations: NA 5. relevance (qualitative judgement of the usefulness of the method to incident-based microbial risk assessment for biothreat agents; high, medium, or low): NA
F. Study Conclusions and Extended	1. conclusions supported by the review: there is some disagreement as to whether RA and HACCP plans should

Applications	be integrated or remain independent; environmental health departments (EHD) operates under a “passive” (self-reporting) surveillance system that significantly under-reports disease incidents; Foodnet is an “active”system that overcomes problems associated with under-reporting and provides a better understanding of incidence and casual factors associated with food borne diseases (FBD); viral diseases are generally aerosol- or direct contact with contamination- based transmission versus food borne; limited viral disease implication due to costs and difficulty identifying pathogen 2. authors’ extrapolations from the observed data to other populations or conditions: NA
G. Data Gaps and Proposed Solutions	1. identification of data gaps: HACCP plans focus less on virus control; up-to-date epidemiological data on viral FBD are not available to complete hazard ID; dose response not established due to lack of human hosts in lab studies; difficulties and costs involved in detecting viruses limits exposures assessments models; 2. assumptions or source of surrogate data to fill gap: UK needs standardized method for collecting FBD data consistently; Kaplan criteria can be applied to outbreaks that “cannot be confirmed”
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: NA
I. Criteria for Exclusion from Compendium	study included no unique data and/or modeling of likely fate and transport or adverse effects of microbial agents
J. Reviewer Comments	other comments by reviewer: this study discusses basic framework and/or components for risk assessment of viral pathogens and how they should be implemented
K. Cross-References	NA

A. Other Exclusions Study Identification (review)	Reij, M.W. and E.D. Den Aantrekker. 2004. Recontamination as a source of pathogens in processed foods. Int. J. Food Microbiol. 91(1): 1-11.
B. Objectives and Type of Study	1. purpose noted by study authors: to review the current state of knowledge about the importance of recontamination (also referred to as *cross-contamination* and *post-process contamination*) as a cause of food-borne disease, and the significant routes and sources of recontamination 2. type: review

C. Publication Attributes	1. sponsors/affiliations: International Life Sciences Institute, European Branch, Belgium; Wageningen University, The Netherlands 2. peer-review mechanism: scientific journal review
D. Data and Study Design	1. type: NA 2. source: NA 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: NA
E. Method/Model/Approach	1. general characteristics: NA 2. specific characteristics: NA 3. assumptions: NA 4. limitations: NA 5. relevance: NA
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: NA 2. extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: NA
I. Criteria for Exclusion from Compendium	review article
J. Reviewer Comments	NA
K. Cross-References	Den Aantrekker et al., 2003; review cites sources that may describe useful models and data, e.g.,: Den Aantrekker, 2002; Den Aantrekker et al. 2003

A. Other Exclusions Study Identification (review)	Rose, J.B. and D.J. Grimes. 2001. Reevaluation of microbial water quality: Powerful new tools for detection and risk assessment. Washington, DC: American Academy of Microbiology.
B. Objectives and Type of Study	1. purpose: future regulatory interest; This report outlines the background and need for new tools to deal with issues of water quality. 2. type: review
C. Publication Attributes	1. sponsors/affiliations: American Society for Microbiology; US Environmental Protection Agency; US Food and Drug Administration; US Office of Naval Research; Water Environment Research Foundation 2. peer-review mechanism: report (not specified)
D. Data and Study Design	1. type: General description of new tools that are suggested to be applied to and be used when performing risk assessments. 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: NA 2. specific characteristics: NA 3. assumptions: NA 4. limitations: NA 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions: Fecal coliform monitoring has led the water industry in the direction of risk reduction of waterborne diseases. These tests have been important first steps in detecting the potential for degraded waters that are unfit for human contact. However, experience has demonstrated the inability of the fecal coliform test to detect many harmful microbes. Reliance on fecal indicators has focused risk management efforts on a system that does not properly characterize or fully understand the nature the hazards associated with water use and consumption. 2. authors' extrapolations: None
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: low

	2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: low 5. defensibility: low
I. Criteria for Exclusion from Compendium	Insufficient data quality or quantity to support rigorous science-based modeling.
J. Reviewer Comments	Document contains a good summary of available tools and a nice description of how they may be used by the engineering and biological communities through collaboration to improve the process used to determine quality of water.
K. Cross-References	NA

A. Other Exclusions Study Identification (review)	Roy E. and P. Robillard. 1994. Effectiveness of and compliance to preventive measures against the occupational transmission of human immunodeficiency virus. Scand. J. Work Environ. Health 20: 393-400.
B. Objectives and Type of Study	1. purpose: scientific; review of compliance as a preventative measure against transmission of HIV 2. type: review
C. Publication Attributes	1. sponsors/affiliations: Center for AIDS Studies, Montreal Public Health Unit, Montreal General Hospital 2. peer-review mechanism: peer reviewed journal
D. Data and Study Design	1. type: no new data presented, historical data presented in a review of past studies 2. source: numerous past studies 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: review, methodology employed in various studies not discussed 2. specific characteristics: NA 3. assumptions: NA

	4. limitations: NA 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions: HIV preventative practices in health care settings are often mixed, despite recommendations from CDC 2. authors' extrapolations: none
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: low 5. defensibility: low
I. Criteria for Exclusion from Compendium	review
J. Reviewer Comments	NA
K. Cross-References	NA

A. Other Exclusions Study Identification (review)	Salisbury, J.G., T.J. Nicholls, A.M. Lammerding, et al. 2002. A risk analysis framework for the long-term management of antibiotic resistance in food-producing animals. Int. J. Antimicrob. Agents 20(3): 153-164.
B. Objectives and Type of Study	1. purpose: future regulatory interest; propose model for risk assessment involving antibiotics, resistant bacteria, and molecular characterization of resistance gene 2. type: review of risk analysis framework
C. Publication Attributes	1. sponsors/affiliations: Commonwealth Department of Agriculture, Forestry and Fisheries, Australia; Population and Public Health branch of Laboratory for Foodborne Zoonoses; Department Microbiology and Infectious Diseases, Women and Children's Hospital, SA. 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: compared design of risk assessment models and developed three staged model to encompass all

	aspects of risk assessment for antibiotics and resistant bacteria 2. source: published studies 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance of data: NA
E. Method/Model/Approach	1. general characteristics: propose a “risk matrix” composed of three separate risk assessments needed on: the antibiotic, antibiotic resistant bacteria, and the antibiotic resistant genes. 2. specific characteristics: NA 3. assumptions: risk assessment for antibiotic use = chemical use, risk assessment for antibiotic resistant bacteria = microbiological risk assessment, and risk assessment of transfer of genetic resistant genes to antibiotic = genetic risk assessment. 4. limitations: data likely to be available for antibiotic sensitive gene/bacterium and it’s fate in environment or influence on human disease (unlikely to find published information for antibiotic resistant bacteria) 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: NA. 2. authors’ extrapolations from the observed data to other populations or conditions: NA
G. Data Gaps and Proposed Solutions	1. identification of data gaps: unlikely to find published information for antibiotic resistant bacteria) 2. assumptions or source of surrogate data to fill gap: continued research
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility (method of uncertain usefulness for incident-based microbial risk assessment of buildings and water systems):low, acknowledges limitations of the available data and offers insights for risk management
I. Criteria for Exclusion from Compendium	Insufficient data quality and quantity to support rigorous science-based modeling; insufficient model documentation to demonstrate viable and credible modeling approaches
J. Reviewer Comments	description of most appropriate uses of risk matrixes for evaluation of the microbial risks involved in introducing antibiotic-resistant microorganisms into natural ecosystems not buildings or water systems
K. Cross-References	NA

A. Other Exclusions Study Identification (review)	Schlundt, J. 2000. Comparison of microbiological risk assessment studies published. Int. J. Food Microbiol. 58(3): 197-202.
B. Objectives and Type of Study	1. purpose: future regulatory interest; propose limitations and inaccuracies in previously developed models and studies of risk assessment 2. type: review
C. Publication Attributes	1. sponsors/affiliations: Danish Veterinary and Food Administration 2. type: overview of risk assessment framework or processes only
D. Data and Study Design	1. type: compared designs of risk assessment models and studies and described their limitations and inconsistencies 2. source: published studies 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance of data: NA
E. Method/Model/Approach	1. general characteristics: proposed risk assessment based studies be more clearly developed by more thoroughly examining food-borne illnesses and more clearly stating assumptions 2. specific characteristics: NA 3. assumptions: NA4. limitations: NA 5. relevance: NA
F. Study Conclusions and Extended Applications	1. conclusions supported by the review: limitations of risk assessment modeling include: often only one food type is studied; microbial growth in food is often not considered; no consideration for uncertainty; building assumptions based upon assumptions of other scientists could lead to “non’ transparent” process; final estimates and purpose/assumptions of risk are often not stated clearly 2. authors’ extrapolations from the observed data to other populations or conditions: ever risk assessment should include a description of the “tool box”used to perform assessment (i.e. models and assumptions), validity of data and uncertainty should be clearly stated, risk assessment and risk management should be kept separate
G. Data Gaps and Proposed	1. identification of data gaps: see conclusions (limitations) above

Solutions	2. assumptions or source of surrogate data to fill gap: develop standardized method for risk assessment studies and pertinent parameters to be presented
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility (method of uncertain usefulness for incident-based microbial risk assessment of buildings and water systems): NA
I. Criteria for Exclusion from Compendium	study included no unique data and/or modeling of likely fate and transport or adverse effects of microbial agents
J. Reviewer Comments	other comments by reviewer: this study outlines biases incorporated into many risk assessment studies and models; useful for trying to correctly construct a useful risk assessment study/model
K. Cross-References	NA

A. Other Exclusions Study Identification (dose-response)	Simmons, J.E., L.K. Teuschler, C. Gennings, et al. 2004. Component-based and whole-mixture techniques for addressing the toxicity of drinking water disinfection by product mixtures. J. Toxicol. Environ. Health, Part A 67: 741-754.
B. Objectives and Type of Study	1. purpose: scientific; To provide improved methods for risk assessment of mixtures and data relevant to the assessment of the health risk of exposure to disinfection by-product (DBP) mixtures. 2. type: DR
C. Publication Attributes	1. sponsors/affiliations: US EPA 2. peer-review mechanism: peer-reviewed journal
D. Data and Study Design	1. type: experimental data based on female CD-1 mice exposed by gavage in an aqueous vehicle daily for 14d. 2. source: laboratory results 3. extent of data: large 4. sampling plan: factorial design based on dose groups, mixing ratios, placement of dose groups along the dose response curves. 5. sample size: extensive sample size (12 dose groups, a vehicle control group; 3 dose levels of DBP A alone;

	3 dose levels of DBP B alone; 3 mixture groups at 1:1 A:B and dose levels of 0.1, 1, and 3 mmol/kg/d). 6. performance characteristics: simple statistics provided 7. relevance: low
E. Method/Model/Approach	1. general characteristics: no modeling provided. Methods have been developed to characterize various brominated and iodinated species during water disinfection. 2. specific characteristics: A method was developed for preparation of water concentrates by concentration through reverse osmosis membranes. 3. assumptions: none reported 4. limitations: NA to biothreat agents of concern 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions: evaluation of defined mixtures is useful for risk assessment, but fails to take into account the toxicity of the unknown DBP fraction. 2. authors' extrapolations: none reported
G. Data Gaps and Proposed Solutions	1. data gaps: none 2. proposed solutions: none
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: low 5. defensibility: low
I. Criteria for Exclusion from Compendium	This study reports data and methods for dose response curves of various chemical species generated during water disinfection. Not relevant to present compendium.
J. Reviewer Comments	Various methods have been developed to characterize brominated and iodinated species during water disinfection. The species have been evaluated for toxicity. Not relevant to the present compendium
K. Cross-References	NA

A. Other Exclusions Study Identification (exposure	Springthorpe, V.S., C.L. Loh and S.A. Sattar. 1997. How good is modelling of microbial survival in fluvial systems? Wat. Sci. Technol. 35(11-12): 253-259.

assessment)	
B. Objectives and Type of Study	1. purpose: scientific; Compares the hollow fibre diffusion (HFD) and static diffusion chamber (DC) methods for the study of regrowth in response to transient nutrient increases. 2. type: EA
C. Publication Attributes	1. sponsors/affiliations: Department of Microbiology and Immunology, University of Ottawa 2. peer-review mechanism: peer-reviewed journal
D. Data and Study Design	1. type: experimental using *E. coli* 2. source: flow rates and growth response of *E. coli* 3. extent of data: two data sets (HFD and DC), each using growth response of *E. coli* as measurement. 4. sampling plan: Spiking conditions used were 1-hour wash, 2- hour spike with a 2-hour wash and four consecutive spikes for 10 minutes each followed by a 20-minute wash. 5. sample size: Samples analyzed at least in triplicate for every sampling period. 6. performance characteristics: growth over time in relation to nutrient spikes (growth curves) 7. relevance: high
E. Method/Model/Approach	1. general characteristics: evaluating growth of microorganisms in man-made environment vs. natural waterway; however need to evaluate man-made systems against each other. 2. specific characteristics: Compares results of HFD and DC methods for regrowth. 3. assumptions: none stated 4. limitations: used only *E. coli* to compare, used high concentrations 5. relevance: high
F. Study Conclusions and Extended Applications	1. conclusions: Use of HFD and DC result in highly different pictures. Qualitative results similar, but quantitative estimates (i.e., growth kinetic) could be very different. 2. authors' extrapolations: could be useful to examine differences in survival/regrowth that may occur in indicator strains. May be useful to examine water distribution systems.
G. Data Gaps and Proposed Solutions	1. data gaps: none identified 2. proposed solutions: none identified
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: high 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: high 5. defensibility: low

I. Criteria for Exclusion from Compendium	There is insufficient data quality or quantity to support rigorous science-based modeling; and there is insufficient model documentation to demonstrate viable and credible modeling approaches.
J. Reviewer Comments	May at some point be useful in the MRA to explain methodological discrepancies, however, may be more important when characterizing occurrence data.
K. Cross-References	NA

A. Other Exclusions Study Identification (review)	Teunis, P.F.M., A.H. Havelaar and G.J. Medema. 1995. A literature survey on the assessment of microbiological risk for drinking water. Rijksinstituut Voor Volksgezondheid en Milieuhygiene Bilthoven. Report nr. 734301006.
B. Objectives and Type of Study	1. purpose: scientific; with future regulatory applications 2. type: a review with analysis of the process of using the quantitative risk assessment method to analyze risks associated with drinking water.
C. Publication Attributes	1. sponsors/affiliations: Dutch Ministry of Housing, Physical Planning and Environment, General Directorate for the Environment. 2. peer-review mechanism: unknown
D. Data and Study Design	1. type: NA 2. source: NA 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low; no original data or analysis presented
E. Method/Model/Approach	1. general characteristics: A literature survey focusing primarily on the assessment of risk from pathogenic organisms in drinking water. 2. specific characteristics: Literature survey that addresses all four components of microbial risk assessment: hazard identification, exposure assessment; dose-response modeling and risk characterization; report also discusses risk management, focusing on the Hazard Analysis Critical Control Point (HACCP) system, and suggests the HACCP system provides a possible framework for incorporating quantitative microbial risk assessment methods into the operation of drinking water treatment facilities. The author also briefly describes methods for modeling repeated exposures, secondary spreading of disease (i.e., person-to-person transmission).

	3. assumptions: NA 4. limitations: NA 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions: NA 2. authors' extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: Author describes data gaps for the Netherlands: more dose-response data for pathogenic microorganisms, particularly data needed to assess the change in the dose-response relation with weakened immune system; data on the efficiency of detection methods; methods for determining the fraction of viable organisms; removal efficiency of water treatment processes. 2. proposed solutions: Research needs are listed in each chapter of the review: hazard identification, exposure assessment, dose-response modeling, and risk characterization and management
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: low
I. Criteria for Exclusion from Compendium	1. insufficient data quality or quantity to support rigorous science-based modeling 2. insufficient model documentation to demonstrate viable and credible modeling approaches
J. Reviewer Comments	The authors objective was to present how quantitative risk assessment is done for microbial risks in drinking water. The presentation is clear and shows the reader the many steps involved is the process. Especially helpful is their discussion of why certain approaches are taken, and where more data would be useful. Aspects of the HACCP system may be applicable to the protection of building drinking water systems.
K. Cross-References	NA

A. Other Exclusions Study Identification (dose-response)	Teunis, P., A. Havelaar, J. Vliegenthart and G. Roessink. 1997a. Risk assessment of *Campylobacter* species in shellfish: Identifying the unknown. Wat. Sci. Technol. 35(11-12): 29-34.
B. Objectives and Type of Study	1. purpose: scientific. Describe the results of a Quantitative Risk Assessment of risks associated with the consumption of *C. lari* and identify data gaps for future studies characterizing the role of shellfish consumption in

	associated diarrheal diseases. 2. type: DR
C. Publication Attributes	1. sponsors/affiliations: Inspectorate for Health Protection, Ministry of Pubic Health, Welfare and Sports, Rijswijk, the Netherlands, under project #284550 2. peer-review mechanism: peer-reviewed journal
D. Data and Study Design	1. type: dose response data for 2 strains of *C. jejuni* (Black et. al., 1988) 2. source: published study 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: Authors note the relationship between infection and dose could be described by the b-Poisson model. Authors describe 2 approaches 1) use the "worst case" estimate for disease, or 2) average the fraction of infected people who will get ill 2. specific characteristics: graph of the dose response relationship with a 95% CI (P_{inf} versus Dose) 3. assumptions: *C. lari* and *C. jejuni* have similar pathogenicity 4. limitations: Details of the human volunteer feeding study are not provided. Only 1 parameter was examined. 5. relevance: medium
F. Study Conclusions and Extended Applications	1. conclusions: The relationship between disease and dose is not linear. The risk of infection is substantial at low doses, but the 95% confidence limit is very wide because no experimental data were available at doses less than 800 cfp 2. authors' extrapolations: none provided
G. Data Gaps and Proposed Solutions	1. data gaps: Limited quantitative data is available. 2. proposed solutions: Experimental data to understand the dose response relationships for infection and disease at low levels is required.
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: unknown 5. defensibility: low

I. Criteria for Exclusion from Compendium	There is insufficient data quality or quantity to support rigorous science-based modeling.
J. Reviewer Comments	The analysis was based on one experimental study using a group of healthy volunteers. Details of the study are not provided.
K. Cross-References	Summarized elsewhere in the compendium for risk characterization and exposure assessment.

A. Other Exclusions Study Identification (exposure assessment)	Teunis, P., A. Havelaar, J. Vliegenthart and G. Roessink. 1997a. Risk assessment of *Campylobacter* species in shellfish: Identifying the unknown. Wat. Sci. Technol. 35(11-12): 29-34.
B. Objectives and Type of Study	1. purpose: scientific. Describe the results of a Quantitative Risk Assessment for risks associated with the consumption of *C. lari* and identify data gaps for future studies characterizing the role of shellfish consumption in associated diarrheal diseases. 2. type: EA
C. Publication Attributes	1. sponsors/affiliations: Inspectorate for Health Protection, Ministry of Pubic Health, Welfare and Sports, Rijswijk, the Netherlands, under project #284550 2. peer-review mechanism: peer-reviewed journal
D. Data and Study Design	1. type: Extrapolated weight of shellfish portion from consumption patterns of either 6 or 12 oysters or mussels (author); semi-quantitative detection of *Campylobacter* in shellfish with graphical representation of *C. lari* levels (author); internal temperature data during preparation (author) 2. source: author 3. extent of data: Limited amount of available data. Author generated a few data points (e.g., 2 reps for determining the temperature inside meat). 4. sampling plan: Not provided. 5. sample size: For detection - unknown; for the effect of preparation - very limited with 2 experimental runs and limited temperature distribution data within the cooking pot. 6. performance characteristics: Limited information relative to analysis was provided. 7. relevance: low
E. Method/Model/Approach	1. general characteristics: Monte Carlo simulation 2. specific characteristics: Provided one example for December 1994 which estimated the dose per unit portion

	and its frequency distribution 3. assumptions: *C. lari* and *C. jejuni* have similar pathogenicity/infectivity; organisms were randomly distributed for the most probable number (MPN) determination; no die-off during storage and transport; weight determination based on a log normal distribution with a geometric mean weight with a 95% CI target range 4. limitations: The assessment was based on very limited information 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions: There is seasonal variation in the levels of *C. lari* in mussels. The standard process of steaming mussels leads to complete inactivation of these bacteria. 2. authors' extrapolations: Health risks are restricted to undercooked or raw shellfish.
G. Data Gaps and Proposed Solutions	1. data gaps: Information on the variation of concentration of the pathogens in the ingested product are limited. 2. proposed solutions: none
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: low 5. defensibility: low
I. Criteria for Exclusion from Compendium	There is insufficient data quality or quantity to support rigorous science-based modeling.
J. Reviewer Comments	Models were not described and the type and amount of data used was very limited.
K. Cross-References	Summarized elsewhere in the compendium for risk characterization and dose response.

A. Other Exclusions Study Identification (risk character.)	Teunis, P., A. Havelaar, J. Vliegenthart and G. Roessink. 1997a. Risk assessment of *Campylobacter* species in shellfish: Identifying the unknown. Wat. Sci. Technol. 35(11-12): 29-34.
B. Objectives and Type of Study	1. purpose: Scientific. Describe the results of a quantitative risk assessment of risks associated with the consumption of *C. lari* and identify data gaps for future studies characterizing the role of shellfish consumption in associated diarrheal diseases. 2. type: RC

C. Publication Attributes	1. sponsors/affiliations: Inspectorate for Health Protection, Ministry of Pubic Health, Welfare and Sports, Rijswijk, the Netherlands, under project #284550 2. peer-review mechanism: peer-reviewed journal
D. Data and Study Design	1. type: dose response data for *C. jejuni* (Black et. al., 1988); exposure assessment using semi-quantitative detection methods and estimated consumption patterns (author) 2. source: published study; author 3. extent of data: NA 4. sampling plan: random (Monte Carlo) 5. sample size: NA 6. performance characteristics: Simple statistics, calculated the average risk for consumption of one portion of shellfish with 95% CI 7. relevance: low
E. Method/Model/Approach	1. general characteristics: sampling (Monte Carlo) from the frequency distribution for the ingested dose and infection response. 2. specific characteristics: Calculated the average risk with a 95% CI 3. assumptions: No immunity is built up 4. limitations: The characterization was based on 1 study with an unknown number of samples, or no understanding of the sampling plan. 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions: The median chance of infection would be 50%for a person who eats one portion of raw shellfish per month. 2. authors' extrapolations: Health risks are restricted to undercooked or raw shellfish.
G. Data Gaps and Proposed Solutions	1. data gaps: Limited quantitative data is available. 2. proposed solutions: Better experimental data is needed.
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: unknown 5. defensibility: low
I. Criteria for Exclusion from Compendium	There is insufficient data quality or quantity to support rigorous science-based modeling.

J. Reviewer Comments	Details were not provide for how the final conclusion was calculated.
K. Cross-References	Summarized elsewhere in the compendium for dose response and exposure assessment.

A. Other Exclusions Study Identification (risk character.)	Todd, E.C.D. 1996. Risk assessment of use of cracked eggs in Canada. Int. J. Food Microbiol. 30(1-2): 125-143.
B. Objectives and Type of Study	1. purpose: regulatory and future regulatory interest - The purpose of this article is to assist risk managers in a decision process for management of cracked eggs. 2. type: RC
C. Publication Attributes	1. sponsors/affiliations: Food Production and Inspection Branch, AAFC, Food Inspection Directorate, Foodborne Disease Reporting Centre and HFB 2. peer-review mechanism: peer-reviewed journal
D. Data and Study Design	1. type: Regulatory review article. No actual data presented. 2. source: Published studies and government databases 3. extent of data: 1990-1996 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: Review of published articles and government statistics and results. 2. specific characteristics: NA 3. assumptions: The rate of reported outbreaks arising from cracked eggs would be the same as that from intact eggs. 4. limitations: NA 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: *B. cereus*, *Campylobacter*, *Salmonella*, *S. aureus*, and *Y. enterocolitica* have been found in the environment or on birds, and could contaminate shells. *Salmonella* is the only organism that has been conclusively linked to human illness from cracked eggs both in Canada and in other countries. The minimum number of *Salmonella* in eggs required to cause illness ranges from 10^5 - 10^9 cells based on illness

	studies. Intact eggs can be penetrated by salmonellae, then it is likely that cracked eggs allow the bacteria to migrate faster onto the membranes and probably in larger numbers. The degree of penetration is dependent on the temperature difference between the egg and the wash water, the concentration of microorganisms in the water, the wash water with appreciable soluble iron, the duration of immersion of eggs in the water, the thickness of eggshell, and the treatment of eggs prior to washing. Growth of *Salmonella* in whole shell eggs is slow and depends on the gradual change of albumen to allow multiplication there and in the yolk. However, it is known that when eggs are broken and the yolk and white are mixed, as in liquid egg preparations, the antibacterial effect of albumen is neutralized, and growth of pathogens and spoilage organisms can proceed rapidly at suitable temperatures. In at least 5 of the 13 outbreaks in Canada involving shell eggs, contaminated cracked eggs were used. The increase in risk of outbreaks from the use of cracks is estimated to be 23:1. The risk for the general population is lower because only some cracked eggs are contaminated with *Salmonella*, most cracked eggs or foods made from cracked eggs used in foodservice establishment or home are refrigerated until use, and most egg products are cooked which could destroy at least some of the salmonellae present. 2. authors' extrapolations: See F1.
G. Data Gaps and Proposed Solutions	1. data gaps: none identified 2. proposed solutions: Require that all cracked eggs to be pasturized in egg breaking stations, present the least risk and are the best control over the potential hazards from cracked eggs. The limited sale of cracked eggs directly to consumers from registered egg stations at the farm gate and seller of multiple producers will be better control the existing situation. AAFC is working with the egg industry to promote an understanding of the problem and to cooperate in improving egg production in Canada through the implementation of HACCP.
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: low 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: high 5. defensibility: low
I. Criteria for Exclusion from Compendium	There is insufficient model documentation to demonstrate viable and credible modeling approaches.
J. Reviewer Comments	NA
K. Cross-References	NA

A. Other Exclusions Study Identification (review)	van Schothorst, M. 1997. Practical approaches to risk assessment. J. Food Protect. 60(11): 1439-1443.
B. Objectives and Type of Study	1. purpose: future regulatory interest; propose limitations and inaccuracies in previously developed models and studies of risk assessment 2. type: overview of risk assessment framework or processes only
C. Publication Attributes	1. sponsors/affiliations: International Association of Milk, Food and Environmental Sanitarians (IAMFES) 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: discussed basic designs of risk assessment models and studies and described their limitations and inconsistencies 2. source: published studies 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics (error structure for analytical data; repeatability; reproducibility; adequacy of analytical and statistical methods; completeness of study; etc.): NA 7. relevance of data: NA
E. Method/Model/Approach	1. general characteristics: short review of risk assessment based studies and how they are applied for different purposes (personal, supplier, food production, government) 2. specific characteristics: NA 3. assumptions: NA4. limitations: NA 5. relevance (qualitative judgement of the usefulness of the method to incident-based microbial risk assessment for biothreat agents; high, medium, or low): NA
F. Study Conclusions and Extended Applications	1. conclusions supported by the review: specific purpose of each risk assessment should be clearly outlined 2. authors' extrapolations from the observed data to other populations or conditions: risk communication between governments, trade partners and consumers is needed
G. Data Gaps and Proposed Solutions	1. identification of data gaps: see conclusions above 2. assumptions or source of surrogate data to fill gap: develop standardized method for risk assessment studies and pertinent parameters to be presented
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA

	4. soundness of study conclusions or internal validity: NA 5. defensibility (method of uncertain usefulness for incident-based microbial risk assessment of buildings and water systems): NA
I. Criteria for Exclusion from Compendium	study included no unique data and/or modeling of likely fate and transport or adverse effects of microbial agents
J. Reviewer Comments	other comments by reviewer: useful for trying to correctly construct a useful risk assessment study/model
K. Cross-References	NA

A. Other Exclusions Study Identification (review)	Vose, D.J. 1998. The application of quantitative risk assessment to microbial food safety. J. Food Protect. 61: 640-648.
B. Objectives and Type of Study	1. purpose: scientific; A review to evaluate a number of modeling techniques that can help produce more realistic and accurate Monte Carlo simulation methods. 2. type: review article
C. Publication Attributes	1. sponsors/affiliations: Ministry of Agriculture, Wellington, New Zealand 2. peer-review mechanism: peer-reviewed journal
D. Data and Study Design	1. type: Review of various processes for probability distributions 2. source: several published literature methods 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: NA
E. Method/Model/Approach	1. general characteristics: several probability distribution methods are reviewed 2. specific characteristics: Models using binomial and Poisson processes and normal distribution are reviewed with theoretical examples. 3. assumptions: NA 4. limitations: Normal distribution is extremely useful in Monte Carlo modeling of microbial risk. However, this mode extends over a range from negative infinity to positive infinity and therefore has the potential to generate

	nonsensical values in a simulation. 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions: NA 2. authors' extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: NA 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: NA
I. Criteria for Exclusion from Compendium	A review article describing various methods that are useful for Monte Carlo modeling of microbial risk. However, no examples are provided to suit this compendium.
J. Reviewer Comments	Good review to understand the various processes, their limitations and acceptances within a given set of parameters. However, this study does not provide direct value to the present compendium, nor does this paper talk about microbial risk of certain biothreat agents.
K. Cross-References	NA

A. Other Exclusions Study Identification (overview)	Voysey, P.A. and M. Brown. 2000. Microbiological risk assessment: a new approach to food safety control. Int. J. Food Microbiol. 58(3): 173-179.
B. Objectives and Type of Study	1. purpose: future regulatory interest; discusses developed MRA models and important components necessary for qualitative assessments 2. type: overview of risk assessment framework or processes only
C. Publication Attributes	1. sponsors/affiliations: Campden and Chorleywood Food Research Association, UK; Unilever Research, UK 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: discussed basic designs of risk assessment models and studies 2. source: published studies

	3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics (error structure for analytical data; repeatability; reproducibility; adequacy of analytical and statistical methods; completeness of study; etc.): NA 7. relevance of data: NA
E. Method/Model/Approach	1. general characteristics: short review of risk assessment based studies and how they are applied for different purposes (personal, supplier, food production, government) 2. specific characteristics: NA 3. assumptions: NA4. limitations: NA 5. relevance (qualitative judgement of the usefulness of the method to incident-based microbial risk assessment for biothreat agents; high, medium, or low): NA
F. Study Conclusions and Extended Applications	1. conclusions supported by the review: Microbial risk assessment components: statement of purpose, hazard identification, exposure assessment, hazard characterization, risk characterization and production of formal report; state general principles of microbial risk assessment as described by the Codex Alimentarius Commission; limitation of MRA include: microbial risks are usually the result of one-time (single) exposures, human response to pathogen bacterium is more variable than to toxic chemicals, pathogens may be diluted, degraded or augmented as a results of food processing steps, microorganisms are remarkably adaptable and can acquire virulent characteristics 2. authors' extrapolations from the observed data to other populations or conditions: NA
G. Data Gaps and Proposed Solutions	1. identification of data gaps: useful/meaningful data difficult to discern 2. assumptions or source of surrogate data to fill gap: Scientific Co-Operation Task (SCOOP) is an European union committee established to examine sources of data, identify gaps and variability of data.
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility (method of uncertain usefulness for incident-based microbial risk assessment of buildings and water systems): NA
I. Criteria for Exclusion from Compendium	study included no unique data and/or modeling of likely fate and transport or adverse effects of microbial agents
J. Reviewer Comments	other comments by reviewer: useful for trying to correctly construct a useful risk assessment study/model

K. Cross-References	NA

A. Other Exclusions Study Identification (review)	Wadhwa, S.G., G.H. Khaled and S.C. Edberg. 2002. Comparative microbial character of consumed food and drinking water. Crit. Rev. Microbiol. 28(3): 249-279.
B. Objectives and Type of Study	1. purpose: future regulatory interest; to assemble from literature the microbial content of food and drinking water to compare and contrast them 2. type: review article
C. Publication Attributes	1. sponsors/affiliations: Clinical Microbiology Laboratory, Yale-New Haven Hospital; Departments of Laboratory and Internal Medicine, Yale University School of Medicine 2. peer-review mechanism: peer-reviewed journal
D. Data and Study Design	1. type: epidemiological and microbial count data 2. source: published studies 3. extent of data: large number of studies of meat, poultry, fish, milk, cheese, eggs, vegetables, spices, and drinking water 4. sampling plan: none 5. sample size: NA 6. performance characteristics: NA 7. relevance: high
E. Method/Model/Approach	1. general characteristics: NA 2. specific characteristics: NA 3. assumptions: NA 4. limitations: NA 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions: Normal flora present in foods and water do not cause human disease, and therefore, their presence should not be regulated for health effects purposes. 2. authors' extrapolations: none stated
G. Data Gaps and Proposed Solutions	1. data gaps: NA

	2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: high 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: NA
I. Criteria for Exclusion from Compendium	There is insufficient data quality or quantity to support rigorous science-based modeling; insufficient model documentation to demonstrate viable and credible modeling approaches; and the study reported detection only without modeling of likely fate and transport or adverse effects.
J. Reviewer Comments	This was a review article that did not present a risk assessment of any kind.
K. Cross-References	NA

A. Other Exclusions Study Identification (risk character.)	Wallace, C. and D. Clayton. 2003. Estimating the relative recurrence risk ratio using a global cross-ratio model. Genetic Epidemiol. 25(4): 293-302.
B. Objectives and Type of Study	1. purpose: scientific; To model the association in cumulative incidence rates between pairs of relatives for complex diseases with genetic and environmental etiologies. 2. type: RC
C. Publication Attributes	1. sponsors/affiliations: British Leprosy Relief Association 2. peer-review mechanism: peer reviewed journal
D. Data and Study Design	1. type: Model testing 2. source: historical leprosy data used only as example for models, not as a study per se 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: low
E. Method/Model/Approach	1. general characteristics: Use maximum likelihood model to estimate risk of disease

	2. specific characteristics: Covariates grouped by whether they cluster in families 3. assumptions: NA 4. limitations: Data limited to sibling pairs, not other relatives 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusion: No strong evidence for genetic susceptibility to leprosy in Karonga 2. authors' extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: might be undetected household contact 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: low 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: low 5. defensibility: low
I. Criteria for Exclusion from Compendium	Not consistent with goals for compendium.
J. Reviewer Comments	Interesting approach to study of genetic and environmental etiologic factors, but does not speak directly to MRA.
K. Cross-References	NA

A. Other Exclusions Study Identification (exposure assessment)	Walls, I. and V.N. Scott. 1997. Use of predictive microbiology in microbial food safety risk assessment. Int. J. Food Microbiol. 36: 97-102.
B. Objectives and Type of Study	1. purpose: regulatory; to present responses to a survey of food industry scientists on the role of predictive microbiology in conducting microbial risk assessments; to present examples of potential risk of foodborne illness from two types of food contaminated with either *Staphylococcus aureus* or *Salmonella* 2. type: EA

C. Publication Attributes	1. sponsors/affiliations: National Food Processors Association 2. peer-review mechanism: peer-reviewed journal
D. Data and Study Design	1. type: experimental data for microbial growth and toxin production; USDA food survey data; *Salmonella* dose-response data 2. source: authors' study, published studies, and government datasets 3. extent of data: cannot determine from paper 4. sampling plan: not described 5. sample size: not described 6. performance characteristics: simple statistics and a few standard model equations, not a true risk assessment 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: probability of infection determined and applied to hypothetical scenarios 2. specific characteristics: *S. aureus* growth and toxin production data fitted to Gompertz equation; probability of infection described by beta distribution model; Pathogen Modeling Program used to predict *Salmonella* growth in hamburger. 3. assumptions: toxin will be absent if fewer than $1.2x10^6$ cfu/g *S. aureus* are present in a cooked meat product 4. limitations: not a true risk assessment 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions: estimated number of infections calculated was higher than expected; Monte Carlo simulations of distribution data needed for more accurate estimates of risk. 2. authors' extrapolations: none stated
G. Data Gaps and Proposed Solutions	1. data gaps: NA; not a true risk assessment 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: low 2. representativeness of data: high 3. generalizability or external validity: low 4. soundness of study conclusions or internal validity: low 5. defensibility: low
I. Criteria for Exclusion from Compendium	There is insufficient data quality or quantity to support rigorous science-based modeling and insufficient model documentation to demonstrate viable and credible modeling approaches.
J. Reviewer Comments	While this paper makes a case for use of microbial risk assessments, it does not describe an actual risk assessment or present data that would be useful in conducting a risk assessment.

K. Cross-References	NA

A. Other Exclusions Study Identification (dose-response)	Watson, A. and D. Keir. 1994. Information on which to base assessments of risk from environments contaminated with anthrax spores. Epidemiol. Infect. 113: 479-490.
B. Objectives and Type of Study	1. purpose: scientific; Provides a literature review of the currently available information relating to health hazards of *B. anthracis*. 2. type: DR
C. Publication Attributes	1. sponsors/affiliations: British Rail Intercity East Coast 2. peer-review mechanism: peer reviewed journal
D. Data and Study Design	1. type: literature review/summary of information for hazard identification and dose response-type studies. 2. source: published literature considered current at the time the article was published 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance: medium
E. Method/Model/Approach	1. general characteristics: summaries of anthrax infections in animals and descriptions of occupational exposures to *B. anthracis*. 2. specific characteristics: No modeling conducted. Only summary of DR found in literature. Anthrax infections summarized for animal species (mice, guinea pigs, monkeys, dogs, sheep, pig) by exposure route, effect, and dose. In addition, a relation between dose to establish infection/number of organisms per milliliter of blood at death was summarized. 3. assumptions: NA 4. limitations: lack of human data; interpretation of animal data 5. relevance: low
F. Study Conclusions and Extended Applications	1. conclusions: Data available from human exposures do not allow establishment of the minimum critical dose; however, man appears to be moderately resistant to anthrax. Infectious dose may be related to body weight. Monkey data appears to be more relevant to man, but this species is more susceptible to infection than man.

	2. authors' extrapolations: NA
G. Data Gaps and Proposed Solutions	1. data gaps: lack of human exposure data 2. proposed solutions: NA
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: high 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: NA
I. Criteria for Exclusion from Compendium	This study does not contain sufficient model documentation to demonstrate viable and credible modeling approaches
J. Reviewer Comments	Does provide data necessary for developing a DR relation using animal data.
K. Cross-References	NA

A. Other Exclusions Study Identification (research for exposure assessment)	Weis, C.P., A.J. Intrepedo, A.K. Miller, et al. 2002. Secondary aerosolization of viable *Bacillus anthracis* spores in a contaminated US Senate office. JAMA 288(22): 2853-2858.
B. Objectives and Type of Study	1. purpose noted by study authors: scientific research on nature and extent of indoor secondary aerosolization of anthrax spores to support development of risk management options for clean up and reoccupancy of office buildings 2. type: basic research to support EA
C. Publication Attributes	1. sponsors/affiliations: US EPA National Enforcement Investigations Center and Region 5; US Army Center for Health Promotion and Preventive Medicine; US Public Health Service; Naval Medical Research Center Biological Defense Directorate 2. peer-review mechanism: full scientific peer-review
D. Data and Study Design	1. type: survey (stationary and personal air samples, surface dust, swab samples) under semiquiescent and simulated office activity in Senate office buildings 2. source: 3. extent of data: three separate building entries on day 25 (Nov. 10) or day 30 (Nov 15, 2001) post-event

	4. sampling plan: targeted plausible exposure pathways beginning 25 days after contamination event 5. sample size: number of observations by entry. 31, 31, and 15 total samples collected for all categories 6. performance characteristics: NA 7. relevance: high
E. Method/Model/Approach	1. general characteristics: NA 2. specific characteristics: NA 3. assumptions: NA 4. limitations: NA 5. relevance: NA
F. Study Conclusions and Extended Applications	1. conclusions supported by the data: estimated exposures as high as 15,000 CFU/hour were possible under conditions of simulated office activity 2. extrapolations: spores detected in/on stationary and personal air samplers, surface swabs, and surface dust could be inputs for modeling dosimetry to target tissue (lung, alveoli)
G. Data Gaps and Proposed Solutions	1. data gaps: mechanistic data for dosimetry modeling 2. proposed solutions: generate targeted data
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: NA
I. Criteria for Exclusion from Compendium	study reporting detection only without modeling of likely fate and transport or adverse effects
J. Reviewer Comments	study included in Appendix 2 and discussed in Executive Summary
K. Cross-References	NA

A. Other Exclusions Study Identification (overview)	Whiting, R.C. 1995. Microbial modeling in foods. Crit. Rev. Food Sci. Nutr. 35: 467-494.

B. Objectives and Type of Study	1. purpose: future regulatory interest; discusses developed models and equation used for MRA 2. type: overview of risk assessment framework or processes only
C. Publication Attributes	1. sponsors/affiliations: US Department of Agriculture 2. peer-review mechanism: full scientific journal review
D. Data and Study Design	1. type: discussed basic equations designed for use in microbial risk assessment models 2. source: published studies 3. extent of data: NA 4. sampling plan: NA 5. sample size: NA 6. performance characteristics: NA 7. relevance of data: NA
E. Method/Model/Approach	1. general characteristics: short review of mathematical equations developed for risk assessment based studies 2. specific characteristics: NA 3. assumptions: NA4. limitations: NA 5. relevance: NA
F. Study Conclusions and Extended Applications	1. conclusions supported by the review: MRA involves accounting for statistical and biological limitations where possible to strengthen model predictions; ultimately models can be used to help estimate risk , determining food spoilage dates, and identify consequences of “out-of-process” events 2. authors’ extrapolations from the observed data to other populations or conditions: NA
G. Data Gaps and Proposed Solutions	1. identification of data gaps: modeling of spoilage microflora; incorporation of additional environmental factors in modeling design; effect of physiological state of pathogen cell 2. assumptions or source of surrogate data to fill gap: more development of MRA models that are physical-chemical, physiological and/or biochemical based
H. Weight of Evidence	1. robustness of method: NA 2. representativeness of data: NA 3. generalizability or external validity: NA 4. soundness of study conclusions or internal validity: NA 5. defensibility: NA
I. Criteria for Exclusion from Compendium	study included no unique data and/or modeling of likely fate and transport or adverse effects of microbial agents

J. Reviewer Comments	other comments by reviewer: this study discusses mathematical equations that have been used and important considerations that may/not have been examined with regards to experimental results
K. Cross-References	NA

APPENDIX B: Secondary Search Results Not Reviewed

Alcantara, F. and M.A. Almeida. 1995. Virological quality of the Ria de Aveiro: Validity of potential microbial indicators. Netherlands J. Aquat. Ecol. 29(3-4): 419-425.

Anderson, M.A., M. Stewart, M.V. Yates, et al. 1998. Modeling the impact of body-contact recreation on pathogen concentrations in a source of drinking water reservoir. Water Res. 32(11): 3293-3306.

Arana, I., P. Santorum, A. Muela, et al. 1999. Chlorination and ozonation of wastewater: comparative analysis of efficacy through the effect on Escherichia coli membranes. J. Appl. Microbiol. 86(5): 883-888.

Araujo, R.M., A. Puig, J. Lasobras, et al. 1997. Phages of enteric bacteria in fresh water with different levels of faecal pollution. J. Appl. Microbiol. 82(3): 281-286.

Ballester, F. and J. Sunyer. 2000. Drinking water and gastrointestinal disease: Need of better understanding and an improvement in public health surveillance. J. Epidemiol. Commun. Health 54(1): 3-5.

Barrell, R.A.E., P.R. Hunter and G. Nichols. 2000. Microbiological standards for water and their relationship to health risk. Commun. Dis. Public Health 3(1): 8-13.

Bemrah, N., H. Bergis and C. Colmin. 2002. Quantitative risk assessment of human salmonellosis from the consumption of a turkey product in collective catering establishments. Int. J. Food Microbiol. 80(1): 17-30.

Bernard, D.T. and V.N. Scott. 1995. Risk assessment and food-borne micro-organisms: The difficulties of biological diversity. Food Control 6(6): 329-333.

Breiman, R.F., W. Cozen, B.S. Fields, et al. 1990. Role of air sampling in investigation of an outbreak of Legionnaires' disease associated with exposure to aerosols from an evaporative condenser. J. Infect. Dis. 161: 1257-1261.

Breiman, R.F. 1996. Impact of technology on the emergence of infectious diseases. Epidemiol. Rev. 18(1): 4-9.

Brion, G.M. and S. Lingireddy. 1999. A neural network approach to identifying non-point sources of microbial contamination. Water Res. 33(14): 3099-3106.

Brookhart ,M.A., A. Hubbard, M. Van der Laan, et al. 2002. Statistical estimation of parameters in a disease transmission model: Analysis of a *Cryptosporidium* outbreak. Stat. Med. 21(23): 3727-3638.

Brown, M.H.. 2002. Quantitative microbiological risk assessment: principles applied to determining the comparative risk of salmonellosis from chicken products. Int. Biodeterior. Biodegrad. 50(3-4): 155-160.

Buche, P., O. Haemmerle and R. Thomopoulos. 2003. Integration of heterogeneous, imprecise, and incomplete data: An application to the microbiological risk assessment. Foundations Intell. Sys. 2871: 98-107.

Chang, F.Y., J.E. Peacock Jr, D.M. Musher, et al. 2003. Staphylococcus aureus bacteremia: Recurrence and the impact of antibiotic treatment in a prospective multicenter study. Medicine 82(5): 333-339.

Chen, Y.M., H.C. Lee, C.M. Chang, et al. 2001. *Clostridium bacteremia*: Emphasis on the poor prognosis in cirrhotic patients. J. Microbiol. Immunnol. Infect. 34: 113-118.

Coleman, M.E. and H.M. Marks. 1999. Qualitative and quantitative risk assessment. Food Control 10: 289-297.

Coleman, M.E. and H.M. Marks. 2000. Mechanistic modeling of Salmonellosis. Quantitiative Microbiol. 2: 227-247.

Coleman, M.E. 2003. Guest editorial: Interactions of predictive microbiology and risk assessment. Risk Anal. 23(1): 175-178.

Dennis, P.J. and J.V. Lee. 1988. Differences in aerosol survival between pathogenic and non-pathogenic strains of *Legionella pneumophila* serogroup 1. J. Appl. Bacteriol. 65: 135-141.

Druett, H.A., D.W. Henderson, L. Packman, et al. 1953. Studies on respiratory infection. I. The influence of particle size on respiratory infection with anthrax spores. J. Hyg. 51: 359-371.

Dull, P.M., K.E. Wilson, B. Kournikakis, et al. 2002. *Bacillus anthracis* aerosolization associated with a contaminated mail sorting machine. Emerg. Infect. Dis. 8(10): 1044- 1047.

Eisenberg, J.N.S. and T.E. McKone. 1998. Decision tree method for the classification of chemical pollutants: Incorporation of across-chemical pollutants: Incorporation of across-chemical variability and within-chemical uncertainty. Environ. Sci. Technol. 32: 3396-3404.

Elliott, A.H. 1998. Prediction of illness risk near ocean outfalls using frequency distributions of bacterial concentrations. Water Res. 32(10): 3182-3187.

FAO/WHO. 2004. Joint FAO/WHO workshop on Enterobacter sakazakii and other microorganisms in powdered infant formula, Geneva, 2-5 February 2004. Food and Agriculture Organization of the United Nations/World Health Organization.

Farber, J. 1997. Introductory note. Int. J. Food Microbiol. 36: 85.

Fewtrell, L., S.M. Macgill, D. Kay, et al. 2001. Uncertainties in risk assessment for the determination of drinking water pollutant concentrations: *Cryptosporidium* case study. Water Res. 35(2): 441-447.

Foegeding, P.M. 1997. Driving predictive modelling on a risk assessment path for enhanced food safety. Int. J. Food Microbiol. 36: 87-95.

Fritz, D.L., N.K. Jaax, W.B. Lawrence, et al. 1995. Pathology of experimental inhalation anthrax in the rhesus monkey. Lab. Invest. 73(5): 691-702.

Gale, P., C. Young, G. Stanfield, et al. 1998. Development of a risk assessment for BSE in the aquatic environment. J. Appl. Microbiol. 84(4): 467-477.

Gibson, C.J., C.N. Haas and J.B. Rose JB. 1998. Risk assessment of waterborne protozoa: Current status and future trends. Parasitology 117: S205-212.

Giovannini, A., V. Prencipe, A. Conte, et al. 2004. Quantitative risk assessment of Salmonella spp. infection for the consumer of pork products in an Italian region. Food Control 15: 139-144.

Gofti, L., D. Zmirou, F.S. Murandi, et al. 1999. Evaluation du risque microbiologique d'origine hydrique: Un etat de l'art et des perspectives. Rev. Epidemiol. Sante Publique 47: 61-73.

Haas, C.N., J.B. Rose and C.P. Gerba. 1999. Risk assessment paradigms. Quantitative microbial risk assessment. New York, NY: John Wiley & Sons, Inc., p. 86-106.

Haas, C.N. 1999. On modeling correlated random variables in risk assessment. Risk Anal. 19(6): 1205-1214.

Haas, C.N., A. Thayyar-Madabusi, J.B. Rose, et al. 2000. Development of a dose-response relationship for *Escherichia coli* O157:H7. Int. J. Food Microbiol. 1748: 153-159.

Haas, C.N. 2003. Book reviews: The microbiological risk assessment of food. Risk Anal. 23(6): 1351-1356.

Haile, R.W., J.S. Witte, M. Gold, et al. 1999. The health effects of swimming in ocean water contaminated by storm drain runoff (abstract only). Epidemiology 10(4): 355-363.

Hartnett, E., L.A. Kelly, G. Gettinby, et al. 2003. A quantitative risk assessment for campylobacters in broilers: Work in progress. Int. Biodeterior. Biodegrad. 50(3- 4): 161-165.

Hathaway, S.C. and R.L. Cook. 1997. A regulatory perspective on the potential uses of microbial risk assessment in international trade. Int. J. Food Microbiol. 36: 127-133.

Hua, I. and J.E. Thompson. 2000. Inactivation of *Escherichia coli* by sonication at discrete ultrasonic frequencies. Water Res. 34(15): 3888-3893.

Hurst, C.J. 2002. Estimating the risk of infectious disease associated with pathogens in drinking water. In: Hurst, C.J., R.L. Crawford, G.R. Knudsen, et al., eds. Manual of environmental microbiology. Washington, DC: ASM Press., p. 309-319.

ILSI Risk Science Institute Pathogen Risk Assessment Working Group. 1996. A conceptual framework to assess the risks of human disease following exposure to pathogens. Risk Anal. 16(6): 841-848.

Inglesby, T.V., D.A. Henderson, J.G. Bartlett, et al. 1999. Anthrax as a biological weapon: Medical and public health management. JAMA 281(18): 1735-1745.

Iversen, C. and S. Forsythe. 2003. Risk profile of *Enterobacter sahazakii*, an emergent pathogen associated with infant milk formula. Trends Food Sci. Technol. 14(11): 443-454.

Jensen, P.A., W.F. Todd, G.N. Davis, et al. 1992. Evaluation of eight bioaerosol samplers challenged with aerosols of free bacteria. Am. Ind. Hyg. Assoc. J. 53(10): 660-667.

Jensen, P.M. and F. Frandsen. 2000. Temporal risk assessment for Lyme borreliosis in Denmark. Scand. J. Infect. Dis. 32: 539-544.

Jensen, P.M., H. Hansen and F. Frandsen. 2000. Spatial risk assessment for Lyme borreliosis in Denmark. Scand. J. Infect. Dis. 32: 545-550.

Jernigan, D.B., P.L. Raghunathan, B.P. Bell, et al. 2002. Investigation of bioterrorism- related anthrax, United States, 2001: Epidemiologic findings. Emerg. Infect. Dis. 8(10): 1019-1028.

Jernigan, J.A., D.S. Stephens, D.A. Ashford, et al. 2001. Bioterrorism-related inhalational anthrax: The first 10 cases reported in the United States. Emerg. Infect. Dis. 7(6): 933-944.

Jolis, D., P. Pitt and R. Hirano. 1999. Risk assessment for *Cryptosporidium parvum* in reclaimed water. Water Res. 33(13): 3051-3055.

Jouve, J.-L. 2000. Special issue: ILSI Europe session on microbiological risk assessment. Int. J. Food Microbiol. 58: 141-142.

Kalberlah, F., U. Fost and K. Schneider. 2002. Time extrapolation and interspecies extrapolation for locally acting substances in case of limited toxicological data. Ann. Occup. Hyg. 46(2): 175-185.

Kang, S.-H., R.L. Kodell and J.J. Chen. 2000. Incorporating model uncertainties along with data uncertainties in microbial risk assessment. Regul. Toxicol. Pharmacol. 32: 68-72.

Kodell, R.L., S.H. Kang and J.J. Chen. 2001. Statistical models of health risk due to microbial contamination of foods. Environ. Ecol. Stat. 9(3): 259-271.

Krishnan, K., J. Paterson and D.T. Williams. 1997. Health risk assessment of drinking water contaminants in Canada: The applicability of mixture risk assessment methods. Regul. Toxicol. Pharmacol. 26: 179-187.

Lammerding, A.M. 1997. An overview of microbial food safety risk assessment. J. Food Prot. 60(11): 1420-1425.

Lammerding, A.M. and G.M. Paoli. 1997. Quantitative risk assessment: An emerging tool for emerging foodborne pathogens. Emerg. Infect. Dis. 3(4): 483-487.

Lammerding, A.M. and A. Fazil. 2000. Hazard identification and exposure assessment for microbial food safety risk assessment. Int. J. Food Microbiol. 58(3): 147-157.

Lathers, C.M. 2001. Role of veterinary medicine in public health: Antibiotic use in food animals and humans and the effect on evolution of antibacterial resistance. J. Clin. Pharmacol. 41: 595-599.

Latimer, H.K., L.-A. Jaykus, R.A. Morales, et al. 2002. Sensitivity analysis of *Salmonella enteritidis* levels in contaminated shell eggs using a biphasic growth model. Int. J. Food Microbiol. 75: 71-87.

Lee, R.J. and A.D. Younger. 2002. Developing microbiological risk assessment for shellfish purification. Int. Biodeterior. Biodegrad. 50: 177-183.

Leoni, E., P.P. Legnani, M.B. Sabattini, et al. 2001. Prevalence of *Legionella spp.* in swimming pool environment. Water Res. 35(15): 3749-3753.

Lewis, D.L. and D.K. Gattie. 1991. Predicting chemical concentration effects on transformation rates of dissolved organics by complex microbiol assemblages. Ecol. Modell. 55: 27-46.

Li, X. and P.A. Rossignol. 1998. Probability model on the use of sentinel animal monitoring for arbovirus. Epidemiology 9(4): 446-451.

Liberman, D.F. 1984. Biosafety in biotechnology: A risk assessment overview. Dev. Ind. Microbiol. 25: 69-75.

Lopez-Pila, J.M. and R. Szewzyk. 2000. Estimating the infection risk in recreational waters from the faecal indicator concentration and from ratio between pathogens and indicators. Water Res. 34(17): 4195-4200.

Makri, A., R. Modarres and R. Parkin. 2004. Cryptosporidiosis susceptibility and risk: A case study. Risk Anal. 24(1): 209-220.

McElroy, D.M., L.A.. Jaykus and P.M. Foegeding. 1999. A quantitative risk assessment for *Bacillus cereus* emetic disease associated with the consumption of Chinese-style rice. J. Food Saf. 19: 209-229.

Membre, J.M., M. Kubaczka, J. Dubois, et al. 2004. Temperature effect on Listeria monocytogenes growth in the event of contamination of cooked pork products. J. Food Protect. 67(3): 463-469.

Meselson, M., J. Guillemin and M. Hugh-Jones, et al. 1994. The Sverdlovsk anthrax outbreak of 1979. Science 266: 1202-1208.

Messner, M.J., C.L. Chappell and P.C. Okhuysen. 2001. Risk assessment for Cryptosporidium: A hierarchical Bayesian analysis of human dose response date. Water Res. 35(16): 3734-3940.

Miller, A.J., R.C. Whiting, J.L. Smith. 1997. Use of risk assessment to reduce listeriosis incidence. Food Technol. 51(4): 100-103.

Molineaux, L., H.H. Diebner, M. Eichner, et al. 2001. *Plasmodium falciparum* parasitaemia described by a new mathematical model. Parasitology 122(4): 379-391.

Muniesa, M. and J. Jofre. 1998. Abundance in sewage of bacteriophages that infect *Escherichia coli* O157:H7 and that carry the shiga toxin 2 gene. Appl. Environ. Microbiol. 64(7): 2443-2448.

Naumova, E.N., A.I. Egorov, R.D. Morris, et al. 2003. The elderly and waterborne *Cryptosporidium* infection: Gastroenteritis hospitalizations before and during the 1993 Milwaukee outbreak. Emerg. Infect. Dis. 9(4): 418-425.

Nauta, M.J. 2000. Separation of uncertainty and variability in quantitative microbial risk assessment models. Int. J. Food Microbiol. 57(½): 9-18.

Nicas, M. 1996. An analytical framework for relating dose risk and incidence: An application to occupational tuberculosis infection. Risk Anal. 16(4): 527-538.

Nicas, M., J. Neuhaus and R.C. Spear. 2000. Risk-based selection of respirators against infectious aerosols: Application to anthrax spores. J. Occup. Environ. Med. 42(7): 737-748.

Nicas, M. and A. Hubbard. 2003. A risk analysis approach to selecting respiratory protection against airborne pathogens used for bioterrorism. Am. Ind. Hyg. Assoc. J. 64: 95-101.

Notermans, S., G. Gallhoff and M.H. Zwietering, et al. 1994. The HACCP concept: Specification of criteria using quantitative risk assessment. Food Microbiol. 11: 397- 408.

Oscar, T.P. 2004. A quantitative risk assessment model for Salmonella and whole chickens. Int. J. Food Microbiol. 93(2): 231-247.

Payment, P., A. Berte, M. Prevost, et al. 2000. Occurrence of pathogenic microorganisms in the St. Lawrence River (Canada) and comparison of health risks for populations using it as their source of drinking water. Can. J. Microbiol. 46(6): 565- 576.

Pepper, I.L. and T.J. Gentry. 2002. Incidence of *Bacillus anthracis* in soil. Soil Sci. 167(10): 627-635.

Perz, J.F., F.K. Ennever and S.M. LeBlancq SM. 1998. Cryptosporidium in tap water-comparison of predicted risks with observed levels of disease. Am. J. Epidemiol. 147(3): 289-301.

Pinelli, C., M.C. Serra and L.C.M. Loffredo. 2000. Efficacy of a microbiological test in caries risk assessment. J. Dent. Res. 79(5): 1164.

Pinsky, P.F. 2000. Assessment of risk from long term exposure to waterborne pathogens. Environ. Ecol. Stat. 7(2): 155-175.

Powell, M., E. Ebel, M. Walderhaug, J. Kause. 2000. Dose response envelope for *Escherichia coli* O157:H7. Quantitative Microbiol. 2: 141-163.

Reissman, D.B., E.A.S. Whitney, T.H. Taylor, et al. 2004. One-year health assessment of adult survivors of *Bacillus anthracis* infection. JAMA 291(16): 1994-1998.

Rocourt, J., P. BenEmbarek, H. Toyofuku, et al. 2003. Quantitative risk assessment of Listeria monocytogenes in ready-to-eat foods: The FAO/WHO approach. FEMS Immunol. Med. Microbiol. 35(3): 263-267.

Rose, J.B., C.N. Haasa and C.P. Gerba. 1995. Linking microbiological criteria for foods with quantitative risk assessment. J. Food Saf. 15(2): 121-132.

Sanaa, M., N. Bemrah, S. Meyer, et al. 2000. Quantification des risques sanitaires lies aux contaminations microbiologiques des aliments. Rev. Epidemiol. Sante Publique 48: S11-S24.

Seigneur, C., E. Constantinou and L. Levin. 1996. Multipathway health risk assessment of power plant water discharges. Water Air Soil Pollut. 90: 55-64.

Serra, J.A., E. Domenech, I. Escriche, et al. 1999. Risk assessment and critical control points from the production perspective. Int. J. Food Microbiol. 46: 9-26.

Soller, J.A., A.W. Olivieri, J. Crook, et al. 2003. Risk-based approach to evaluate the public health benefit of additional wastewater treatment. Environ. Sci. Technol. 37: 1882-1891.

Soller, J.A., A.W. Olivieri, J.N.S. Eisenberg, et al. 2004. Evaluation of microbial risk assessment techniques and applications. Alexandria, VA: Water Environment Research Foundation.

Teunis, P.F., N.J. Nagelkerke, C.N. Haas. 1999. Dose response models for infectious gastroenteritis. Risk Anal. 19(6): 1251-1260.

The Safety in Biotechnology Working Party of the European Federation of Biotechnology. 1999. Safe biotechnology 9: Values in risk assessment for the environmental application of microorganisms. Trends Biotechnol. 17(8): 307-311.

Tryland, I., M. Pommepuy and L. Fiksdal. 1998. Effect of chlorination on beta-D- galactosidase activity of sewage bacteria and *Escherichia coli*. J. Appl. Microbiol. 85(1): 51-60.

Turnbull, P.C.B., P.M. Lindeque, A.M. Bennett, et al. 1998. Airborne movement of anthrax spores from carcass sites in the Etosha National Park, Namibia. J. Appl. Microbiol. 84: 667-676.

Vanderlinde, P. 1998. Quantitative microbial risk assessment. An Australian perspective. Food Australia 50(12): 626-628.

van Gerwen, S.J.C., M.C. te Giffel, K. van't Riet, et al. 2000. Stepwise quantitative risk assessment as a tool for characterization of microbiological food safety. J. Appl. Microbiol. 88(6): 938-951.

van Schothorst, M. 2002. Microbiological risk assessment of foods in international trade. Saf. Sci. 40: 359-382.

Vialette, M., A. Pinon, E. Chasseignaux, et al. 2003. Growths kinetics comparison of clinical and seafood Listeria monocytogenes isolates in acid and osmotic environment. Int. J. Food Microbiol. 82(2): 121-131.

Vynnycky, E. and P.E. Fine. 2000. Lifetime risks incubation period and serial interval of tuberculosis. Am. J. Epidemiol. 152(3): 247-263.

Walker, D.H., O. Yampolska and L.M. Grinberg. 1994. Death at Sverdlovsk: What have we learned? Am. J. Pathol. 144(6): 1135-1141.

Watson, A. and D. Keir. 1994. Information on which to base assessments of risk from environments contaminated with anthrax spores. Epidemiol. Infect. 113: 479-490.

Webb, G.F. and M.J. Blaser. 2002. Mailborne transmission of anthrax: Modeling and implications. Proc. Natl. Acad. Sci. U S A 99(10): 7027-7032.

Weis, C.P., A.J. Intrepido, A.K. Miller, et al. 2002. Secondary aerosolization of viable *Bacillus anthracis* spores in a contaminated US Senate office. JAMA 288(22): 2853-2858.

Whiting, R.C. and R.L. Buchanan. 1994. Microbial modeling. Food Technol. 48(6): 113-120.

Wilson, M.E. 1995. Infectious diseases: An ecological perspective. Br. Med. J. 311(7021): 1681-1684.

Winter, H. and R.M. Pfisterer. 1991. Inhalationsanthrax bei einem textilarbeiter: Ein nicht-letaler verlauf. Schweiz Med. Wochenschr. 121: 832-835.

Yates, M.V. and W.A. Jury. 1995. On the use of virus transport modeling for determining regulatory compliance. J. Environ. Qual. 24(6): 1051-1055.

Young, G.A., M.R. Zelle and R.E. Lincoln. 1946. Respiratory pathogenicity of *Bacillus anthracis* spores. J. Infect. Dis. 79: 233-246.

Young, P.L. and S.J. Komisar. 1999. The variability introduced by partial sample analysis to numbers of *Cryptosporidium* oocysts and *Giardia* cysts reported under the Information Collection Rule. Water Res. 11: 2660-2668.

APPENDIX C: Modeling Citations for Particulate Deposition

Anjilvel, S. and B. Asgharian. 1995. A multiple-path model of particle deposition in the rat lung. Fundam. Appl. Toxicol. 28: 41-50.

Asgharian, B., R. Wood, R.B. Schlesinger. 1995. Empirical modeling of particle deposition in the alveolar region of the lungs: A basis for interspecies extrapolation. Fundam. Appl. Toxicol. 27: 232-238.

Asgharian, B. and S. Anjilvel. 1998. A multiple-path model of fiber deposition in the rat lung. Toxicol. Sci. 44: 80-86.

Asgharian, B., J.T. Kelly and E.W. Tewksbury. 2003. Respiratory deposition and inhalability of monodisperse. Toxicol. Sci. 71:.104-111.

Balashazy, I., A. Farkas, I. Szoke, et al. 2003. Simulation of deposition and clearance of inhaled particles in central human airways. Radiat. Prot. Dosim. 105(1- 4): 129-132.

Bolch, W.E., E.B. Farfan, C. Huh, et al. 2001. Influence of parameter uncertainties within the ICRP 66 respiratory tract model: Particle deposition. Health Phys. 81(4): 378-394.

Bolch, W.E., T.E. Huston, E.B. Farfan, et al. 2003. Influences of parameter uncertainties within the ICRP-66 respiratory tract model: Particle clearance. Health Phys. 84(4): 421-435.

Brand, P., C. Rieger, T. Beinert, et al. 1995. Aerosol derived airway morphometry in healthy subjects. Eur. Resp. J. 8: 1639-1646.

Cassee, F.R., H. Muijser, E. Duistermaat, et al. 2002. Particle size-dependent total mass deposition in lungs determines inhalation toxicity of cadmium chloride aerosols in rats. Application of a multiple path dosimetry model. Arch. Toxicol. 76: 277-286.

Cullen, R.T., C.L. Tran, D. Buchanan, et al. 2000. Inhalation of poorly soluble particles. I. Differences in inflammatory response and clearance during exposure. Inhal. Toxicol. 12: 1089-1111.

Darquenne, C. and M. Paiva. 1994. One-dimensional simulation of aerosol transport and deposition in the human lung. J. Appl. Physiol. 77(6): 2889-2898.

Darquenne, C. and M. Paiva. 1996. Two- and three-dimensional simulations of aerosol transport and deposition in alveolar zone of human lung. J. Appl. Physiol. 80(4): 1401- 1414.

Darquenne, C., P. Brand, J. Heyder, et al. 1997. Aerosol dispersion in human lung: comparison between numerical simulations and experiments for bolus tests. J. Appl. Physiol. 83(3): 966-974.

Dowd, S.E., C.P. Gerba, I.L. Pepper, et al. 2000. Bioaerosol transport modeling and risk assessment in relation to biosolid placement. J. Environ. Qual. 29(1): 343-348.

Dubaniewicz, A., Z. Szczerkowska and A. Hoppe. 2003. Comparative analysis of HLA class I antigens in pulmonary sarcoidosis and tuberculosis in the same ethnic group. Mayo Clin. Proc. 78(4): 436-442.

Finlay, W.H., K.W. Stapleton, H.K. Chan, et al. 1996. Regional deposition of inhaled hygroscopic aerosols: *In vivo* SPECT compared with mathematical modeling. J. Appl. Physiol. 81(1): 374-383.

Foster, W.M., D.M. Walters, M. Longphre, et al. 2001. Methodology for the measurement of mucociliary function in the mouse by scintigraphy. J. Appl. Physiol. 90: 1111-1118.

Haber, S., D. Yitzhak and A. Tsuda. 2003. Gravitational deposition in a rhythmically expanding and contracting alveolus. J. Appl. Physiol. 95: 657-671.

Harvey, R.P. and D.M. Hamby. 2002. Age-specific uncertainty in particulate deposition for 1 m AMAD particles using the ICRP 66 lung model. Health Phys. 82(6): 807-816.

Hattis, D., A. Russ, R. Goble, et al. 2001. Human interindividual variability in susceptibility to airborne particles. Risk Anal. 21(4): 585-599.

Hofmann, W. and B. Asgharian. 2003. The effect of lung structure on mucociliary clearance and particle retention in human and rat lungs. Toxicol. Sci. 73: 448-456.

Kim, C.S. and S.C. Hu. 1998. Regional deposition of inhaled particles in human lungs: comparison between men and women. J. Appl. Physiol. 84(6): 1834-1844.

Kim, C.S. 2000. Methods of calculating lung delivery and deposition of aerosol particles. Resp. Care 45(6): 695-711.

Kreyling, W.G., J.D. Blanchard, J.J. Godleski, et al. 1999. Anatomic localization of 24- and 96-h particle retention in canine airways. J. Appl. Physiol. 87(1): 269-284.

Kreyling, W.G., M. Semmler, F. Erbe, et al. 2002. Translocation of ultrafine insoluble iridium particles from lung epithelium to extrapulmonary organs is size dependent but very low. J. Toxicol. Environ. Health A 65: 1513-1530.

Kuempel, E.D., C.L. Tran, A.J. Bailer, et al. 2001. Methodological issues of using observational human data in lung dosimetry models for particulates. Sci. Total Environ. 274: 67-77.

Lazaridis, M., D.M. Broday, O. Hov, et al. 2001. Integrated exposure and dose modeling and analysis system. 3. Deposition of inhaled particles in the human respiratory tract. Environ. Sci. Technol. 35: 3727-3734.

Martonen, T.B., J.D. Schroeter, D. Hwang, et al. 2000. Human lung morphology models for particle deposition studies. Inhal. Toxicol. 12: 109-121.

Martonen, T.B., C.J. Musante, R.A. Segal, et al. 2000. Lung models: Strengths and limitations. Resp. Care 45(6): 712-736.

Martonen, T.B., I.M. Katz and C.J. Musante. 2001. A nonhuman primate aerosol deposition model for toxicological and pharmaceutical studies. Inhal. Toxicol. 13: 307-324.

Martonen, T.B. and J.D. Schroeter. 2003. Risk assessment dosimetry model for inhaled particulate mater: II Laboratory surrogates (rat). Toxicol. Lett. 138(1-2): 133-142.

Martonen, T.B. and J.D. Schroeter. 2003. Risk assessment dosimetry model for inhaled particulate matter: I Human subjects. Toxicol. Lett. 138(1-2): 119-132.

Mauderly, J.L. 2000. Animal models for the effect of age on susceptibility to inhaled particulate matter. Inhal. Toxicol. 12: 863-900.

Musante, C.J. and T.B. Martonen. 2000. Computer simulations of particle deposition in the developing human lung. J. Air Waste Manage. Assoc. 50: 1426-1432.

Nowak, K., P.P. Kakade and A.V. Annapragada. 2003. Computational fluid dynamics simulation of airflow and aerosol deposition in human lungs. Ann. Biomed. Eng. 31(4): 373-390.

Paoletti, L. 1997. Mineral particles in bronchoalveolar lavage fluid (BALF): An attempt at designing a quantitative model. Arch. Environ. Health. 52(5): 384-389.

Phalen, R.F. and M.J. Oldham. 2001. Methods for modeling particle deposition as a function of age. Respir. Physiol. 128(1): 119-130.

Sarangapani, R. and A.S. Wexler. 2000. The role of dispersion in particle deposition in human airways. Toxicol. Sci. 54: 229-236.

Seaton, A., A. Soutar, V. Crawford, et al. 1999. Particulate air pollution and the blood. Thorax 54: 1027-1032.

Segal, R.A., T.B. Martonen and C.S. Kim. 2000. Comparison of computer simulations of total lung deposition to human subject data in healthy test subjects. J. Air Waste Manage. Assoc. 50: 1262-1268.

Stober, W. 1999. Pock model simulations of pulmonary quartz dust retention data in extended inhalation exposures of rats. Inhal. Toxicol. 11: 269-292.

Tanpowpong, K. and C. Chiratthiti. 2001. The Ramathibodi nasal filter in a simulated human airway: Evaluated with laser smoke particles and a laser diode dust portable monitor. J. Med. Assoc. Thai. 84: 1667-1673.

Tawhai, M.H., A.J. Pullan and P.J. Hunter. 2000. Generation of an anatomically based three-dimensional model of the conducting airways. Ann. Biomed. Eng. 28: 793-802.

Warheit, D.B., B.R. Laurence, K.L. Reed, et al. 2004. Comparative pulmonary toxicity assessment of single-wall carbon nanotubes in rats. Toxicol. Sci. 77: 117-125.

Webster, I., B. Goldstein, F.S.J. Coetzee, et al. 1993. Malignant mesothelioma induced in baboons by inhalation of amosite asbestos. Am. J. Ind. Med. 24: 659-666.

Zhang, Z., C. Kleinstreuer and C.S. Kim. 2001. Effects of curved inlet tubes on air flow and particle deposition in bifurcating lung models. J. Biomech. 34: 659-669.

Zhang, Z., C. Kleinstreuer and C.S. Kim. 2002. Computational analysis of micron-particle deposition in a human triple bifurcation airway model. Computer Methods in Biomechanics and Biomedical Engineering 5(2): 135-147.

Appendix D: Acronyms

AAAS	**American Association for the Advancement of Science**
ASM	**American Society for Microbiology**
BSE	**bovine spongiform encephalopathy**
DR	**dose-response**
EA	**exposure assessment**
EPA	**Environmental Protection Agency**
FAO	**Food and Agricultural Organization (United Nations)**
FDA	**Food and Drug Administration**
HACCP	**Hazard Analysis Critical Control Point (program/system)**
HIV	**human immunodeficiency virus**
HSPD	**Homeland Security Presidential Directive**
ILSI	**International Life Sciences Institute**
LOAEL	**lowest observable adverse effect level**
NAS	**National Academy of Sciences**
NHSRC	**National Homeland Security Research Center**
NOAEL	**no observable adverse effect level**
NTIS	**National Technical Information Service**
PBPK	**physiologically based pharmacokinetic**
RC	**risk characterization**
SOT	**Society of Toxicology**
SRA	**Society for Risk Analysis**
TCAD	**Threat and Consequence Assessment Division**
TSE	**transmissible spongiform encephalopathy**
URL	**uniform resource locator (Web address)**
USDA	**U.S. Department of Agriculture**
WHO	**World Health Organization**

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