参考資料4

Food and Agriculture Organization of the United Nations

World Health Organization

Joint FAO/WHO Expert Meetings on Microbiological Risk Assessment (JEMRA) on Methodologies of Microbiological Risk Assessment

Draft Guidance of Microbiological Risk Assessment for Food

Public consultation

Posted on 15 June 2020

Background information

Risk assessment of microbiological hazards in foods, commonly referred to as Microbiological Risk Assessment (MRA), has previously been identified as one of the priority areas of work by the Codex Alimentarius Commission (CAC). Following the work of the Codex Committee on Food Hygiene (CCFH), CAC adopted Principles and Guidelines for the Conduct of Microbiological Risk Assessment (CXG-30) in 1999.
Subsequently, the CCFH identified a number of areas in which it required expert risk assessment advice.
In response to the needs of their member countries and Codex, FAO and WHO launched a programme of work in the early 2000's with the objective of providing expert advice on risk assessment of microbiological hazards in foods, including technical guidance on microbiological risk assessment. Three technical guidance documents were published in the Microbiological Risk Assessment Series: Hazard characterization for Pathogens in food and water (2003), Exposure assessment of microbiological hazards in food (2008), and Risk characterization of microbiological hazards in food (2009).
Science has evolved over the last decade and there is a need to update and incorporate new developments in the principles and methods for risk assessment of microbiological hazards.
To consolidate and update the existing technical guidance documents on microbiological risk assessment, FAO and WHO established a group of experts and convened the Expert Meetings in Rome, Italy on 11-15 March 2019. In addition, the draft document was also subject to peer review by external reviewers.

Comments

If you have any comments, please contact us at both jemra@fao.org and jemra@who.int no later than **15 July 2020**. When you provide us your comments, please indicate line number (left) for specific chapters/sections.

(DRAFT) Guidance of Microbiological Risk Assessment for Food

Joint FAO/WHO Expert Meetings on Microbiological Risk Assessment (JEMRA) on Methodologies of Microbiological Risk Assessment

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Glossary

Baseline risk (Inherent risk): The level of food safety risk posed by a hazard in a food supply chain without any changes to the current system, i.e. without additional risk management options being implemented.

Dose-Response Assessment: The determination of the relationship between the magnitude of exposure (dose) to a chemical, biological or physical agent and the severity and/or frequency of associated adverse health effects (response). (CAC, 2019)

Exposure Assessment: The qualitative and/or quantitative evaluation of the likely intake of biological, chemical, and physical agents via food as well as exposures from other sources if relevant. (CAC, 2019)

Hazard: a biological, chemical or physical agent in, or condition of, food with the potential to cause an adverse health effect. (CAC, 2019)

Hazard Characterization: The qualitative and/or quantitative evaluation of the nature of the adverse health effects associated with biological, chemical and physical agents which may be present in food. (CAC, 2019)

Hazard Identification: The identification of biological, chemical, and physical agents capable of causing adverse health effects and which may be present in a particular food or group of foods. (CAC, 2019)

Qualitative Risk Assessment: A risk assessment based on data which, while forming an inadequate basis for numerical risk estimations, nonetheless, when conditioned by prior expert knowledge and identification of attendant uncertainties permits risk ranking or separation into descriptive categories of risk. (CAC, 1999)

Quantitative risk assessment: A risk assessment that provides numerical expressions of risk and indication of the attendant uncertainties. (CAC, 1999)

Ranking: The process of ranking different hazard-food product combinations for risk assessment and/or risk management priority.

Risk: A function of the probability of an adverse health effect and the severity of that effect, consequential to a hazard(s) in food. (CAC, 2019)

Risk Analysis: A process consisting of three components: risk assessment, risk management and risk communication. (CAC, 2019)

Risk Assessment: A scientifically based process consisting of the following steps: (i) hazard identification, (ii) hazard characterization, (iii) exposure assessment, and (iv) risk characterization. (CAC, 2019)

Risk Characterization: The process of determining the qualitative and/or quantitative estimation, including attendant uncertainties, of the probability of occurrence and severity of known or potential adverse health effects in a given population based on hazard identification, hazard characterization and exposure assessment. (CAC, 2019)

Risk Communication: The interactive exchange of information and opinions throughout the risk analysis process concerning risks, risk-related factors and risk perceptions, among risk assessors, risk managers, consumers, industry, the academic community and other interested parties, including the explanation of risk assessment findings and the basis of risk management decisions. (CAC, 2019)

Risk estimate: The qualitative and/or quantitative estimation of risk resulting from risk characterization. (CAC, 2019)

Risk Management: The process, distinct from risk assessment, of weighing policy alternatives, in consultation with all interested parties, considering risk assessment and other factors relevant for the health protection of consumers and for the promotion of fair trade practices, and, if needed, selecting appropriate prevention and control options. (CAC, 2019)

Risk profile: The description of the food safety problem and its context. (CAC, 2019)

Semi-quantitative risk assessment: Semi-quantitative risk assessment involves assigning numbers to qualitative estimates of exposure and the dose-response relationship, in the form of probability ranges, weights or scores, and combining them by addition, multiplication, or other mathematical operation, to arrive at a risk estimate with the objective of achieving a greater level of objectivity compared to a qualitative risk assessment approach.

Sensitivity analysis: A method used to examine the behaviour of a model by measuring the variation in its outputs resulting from changes to its inputs. (CAC, 1999)

Transparent: Characteristics of a process where the rationale, the logic of development, constraints, assumptions, value judgements, decisions, limitations and uncertainties of the expressed determination are fully and systematically stated, documented, and accessible for review. (CAC, 1999)

Uncertainty analysis: A method used to estimate the uncertainty associated with model inputs, assumptions and structure/form. (CAC, 1999)

1. Introduction

1.1 FAO/WHO Series of Guidelines on Microbiological Risk Assessment

The General Agreement on Tariffs and Trade (GATT), was established under the United Nations in 1947 as a series of international meetings at which nations would work together to reduce tariffs and other barriers to eliminate unfair and discriminatory practices in international commerce. In relation to food, the overarching principle was that, for nations to develop, export income from agricultural products was the first step in the economic development of those nations. Completion of the eighth, or 'Uruguay round', of GATT negotiations, in 1994, led to the creation of the World Trade Organization (WTO).

Importantly, the rules and disciplines of the WTO Agreements – the Sanitary and Phytosanitary (SPS) and the Technical Barriers to Trade (TBT) Agreements – are designed to minimise the negative effect on trade of food safety regulations that cannot objectively be justified. What this means is that scientific data and arguments and conclusions based on them, i.e. 'science-based' arguments, are the only basis for restrictions to international trade in foods.

The WTO recommendations specified the need for science-based food safety regulations but, when those rules were introduced, there were no established, internationally accepted, procedures for science-based assessment of microbiological food safety risk. The development of science-based standards was considered the role of Codex. Accordingly, FAO and WHO established the Joint Expert Meetings on Microbiological Risk Assessment (JEMRA[1]) – similar to the already well-established Joint FAO/WHO Expert Committee on Food Additives (JECFA[2]) – to develop the methods and the tools needed to facilitate the WTO ambitions. As part of that process Codex also developed a set of principles and guidelines for the conduct of microbiological food safety risk assessment (CAC, 1999).

In response to the needs of their member countries and Codex, FAO and WHO, through JEMRA, launched a programme of work in the early 2000's with the objective of providing expert advice on risk assessment of microbiological hazards in foods. FAO and WHO undertook development of guideline documents for the hazard characterization (FAO/WHO, 2003), exposure assessment (FAO/WHO, 2008), and risk characterization (FAO/WHO, 2009a) steps of risk assessment. The need for such guidelines was highlighted in the work being undertaken by FAO and WHO on risk assessment of specific commodity-hazard combinations and it was recognized that reliable and consistent estimates of risk in the risk characterization step were critical to risk assessment.

Over the years, since the guidelines were first developed, much experience has been gained in risk assessment. By 2017, FAO and WHO recognized that a single, updated document on risk assessment was needed, including additional guidance on hazard identification. To this end, this FAO/WHO guideline is intended to provide practical guidance and a structured framework for carrying out each of the four components of a microbiological risk assessment described below, whether as part of a full risk assessment, as an accompaniment of other evaluations, or as a stand-alone process.

These guidelines are not intended to be prescriptive, nor do they identify pre-selected compelling options. They provide descriptive guidance on how to conduct a risk assessment, utilizing a variety of tools and techniques. They have been developed in recognition of the fact that reliable estimation of risk combined with appropriate uncertainty analysis is critical for transparent and consistent risk

[1] http://www.fao.org/food/food-safety-quality/scientific-advice/jemra/en/ accessed 6 August 2019
[2] http://www.fao.org/food/food-safety-quality/scientific-advice/jecfa/en/ accessed 6 August 2019

management decision making as well as for effective risk communication within the risk analysis framework.

1.2 Scope and Purpose of these guidelines

This document provides guidance on undertaking risk assessment of all microbial hazards which may adversely affect human health in foods along the food supply chain; included are microbial toxins that result in acute illness and where the dose of the microbial toxin is stoichiometrically related to the level of contamination of the toxigenic organism in the food. This document is also intended to provide practical guidance on a structured framework for carrying out risk assessment of microbiological hazards in foods, focusing on the four components including hazard identification, hazard characterization, exposure assessment and risk characterization. These guidelines therefore represent the best practice at the time of their preparation, and it is hoped that they will help stimulate further developments and disseminate the current knowledge.

The overarching objectives of these guidelines are to help the reader to:

- identify the key issues and features of a microbiological risk;
- recognize the properties of a best-practice risk assessment;
- avoid some common pitfalls of risk assessment; and
- perform risk assessments that are responsive to the needs of risk managers.

1.3 Guiding the reader through this document

The primary audience for this MRA guideline is the global community of scientists and risk assessors, both experienced and inexperienced, in risk assessment, and the risk managers or others responsible for risk decision making and/or communication.

Ideally, the reader would begin with the Report of a Joint FAO/WHO Consultation entitled Principles and guidelines for incorporating microbiological risk assessment in the development of food safety standards, guidelines and related texts (FAO/WHO, 2002a). That report appropriately establishes the purpose of risk assessment as meeting the needs of risk managers. With that report as background the reader would ideally read the current guidelines for risk assessment next.

On some issues, an approach is advocated based on a consensus view of experts to provide guidance on the current science in risk assessment. On other issues, the available options are compared and the decision on the approach appropriate to the situation is left to the analyst. In both of these situations, transparency requires that the approach and the supporting rationale be documented.

1.4 How to begin with risk assessment

Microbial risk assessment can often seem overwhelming to those faced with the task of developing a risk assessment for the first time. There are several books that can be helpful for the beginner or the advanced beginner. Training courses are also available from recognized experts in the field. Finally, and perhaps of greatest value, is to work with an experienced practitioner over an extended period to develop a risk assessment. The list of books and training providers below are not meant to be all-inclusive, nor do they imply endorsement, but they represent a good starting place.

Books

- Haas, Charles N., Joan B. Rose, and Charles P. Gerba. Quantitative Microbial Risk Assessment. 2nd Ed. John Wiley & Sons, 2014.
- Schaffner, Donald W (editor). Microbial Risk Analysis of Foods. ASM Press, 2008.
- Vose, David. Risk analysis: A Quantitative Guide. John Wiley & Sons, 2008.

- WHO/FAO. Food safety risk analysis: A guide for national food safety authorities, 2007.

Training

- Center for Advancing Microbial Risk Assessment http://camra.msu.edu/
- Epiχ Analytics https://www.epixanalytics.com/
- FAO/WHO/ICD basic awareness course on Microbiological risk assessment available at: http://www.fao.org/waicent/faoinfo/food-safety-quality/mra/mra_en/index.html
- Joint Institute for Food Safety and Applied Nutrition https://jifsan.umd.edu/training/risk/registration/catalog
- Risk Sciences International, Inc. https://www.risksciences.com/course/quantitative-food-safety-risk-assessment/

Part 1 General Considerations

2. Risk Assessment in Context

2.1 Risk Analysis Framework

Risk analysis is defined by Codex Alimentarius Commission (CAC) as "a process consisting of three components: risk assessment, risk management and risk communication" (CAC, 2018), with the three components defined as follows:

- Risk Assessment – A scientifically based process consisting of the following steps: (i) hazard identification, (ii) hazard characterization, (iii) exposure assessment, and, (iv) risk characterization
- Risk Management – The process, distinct from risk assessment, of weighing policy alternatives, in consultation with all interested parties, considering risk assessment and other factors relevant for the health protection of consumers and for the promotion of fair-trade practices, and, if needed, selecting appropriate prevention and control options.
- Risk Communication – The interactive exchange of information and opinions throughout the risk analysis process concerning risk, risk-related factors and risk perceptions, among risk assessors, risk managers, consumers, industry, the academic community and other interested parties, including the explanation of risk assessment findings and the basis of risk management decisions.

Risk analysis is used to develop an estimate of the risks to human health, to identify and implement appropriate measures to control the risks, and to communicate with stakeholders about the risks and measures applied. It can be used to support and improve the development of standards, as well as to address food safety issues that result from emerging hazards or breakdowns in food control systems. It provides risk managers with the information and evidence they need for effective decision-making, contributing to better food safety outcomes and improvements in public health. Regardless of the institutional context, the discipline of risk analysis offers a tool that all food safety authorities can use to improve food safety.

2.2 Risk Management

A generic process for carrying out risk management is presented in Figure 1. Such frameworks developed at the international level provide useful templates for countries developing their own risk management systems. In addition, the CAC has developed principles and guidelines for the conduct of microbiological risk management (CAC, 2008).

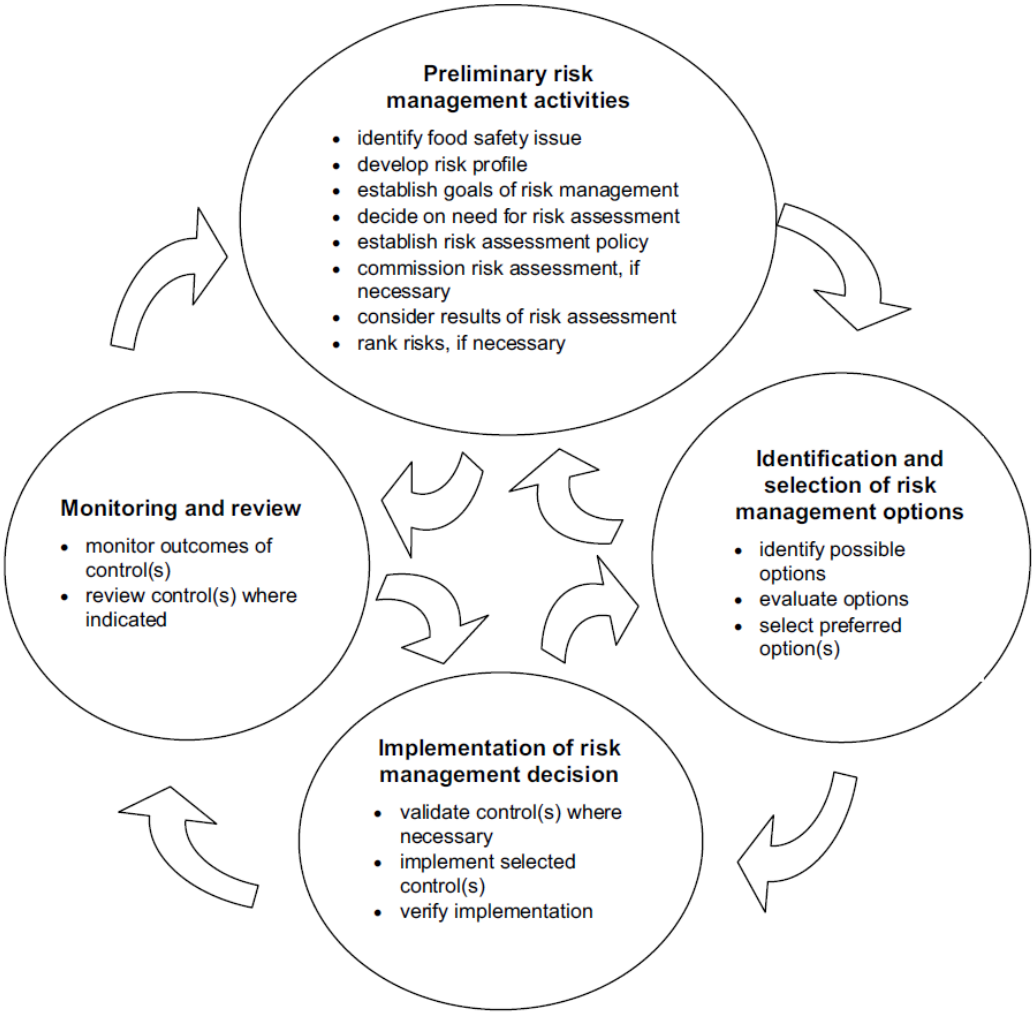


Figure 1: Generic Risk Management Framework (RMF) as presented by FAO/WHO (2006, Figure 2.1)

The first phase of the Risk Management Framework (RMF) shown in Figure 1 consists of "preliminary risk management activities". After a food safety issue has been identified, available scientific information is aggregated into a risk profile that will guide further action.

The second phase of the RMF consists of identifying and evaluating a variety of possible options for managing (e.g. controlling, preventing, reducing, eliminating or in some other manner mitigating) the risk.

The third phase of the RMF refers to the implementation of the selected risk management options by the relevant stakeholders. In many countries, industry has the primary responsibility for implementing regulatory standards or other food safety measures under government or customer oversight. National food safety authorities, or certified 'third party' auditors, must verify implementation of regulatory standards and verify the implementation and effectiveness food safety programs, such as HACCP. In addition, some risk management options may be adopted, such as quality assurance schemes at the farm level, or consumer education packages for food handling in the home that can also contribute to risk reduction. Guidelines on the translation of microbial food safety risk assessment into risk management actions are presented in FAO/WHO (2006b).

Once control measures have been implemented, monitoring and review activities should be carried out (the fourth phase of the RMF). The goal is to determine whether the measures that were

selected and implemented are, in fact, achieving the risk management goals they were meant to achieve, and also whether they are having any other *unintended* effects. Both industry and government bodies are likely to be involved in monitoring and review activities. Both sectors usually monitor levels of hazard control, while government generally carries out surveillance of the level of food-borne illness in the population. If monitoring information indicates a need to review the risk management options, the risk management process can begin a new cycle, with all interested parties participating as appropriate.

When dealing with a given specific food safety issue, the RMF can be entered at any phase and the cyclical process can be repeated as many times as is necessary. Further details can be found in the food safety risk analysis guide published by WHO/FAO (2006).

2.3 Risk Assessment

Risk assessment is a 'decision support' tool. Its purpose is not necessarily to further extend scientific knowledge but to provide risk managers with a rational and objective picture of what is known, or believed to be known, about health risk and its causes at a particular point in time. It is the risk manager's responsibility to consider the risks alongside other decision criteria (sometimes referred to in WTO as "other legitimate factors"), such as nutrition, food security, social & cultural aspects, technical feasibility, cost-vs-benefit, and environmental and economic aspects (FAO, 2017). Nevertheless, risk assessment may also involve judgments and choices that are not entirely scientific, and risk managers need a sound understanding of scientific approaches and assumptions used by risk assessors.

In several frameworks, risk assessment is broken down into a number of stages but, in general, risk assessment is the 'umbrella' term used to describe the complete process of assessing a risk. The Codex guideline CAC/GL-30 (CAC, 1999) defined risk assessment for microbiological hazards in foods as a scientifically based process comprising four components (Figure 2), which are described below and systematically addressed in the various parts of this guidance document. For all components, the sources and magnitude of variability and uncertainty (see Chapter 14) should be described, although the extent to which this can be done will depend on the data available and the risk assessment approach being taken.

- **Hazard Identification** (Chapter 4) is a qualitative process intended to identify microbial hazards of concern in food. Microbial hazards can include infectious agents or toxins produced by microorganisms. For well-documented microbiological hazards, this step is straightforward while more work will be required if the hazard is new or emerging. If a comprehensive risk profile has already been developed, then this step may be very simple. During hazard identification, the associations between microbiological hazards and specific food commodities and certain high-risk groups in the population should be identified.
- **Exposure Assessment** (Chapter 5) is the qualitative and/or quantitative evaluation of the likely intake of a microbial hazard via specific foods with the potential to cause an adverse health effect. It should provide a qualitative and/or quantitative estimate of the likelihood and level of the hazard in a specified consumer portion of that food or a specified volume of water, taking into account all pertinent parts of the food chain and pathways. The exposure assessment may also identify the frequency and amount of food and water consumed in a given period for a given (sub-) population and may combine the information to estimate the population exposure to a microbiological hazard. Often the exposure assessment will detail the various steps of the farm-to-fork pathway so that the influence of individual

steps/processes, or changes to them, can be assessed. This is often very powerful information for assessing risk management options.

- **Hazard Characterization** (Chapter 6) provides a description of the adverse effects that may result from ingestion of a hazard, whether that is a microorganism or its toxin, and articulation of a dose-response relationship where possible. Those health effects include, for example, diarrhoeal illnesses, hospitalizations and deaths, and in the context of MRA are usually considered to be acute, rather than chronic illnesses. This component may include identification of different adverse effects, including sequalae and their likelihood, for different subpopulations, such as neonates or immunocompromised people.
- **Risk Characterization** (Chapter 7) is the integration of the three previous steps to derive a risk estimate, i.e. an estimate of the likelihood and severity of the adverse effects that occur in a given (sub-)population, with associated uncertainties from consumption of a food contaminated with the hazard. It is in the risk characterization step that the results of the risk assessment are presented. These results are provided in the form of risk estimates and/or risk descriptions that provide answers to the questions that the risk managers posed to the risk assessors. These answers, in turn provide the best available science-based evidence to be used by risk managers to assist them in managing food safety risks.

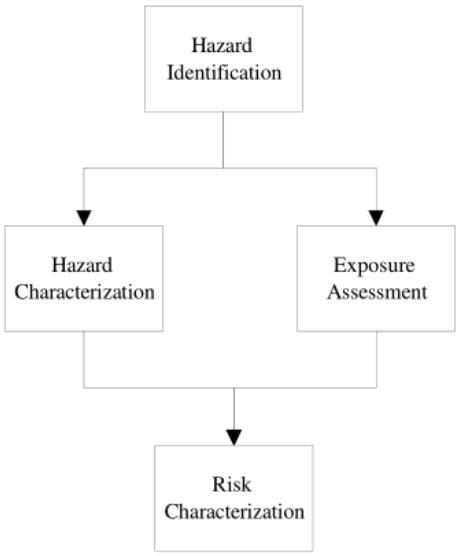


Figure 2: Components of a Risk Assessment

The World Organisation for Animal Health (OIE) has also defined the risk assessment (OIE, 2018). However, as the OIE guidelines focus on risk assessment from the perspective of import and export of aquatic and terrestrial animals the steps are slightly different.

2.4 Risk Communication

The ultimate objective of risk communication is to inform and enhance risk assessment and risk management strategies, inform people who may be involved in risk mitigation, i.e. implementing chosen risk management options, and to enable people who are exposed to the risk to be involved in how they protect their own and others' health from the food safety risk. Risk communication is an integral and ongoing part of the risk analysis process and, ideally, all stakeholder groups should be involved from the start. This means that risk communication is a two-way process which involves understanding and consideration of all stakeholder feedback, perceptions and willingness to accept risk into the risk analysis process and the formulation of the most appropriate risk management strategies. Therefore, a risk communication strategy should be developed early in the risk analysis

process, i.e. prior to commissioning a risk (e.g. Ch 7 in FSANZ, 2013). To assist risk managers in communicating food safety risk information more effectively, FAO has developed a handbook on the subject (FAO/WHO, 2016).

Communication of relevant scientific information to risk managers by risk assessors can be challenging, especially when there is uncertainty about risk-affecting factors and the ultimate risk to consumers. For this reason, the interaction between risk assessors and risk managers should be ongoing throughout the process. Risk assessors and risk managers should discuss and agree on which stakeholders are consulted throughout the process. While risk managers of the competent authority have the ultimate responsibility for risk management, the risk perception of stakeholders, including industry and consumers, as well as their willingness to operationalise risk management options must be understood. In presenting the results of a risk assessment, the following points should be taken into consideration:

- Results should be presented in a transparent, objective manner. They should be in a form that enables people with little mathematical or statistical background to understand the essential aspects of the risk characterization. For example, a 'technical document' with all modelling details could be paired with a less technical 'interpretive summary'. Additionally, the use of illustrations, graphs and tables for presentation of quantitative information from the model will be more informative than giving just parameter estimates or other statistics as numerical risk outputs.
- Numerical estimates should be supported, and communicated, by qualitative information about the nature of the risk and about the weight of evidence that defines and supports it.
- All assumptions, and their consequences for the risk estimates, sources of variation and uncertainty should be fully presented and acknowledged.
- All the information and data used in the MRA should be explicitly described in the report.
- To ensure transparency, all sources of information or data should be given and cited appropriately and unambiguously in the report and detailed in the references list. A copy of any ephemeral information (e.g. from a Web site) should be saved and filed for reference.
- Any identified needs for additional data should be clearly communicated.

3. Food Microbiological Risk Assessment (MRA)

3.1 Properties and principles of best-practice risk assessments

Codex Guidelines CAC/GL-30 (CAC, 1999) for microbiological risk assessment contain a list of general principles of microbiological risk assessment, including that:

- Risk assessment be objective and soundly based on the best available science and presented in a transparent manner;
- Constraints that affect the risk assessment, such as cost, resources or time, be identified and their possible consequences described;
- Microbiological risk assessment should clearly state the purpose, including the form of risk estimate that will be the output;
- The dynamics of microbiological growth, survival, and death in foods and the complexity of the interaction (including sequelae) between human and agent following consumption (as well as the potential for further spread) be specifically considered;
- Data should be such that uncertainty in the risk estimate can be determined;
- Data and data collection systems should, as far as possible, be of sufficient quality and precision that uncertainty in the risk estimate is minimized;
- The risk estimate should include a description of the uncertainty and where that uncertainty arose; and
- MRA should be conducted according to a structured approach that includes Hazard Identification, Hazard Characterization, Exposure Assessment and Risk Characterization.

The scope of the exposure assessment in terms of content and timeframe should be appropriate to meet its objectives and fulfil the needs of the risk managers. As such, before embarking on a risk assessment, the purpose and scope should be clearly identified and articulated by those who commission it.

Risk assessments should be initiated in response to well-defined risk management questions; where possible these questions should target the evaluation of the specific risk management options under consideration. Discussions with risk managers are needed to define what information is required to support the decisions they have to make and the type of work that needs to be undertaken to provide it. Depending on the risk question(s), this may include provision of surveillance data, or epidemiological data, through to a qualitative risk assessment or a quantitative production-to-consumption exposure assessment. Even if a fully quantitative risk assessment is thought to be necessary, it may be useful to commence with a qualitative approach to better define the nature of the work, the feasibility and the time needed to meet the risk manager's requirements. This again highlights the likely iterative nature of risk assessments.

The risk assessment for microbiological hazards should provide risk managers with a 'best estimate' that is as free of bias as is possible, along with discussion or analysis of the uncertainties and variability in the estimate. Bias describes forms of error that lead to consistent over- or underestimation of the true risk. The basis of the 'best estimate', whether the average risk (mean), or the most likely risk (mode), or some other metric, should be clearly communicated, including a description of why that metric is the best measure of risk. If bias (e.g. the decision to use a worst-case estimate) cannot be eliminated, that bias and the reasons for it should be clearly stated.

Risk assessments should represent the 'real world' situation as closely as possible and reflect the full range of possible outcomes (i.e. probabilities and levels of exposure and consequent risk, e.g. through a distribution of risk per serving), unless risk managers express the need for information on

a particular subset of outcomes, such as 'most likely' or 'worst-case' scenarios. It should be noted, however, that deliberately conservative estimates can reduce the usefulness of the estimate for cost-benefit and cost-effectiveness studies and decrease the ability to describe the uncertainty of the risk estimates. They may be useful in certain situations, however, e.g. to better understand the impact of risk mitigations (see also Section).

Specification of uncertainty and variability are critical in terms of correctly understanding and appropriately using the estimate of risk. It is important to identify variability and uncertainty to the greatest extent possible, discuss their implications for the risk estimate(s) and to provide a description of uncertainty and variability as part of the final risk estimate. Uncertainty and variability are discussed in more detail in Chapter 14.

Independence and functional separation of the risk assessment from the risk management process are highly desirable. Nevertheless, interaction between managers and assessors is also essential to ensure that the risk assessment provides the best possible support for the decision(s) that the risk managers have to make, and to ensure that risk managers understand the principles and assumptions underlying the specific risk assessment.

The need for transparency of the risk assessment requires full documentation of the process. This includes transparency in the process, including calls for data and information, scientific peer review and public review, etc. The report should include an explanation of data used, a description of the models used to assess risk, and explanations of any assumptions made, including the effect of those assumptions on the outcome of the risk assessment.

3.2 Purpose and scope of MRA

Risk assessment is commonly undertaken to help risk managers understand which, if any, intervention strategies can best serve the needs of food safety, or if current risk management actions are adequate.

Before beginning a risk assessment, the purpose and scope should be clearly defined, either explicitly or implicitly through the risk management questions. This may involve a discussion between all relevant parties, including the risk managers, risk assessment team, risk communication specialist, and, when appropriate, relevant stakeholders and interested parties. Definition of the purpose and scope usually specifically identifies the population that should be protected (e.g. general population, young children, pregnant women, immunologically compromised), the stages of the food supply chain that are to be included, as well as the metrics of risks best suited for decision-making. The scope may need to be revised during the preparation of the risk assessment if it becomes evident that the original scope cannot be achieved; any change in scope should be discussed and agreed with the risk manager.

If the risk assessment aims to find the best option to reduce a risk, then a statement of purpose should be prepared to identify all potential risk management options to be considered. The questions and the statement of purpose will, to a great extent, guide the choice of the approach to be taken to characterize the risk. Clearly, this should be done prior to commencing the risk assessment so that the relevant data are gathered, synthesized and analysed in a way that most effectively informs the risk manager. However, if the purpose of the risk assessment is not clear initially, inappropriate data and information may be collected and analysed in ways that, while providing insight into some aspects of the risk, do not provide clear answers to inform the risk manager appropriately.

Risk managers initially define the intended use of a risk assessment in their *Preliminary risk management activities* (CAC, 2007). They may need to interact with risk assessors in an iterative fashion, to refine the specific questions to be answered, the scope, focus or outputs of the risk assessment, possibly throughout the conduct of the risk assessment. Risk managers are expected to ask risk assessors to answer a specific questions about potential risk management options, which when answered, provide the managers with the information and analysis they need to support their food safety decisions (FAO, 2017).

One of the more important preliminary risk management activities is the elaboration of a risk profile (CAC, 2008). A risk profile comprises a systematic collection of the information needed to make a risk management decision and whether a full risk assessment is needed, as outlined by the Codex Guidelines CAC/GL-63 (CAC, 2008). Typically, the risk profile would be a short document, although sometimes it is expanded to a preliminary risk assessment, e.g. the approach used in New Zealand (e.g. Lake and Cressey, 2013) and in the Netherlands' CARMA Project (Bogaardt *et al.*, 2004). This may help to determine the structure of the risk assessment, to fine-tune risk management questions, and assess the feasibility of a more comprehensive risk assessment. While the elaboration of a risk profile is the responsibility of the risk manager it may, in reality, be commissioned out to other parties, including risk assessors.

The purpose and scope of risk assessment can vary depending on the risk managers' questions. The following sections contain a discussion of three possible approaches to 'risk assessment'. No 'correct' approach can be recommended or specified: the choice of approach depends on the risk assessment question, the data and resources available, etc. The three approaches, considered as examples, are:

- Estimating a baseline risk
- Comparing risk intervention strategies
- Research-related study or model

3.2.1 *Estimating 'baseline risk'*

A common and practical starting point for a risk assessment is to estimate the existing level of risk, often termed the 'baseline risk', i.e. the level of food safety risk posed without any changes to the current system. This risk estimate is most frequently used as the baseline against which intervention strategies can be evaluated, if desired (Figure 3). Using the current risk level as a baseline has several advantages, among them being that it is the easiest to estimate the effect of changes by estimating the magnitude of the risk after the changed conditions relative to the existing level of risk. This approach implicitly accepts the starting point of any risk management actions as being changes to the current system. For some purposes, a baseline other than the existing level of risk might be used as a point of comparison. For example, the baseline risk could be set as that which would exist under some preferred (e.g. least costly) risk management approach, and the risk under alternative approaches compared with that.

Estimating a baseline risk may not be for the immediate purpose of managing the risk so much as to measure or bound the severity of a food safety problem and hence decide whether the risk merits further management. Whilst in theory it may not be necessary to determine a baseline risk to evaluate intervention strategies, it is nonetheless almost always carried out in practice. Baseline risk does not always need a fully detailed farm-to-fork risk assessment and could instead rely mostly on epidemiological data and knowledge of underreporting rates (see also Section 3.2.2).

3.2.2 *Comparing risk management strategies*

Ideally, agencies with responsibility for safety of foods would consider all possible risk management interventions along the food chain without regard to who has the authority to enact them. This objective has led to the creation of integrated food safety authorities in many nations and regions. For example, Berends *et al.* (1998) considered the likely effects on exposure (i.e. *Salmonella* contamination of pork retail cuts) under different intervention strategies, covering various steps in the farm-to-retail continuum.

A farm-to-table model may be most appropriate for this purpose. In practice, however, the scope of the assessment may be limited to those sections of the food chain within the risk manager's area of authority, but a more comprehensive risk assessment might identify relationships outside that area of authority that would motivate the risk manager to seek the authorisation required to intervene effectively or to request others with authority to take appropriate actions. For some risk questions, analysis of epidemiological data or a model of part of the food chain may be adequate. As discussed elsewhere, some risk assessments may be undertaken to ascertain whether existing food safety regulations and existing intervention strategies are adequate, or most appropriate, and if they require review.

Evaluations of putative risk management actions are often based on comparisons of a baseline risk estimate with a forecast risk that could result from pursuing various alternative strategies (FAO/WHO, 2009b; USFDA, 2005) as shown in Figure 3, sometimes called 'what-if' scenarios. One includes a future with no new intervention (the future status quo), the other a future with a new intervention. Initially, a baseline model (i.e. the 'without intervention' scenario) is constructed and run to give a baseline estimate of risk. Then the model or selected model parameters are changed to determine the probable effect of the putative intervention(s).

The differences between the two risk estimates offer indications of the public health benefits of the proposed intervention(s) and, if possible, could also indicate the costs required to attain them. Combinations of interventions can be investigated in a similar fashion, to determine their joint effect, in an effort to find the optimal strategy. However, risk managers should also consider sub-optimal strategies in the broader context, i.e. taking into account the multi-dimensional nature of risk management (FAO, 2017). In some cases, it is possible to estimate the change in risk without producing an estimate of the baseline risk, but caution must be used in these cases. For example, a risk assessment might determine that it is technically feasible to reduce a particular risk one-hundred-fold, but if this risk was negligible at the start, then reducing it one-hundred-fold may not be a worthwhile course of action.

There are many ways to approach an evaluation of risk management options, including gap analysis, before and after comparison, and with and without comparison (as illustrated in this example). The risk estimates, special studies, economic and environmental analyses, opinion surveys, analysis of the legal implications of proposed actions, and the like will vary from case to case. Not all of these elements are within the domain of risk assessment, but a few generic steps in the process can be identified. These include:

- Describe the existing baseline risk condition, i.e. the current state of the risk, given the intervention strategies already in place.
- Describe the most likely future condition in the absence of a change in risk management intervention, i.e. the 'without' condition. Every option is evaluated against this same 'without' condition, labelled 'Future No Action' below. This future may exhibit an increasing, decreasing, flat or mixed trend.
- Describe the most likely future condition anticipated with a specific risk-management intervention in place, i.e. the 'with' condition. Each intervention has its own unique 'with' condition: in the example below, it is labelled 'Future With Intervention A'.
- Compare 'with' and 'without' conditions for each intervention option.
- Characterize the effects of this comparison: not all effects are equal in size, some are desirable, others are not.

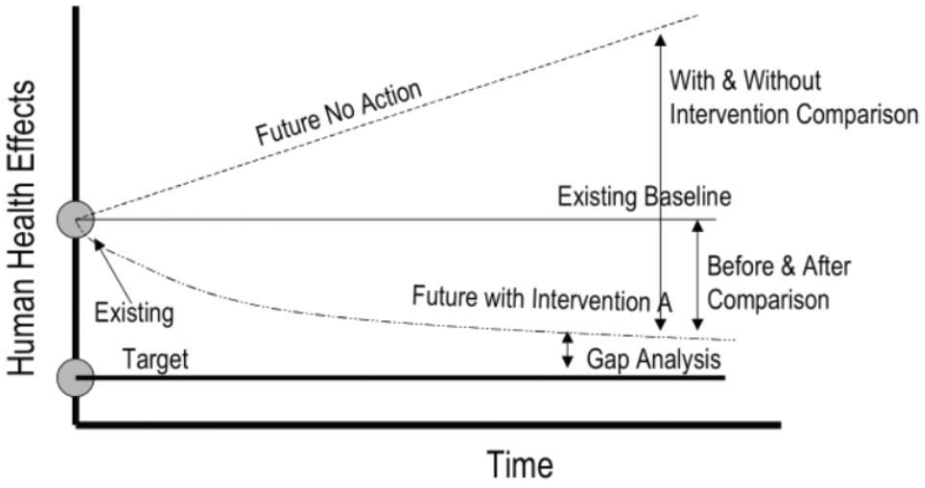


Figure 3: 'With' and 'without' intervention scenarios and changes in risk over time (FAO/WHO, 2009a, Box 2.2).

3.2.3 *Research-related study or model*

Research findings are needed to do good risk assessment. There are a number of large microbiological risk assessment models in existence that have been initiated as academic exercises (Guo *et al.*, 2015; Pang *et al.*, 2017; Van Abel *et al.*, 2017). These models have helped advance the field of microbiological risk assessment by allowing us to see what techniques are necessary, developing new techniques, and stimulating research that can now be seen to have value within a risk assessment context. In some situations, those models have subsequently been used by risk managers to assist in risk management decisions. Such models have also made apparent the changes in collection and reporting methods for microbiological, epidemiological, production, dietary and other data that would make the data more useful for risk assessment.

Risk assessment is also a very useful aid in identifying where gaps in knowledge exist and thus where additional information is needed. A risk assessment may be undertaken specifically or incidentally to identify research needs, to establish research priorities, and to help design commissioned studies. Experience with microbiological risk assessments has proven these assessments to be valuable in aiding the understanding of complex systems. The very process of systematically investigating a food

chain has contributed to the ability to both appreciate and understand the complexity of the systems that make up the food chain.

3.3 The role of best- and worst-case scenarios

It may be useful to evaluate the best- or worst-case scenarios to get a sense of 'how good could it be' or 'how bad could it be' as a filtering technique or as part of a risk profile. The worst-case scenario can be used to filter out whether a risk or an exposure pathway is worth worrying about. No further analysis is necessary if the most pessimistic estimate shows the risk level to be below some threshold of interest (e.g. a negligible-risk level or an acceptable level of risk as defined by a competent authority).

Conversely, a best-case scenario can be used as a preliminary filter of possible risk management options. The risk manager can discount any options for which the most optimistic estimate of the benefits the options could offer does not justify the cost of that option.

Best- and worst-case scenarios operate like extreme 'what-if' scenarios. Where there is considerable but quantified uncertainty about a model parameter, a value is used that gives the required extreme. This will usually be an extreme value from the uncertainty distribution of the parameter, e.g. its 1st or 99th percentile. Where there is uncertainty about exposure pathways and risk attribution, the extreme risk estimate is achieved by picking the most pessimistic (or optimistic) pathway: for example, 'imagine that all *Salmonella* came from chicken'.

Potential problems with worst-case analyses include focusing the analysis on the consequences of the worst case, without the context of the probability of that worst-case scenario occurring, and the difficulty in specifying the conditions that might lead to the worst (or best) case: absolute extremes may be limited only by our imaginations no matter how unlikely. Conversely, when parameter values or exposure pathways are known with considerable certainty, they should be used to avoid exaggerating the extreme scenario beyond what is likely. The concept of *compounding* or *compounded conservatism* is well known in chemical risk assessment. While a detailed explanation of the concept is beyond the scope of this document, the interested reader is directed towards scientific literature (Bogen, 1994; Burmaster and Harris, 1993; Cullen, 1994), including Cassin *et al.* (1996) who specifically discuss the dangers of compounding conservatism in quantitative microbial risk assessment.

3.4 Assessing the results of a risk assessment

When undertaking a risk assessment, the risk assessor needs to consider two basic probability concepts that can affect the outcome. The first is the apparently random nature of the world; the second is the level of uncertainty about how the real world is operating. Together, they limit the ability to predict the future and the consequences of decisions made that may affect the future. Inevitably, a risk assessment will not have included all possible information about a risk issue because of limited data access (for example, time constraints for the collection of data, or unwillingness of data owners to share information) or because the data simply do not exist. Complying with all the requirements of transparency, of describing model and parameter uncertainties, and all the explicit and implicit assumptions, does not necessarily communicate to risk managers the degree of confidence that the risk assessor has in the results of the risk assessment or limitations in its application. Thus, risk assessors must clearly explain the level of reliability, or confidence, they attach to the risk assessment results. The reliability of the results depends on the extent of variability and uncertainty in the model outcomes.

All assumptions should be acknowledged and made explicit in a manner that is meaningful to the risk manager. In particular, it should be explained what the assumption is, why the assumption was made and why it is appropriate, and what the expected effect is if the assumption doesn't hold.

The process of microbiological food safety risk assessment is most affected by uncertainty: uncertainty about what is really happening in the exposure pathways resulting in human illness; uncertainty about processes that lead from ingestion through to infection and illness and that dictate the severity of the illness in different people; and uncertainty about the values of the parameters that would describe those pathways and processes. In general, risk assessments should be as simple as possible whilst meeting the risk manager's needs. The MRA should strive to balance greater detail and complexity (e.g. through addressing more questions or alternative scenarios) against having to include more assumptions that this would entail, because more assumptions increase the uncertainty and decrease the reliability of the conclusions. A draft risk assessment, in which the data gaps and assumptions are clearly identified, may elicit new information, if distributed widely to important stakeholders.

Sometimes what is known at a particular time is insufficient for a risk manager to be comfortable in selecting a risk management option. If the risk manager's criteria for making a particular decision (i.e. the 'decision rule') are well defined, a risk assessment carried out based on current knowledge can often provide guidance as to what, and how much, information would make a decision clearer. Another benefit of the risk assessment methodology is that it provides a basis for rational discussion and evaluation of data and potential solutions to a problem. Thus, it acts to create consensus among stakeholders around risk management strategies or helps to identify where additional data are required.

The purpose of a risk assessment is to help the risk manager make a more informed choice and to make the rationale behind that choice clear to all stakeholders. Thus, in some situations, a very quick and simple risk assessment may be sufficient for a risk manager's needs. For example, imagine the risk manager is considering some change that has no cost associated with it, and a crude analysis demonstrates that the risk under consideration would be 10-90% less likely to occur following implementation of the change, with no secondary risks. For the risk manager, this may be sufficient information to authorize making the change, despite the high level of uncertainty and despite not having determined what the base risk was in the first place. Of course, most risk issues are far more complicated, and require balancing the benefits (usually human health effect avoided) and costs (usually the commitment of available resources to carry out the change, as well as human health effects from any secondary risks) of different intervention strategies. Thus, depending on the specific question posed, an exposure estimate may be enough to allow comparison between different interventions to be made, allowing the risk manager to make an informed decision.

In the process of performing a risk assessment one usually learns which gaps in knowledge are more, and which are less, critical and some of those uncertainties are readily quantified with statistical techniques where data are available, which gives the risk manager the most objective description of uncertainty. If, however, a risk assessment assumes a particular set of pathways and causal relationships that are incorrect, then the assessment will be flawed. This is clearly different from variability and uncertainty (Chapter 14) and should be avoided as much as possible.

3.5 Choosing the type of risk assessment to perform

Risk assessments methods span a continuum from qualitative through semi-quantitative to fully quantitative. These approaches may vary in their key attributes, for example: quality of risk inference, timeliness, complexity, assessor training requirements, and data requirements (note that

783 a scientifically sound risk assessment requires collection of suitable information/data/assumptions
784 which are documented and fully referenced and synthesized in a logical and transparent manner,
785 regardless of where on the methodology continuum the approach sits). All are valid approaches to
786 food safety risk assessment, but the appropriateness of a particular method ultimately depends on
787 the ability of the risk assessment to address the specific risk question and that it is "fit-for-purpose"
788 to support the risk management decision. A benefit of risk assessment as a whole is that solutions to
789 minimize risk often present themselves out of the formal process of modelling risk, whether the risk
790 assessment that has been conducted is qualitative, semiquantitative, quantitative, or a combination
791 with elements spanning the continuum.

792 • **Qualitative Risk Assessment:** Qualitative risk assessments are descriptive or categorical
793 treatments of information. A qualitative assessment may be undertaken as part of a first
794 evaluation of a food safety issue, to determine if the risk is significant enough to warrant a
795 more detailed analysis; this again highlights that risk assessments tend to be, and frequently
796 are, iterative. Nevertheless, a qualitative exposure assessment alone may, in some
797 circumstances, provide all the decision support needed by the risk manager. If a more
798 detailed analysis is warranted, then a fully quantitative assessment is usually the preferred
799 approach if data, time and resources are available to support it.
800 • **Semi-Quantitative risk assessment:** Semi-quantitative risk assessment provides an
801 intermediary level between the textual evaluation of risk that characterises qualitative risk
802 assessment and the numerical evaluation of quantitative risk assessment, by evaluating risks
803 with a score. It offers a more consistent and rigorous approach to assessing and comparing
804 risks and risk management strategies than qualitative risk assessment and avoids some of
805 the ambiguities that a qualitative risk assessment may produce. It does not require the same
806 mathematical skills of quantitative risk assessment, nor does it require the same amount of
807 data, which means it can be applied to risks and strategies where precise data are missing.
808 • **Quantitative risk assessment:** Quantitative risk assessments provide numerical estimates of
809 risk, although most models use combinations of mathematics and logic statements.
810 Quantitative risk assessments require the development of mathematical models in which all
811 relationships between factors affecting exposure can be quantified or explained using logical
812 tests and conditional statements. An exposure estimate may be combined with a
813 mathematical function that quantifies the dose-response relationship to provide an estimate
814 of risk.

815 It should be noted that there is a gradation of model types from qualitative to fully quantitative and
816 while such classifications may be helpful, they are not strictly defined categories.

817 The importance of matching the type of risk assessment to its purpose has been emphasized
818 previously. The USA National Advisory Committee on Microbiological Criteria for Foods noted
819 (USNACMCF, 2004):

820 *"Risk assessments can be quantitative or qualitative in nature, but should be adequate*
821 *to facilitate the selection of risk management options. The decision to undertake a*
822 *quantitative or qualitative risk assessment requires the consideration of multiple factors*
823 *such as the availability and quality of data, the degree of consensus of scientific opinion*
824 *and available resources."*

825 The Australian National Health and Medical Research Council (NHMRC, 2018, p38) cautions that:

"Realistic expectations for hazard identification and risk assessment are important. Rarely will enough knowledge be available to complete a detailed quantitative risk assessment. ... Staff should have a realistic understanding of the limitations of these predictions, and this should also be conveyed to the public."

The decision on the appropriate balance of the continuum of methods from qualitative to quantitative will be based on several factors, including those considered below.

3.5.1 *Consistency*

Risk assessments should limit subjectivity as far as possible and aim for consistency. On the one hand, qualitative and semi-quantitative risk assessment can be made simple enough to be applied repeatedly across a range of risk issues, whereas quantitative risk assessment is more driven by the availability of data and may have to employ quite disparate methods to model different risks. Subjectivity can occur across the spectrum. Qualitative risk assessment is more prone to subjective judgements involved in converting data or experience into categories such as 'high', 'intermediate' and 'low' because it may be difficult to unambiguously define these terms, so repeatability of an analysis by others is less certain. On the other hand, quantitative risk assessments may involve subjective choices regarding model form and data analysis, e.g. in approaches to the selection and analysis of data. In all cases the basis of these judgements can, and should, be documented in a way that enables others to understand the reasoning and replicate the results.

3.5.2 *Resources*

Some basic capacities are needed to conduct MRA or its components. Risk assessments conducted at the international level (e.g. JEMRA) can assist countries by providing modules or building blocks that can be adapted or modified to suit other exposure or risk assessments. For example, FAO/WHO's Food Safety Risk Analysis Tools website[3] contains a risk assessment tool for *Cronobacter* spp. in powdered infant formula and a risk management tool for the control of *Campylobacter* and *Salmonella* spp. in chicken meat, and the US FDA's FDA-iRISK® tool[4] allows sharing of risk assessment models/modules. However, it must be remembered that the risk assessment usually requires also some country- or region-specific data.

The basic capacities needed include:

- **Access to expertise**. While the assessment may be carried out by one individual or a small team, access to a range of other expertise, from multiple disciplines, usually is needed. Depending on the task, this is likely to include trained risk assessors, modellers, mathematicians, statisticians, microbiologists, food technologists, animal and plant health specialists, agriculture technologists, human and veterinary epidemiologists, public health specialists, and other experts as needed. Quantitative risk assessments typically require that at least part of the assessment team have rigorous mathematical training. If this resource is in limited supply, then this may make qualitative risk assessment more practical, provided the risk question is amenable to this approach. Note that, though qualitative risk assessments may not be demanding in terms of pure mathematical ability, they place a considerable burden of judgement on the analyst to combine evidence in an appropriate and logical manner, and the technical capability necessary to collate and interpret the current scientific knowledge is almost the same.

[3] www.fstools.org accessed 20 June 2019
[4] irisk.foodrisk.org accessed 20 June 2019

- **Informed risk managers and policymakers** who are aware of the need for, use of and limitations of risk assessment, working in the context of an appropriate risk management framework, whether in government or industry. This framework must facilitate data collection, decision-making and implementation.
- **Financial and human resources** to complete the risk assessment in a timely manner and to an acceptable level that provides useful support for risk management decisions. For very large MRA projects, a dedicated project manager may be desirable.
- **Communication channels**. Good communication is needed between technical experts, risk managers and the risk assessors to facilitate efficient exchange of data and knowledge.
- **Information technology**. Computing facilities, both hardware and software and access to appropriate information networks are needed, to collect, collate and process data, and to provide outputs in a form suitable for communication of results. This should include access to international networks and databases, including access to scientific publications.
- Where data on microbiological hazards are not available, **the capacity to conduct surveillance for microbiological hazards**, including access to microbiologists, epidemiologists, trained field staff and competent laboratories, is needed.

While the above list is an ideal, benefits can also be obtained from conducting more modest risk assessments, but still according to the principles in these Guidelines, even from teams with limited expertise. To assist groups with fewer resources, communication (e.g. including training, mentoring and technology transfer) with more established groups should be actively encouraged.

With respect to scientific publications, access to subscription-based journals has repeatedly been identified as a substantial limitation in many developing countries. It is worthwhile to note that Research4Life (www.research4life.org) provides developing countries with free or low-cost access to academic and professional peer-reviewed content online. To assist the risk assessors with their tasks, a range of software tools have been developed, including those listed by Bassett *et al.* (2012) and those at the QMRA Wiki.[5] These tools are not necessarily specific to food safety risk assessments, although a range of food safety specific models and tools are also identified, covering areas of risk ranking, predictive microbiology, specific risk assessment and sampling tools. The idea and application of predictive microbiology in exposure assessment described in Section 12.2, with examples of the necessary fine detail given in Section 12.2.

3.5.3 *Theory or data limitations*

Quantitative risk assessments tend to be better suited for situations where mathematical models are available to describe phenomena, e.g. Dose-Response models, and where data are available to estimate the model parameters. If either the theory or data are lacking, then a more qualitative risk assessment is appropriate.

3.5.4 *Breadth of application*

When considering risks across a spectrum of hazards and pathways, there may be problems in applying quantitative risk assessment consistently across a diverse base of theory and evidence, such as comparing microbiological and chemical hazards in food. The methodologies and measurement approaches may not yet be able to provide commensurate risk measurements for decision-support where scope is broad.

[5] http://qmrawiki.canr.msu.edu/index.php accessed 18 June 2019

3.5.5 *Speed*

Qualitative and semi-quantitative risk assessments generally require much less time to generate conclusions compared with quantitative risk assessment. This is particularly true when the protocols for qualitative and semi-quantitative risk assessments have been firmly established with clear guidance in the interpretation of evidence. There may be some exceptions where the process of qualitative risk assessment relies on a process of consultation (e.g. when relying heavily on structured expert elicitation) that requires considerable planning, briefing, and scheduling. Quantitative risk assessment may take longer to develop; if it is to be repeated once the model is established, then the speed to generate conclusions is similar to qualitative or semi-quantitative approaches.

3.5.6 *Transparency*

Transparency, in the sense that every piece of evidence and its exact effect on the assessment process is made explicit, is more easily achieved by quantitative risk assessment. However, accessibility, where a large audience of interested parties can understand the assessment process, may be better achieved through qualitative or semi-quantitative risk assessment. Quantitative microbiological risk assessment often involves specialized knowledge and a considerable time investment. As such, the analysis may only be accessible to specialists or those with the time and resources to engage them. Strict transparency is of limited benefit where interested parties are not able, or find it excessively burdensome, to understand, scrutinize and contribute to the analysis and interpretation, and errors in quantitative risk assessments may also be more difficult to find. Qualitative or semi-quantitative approaches may be easier to understand by a larger range of stakeholders, who will then be better able to contribute to the risk analysis process.

3.5.7 *Stage of analysis*

Qualitative and quantitative risk assessment need not be mutually exclusive. Qualitative risk assessment is very useful in an initial phase of risk management to provide timely information regarding the approximate level of risk and to decide on the scope and level of resources to apply to quantitative risk assessment. As an example, qualitative risk assessment may be used to decide which exposure pathways (e.g. air, food, water; or raw versus ready-to-eat foods) will be the subject of a quantitative risk assessment.

Where available, comparing the outputs from both approaches, or from different stages of the analysis, may help the detection of errors that may have been made in either assessment.

3.5.8 *Responsiveness*

A major concern often expressed in regulatory situations is the lack of responsiveness of risk assessment conclusions when faced with new evidence. Consider a situation where a risk assessment has been carried out with older data indicating that the prevalence of a pathogen is 10%. After the risk assessment is published, it is found that the prevalence has been reduced to 1%. In most quantitative risk assessments, there would be a clear effect of the reduced prevalence on the risk characterization. In some qualitative risk assessments, this effect may not be sufficiently clear. Qualitative risk assessments, particularly where the link between evidence and conclusion is ambiguous, may contribute to foster or support this lack of responsiveness. The unresponsiveness can generate mistrust and concern for the integrity of the risk assessment process.

4. Hazard Identification

Hazard identification (HI) is conventionally the first step in risk assessment. For the purposes of the Codex guideline , hazard identification related to food safety is defined as "the identification of biological, chemical and physical agents capable of causing adverse health effects and which may be present in a particular food or group of foods" (CAC, 1999). In particular, for microbiological agents "the purpose of hazard identification is to identify the microorganisms or the microbial toxins of concern with food" (CAC, 1999). In general, hazard identification is largely a qualitative examination of the foodborne hazard and associated potential adverse health outcomes due to specific foodborne exposure, which is supported by a critical review of knowledge about the hazards and/or food in question. In the context of MRA, the term *hazard* encompasses any microbiological agent able to cause harm, including bacteria, viruses, parasites, fungi, algae, including their toxins and metabolites, as well as prions.

4.1 Objectives of hazard identification

The main purpose of hazard identification is to identify the microbiological hazard(s) found in food that is/are the cause of specific adverse health outcomes. Since a wide range of microbiological hazards can cause food-borne illness, hazard identification should identify whether a potential hazard is realistic for the food product of interest. In some situations, i.e. depending on the risk managers' questions, the hazard characterization may include a list of hazards and therefore, the final product of the hazard identification procedure is a practical list of microbiological hazards related to the specific food product (e.g. FAO/WHO, 2006a, 2007).

4.2 The process of hazard identification

Essentially, the hazard identification serves to establish the hazard as likely or real in the food product and to document the important information known about the relationships and interactions between the hazard, the food (including intrinsic characteristics, environmental factors and production conditions) and host, as well as their relationship to human illness (Figure 4). There is some overlap between the information collated as part of the hazard identification step and the exposure assessment and hazard characterization steps – the hazard identification may provide only a general overview, while the latter steps document the detailed information, e.g. extent of exposure to the hazard and dose-response relationship. The information is documented to address general questions as part of microbiological hazard identification, including:

- What is/are the hazard(s) of concern associated with specific food in question?
- Is the hazard of concern to public health and what is the likelihood of the hazard causing an adverse health effect?
- What is the population at risk?
- What is the epidemiological evidence, including outbreaks and sporadic illness, that this hazard poses a potential risk in the food product of concern?
- What adverse health effects could be associated with the exposure to the hazard and through what mechanisms?
- What host factors and life stages could potentially influence the sensitivity and the type and severity of adverse health outcomes among population at risk?
- How do common exposure pathways link the adverse health effects with the hazard?
- How often does the hazard occur in the food product of interest?
- How do environmental conditions affect the hazard's transfer and fate along the exposure pathway?

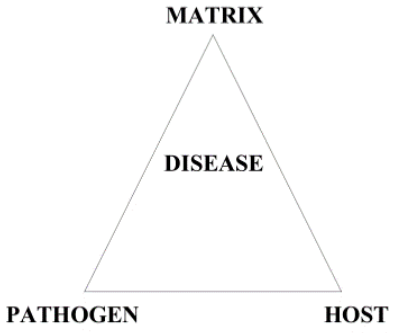


Figure 4: The epidemiology triangle (modified from Coleman and Marks, 1998).

A wide range of microbiological hazards are associated with food-borne illness. To identify the most significant hazards in the food of concern, characteristics of a range of hazards can be collectively evaluated, including inherent properties of hazards such as invasiveness, virulence, pathogenicity, natural reservoir, transmissibility and resistance to environment factors and interventions as part of the food supply chain.

In addition, hazard identification highlights issues such as sensitive populations, acute versus chronic disease and other complications such as long-term sequelae for later detailed consideration in the hazard characterization (Chapter 6). Sensitivity to infection depends on the integrity of the hosts' immune system, the virulence/potency of the hazard and exposure levels of the hazard. The integrity of hosts' immune system can be influenced by life stage and health conditions. For example, young children and the elderly may be more sensitive to microbiological infection compared to young healthy adults due to their immature or compromised immune systems, leading to more serious and longer-lasting health outcomes. The exposure level of and ability of a hazard to elicit an adverse health effect at the time of consumption can be cumulatively affected by a series of environmental conditions throughout the food chain. The physical and chemical property of the food matrix may influence the hazards' survival and persistence and these, together with growth, inactivation and survival characteristics of the hazard can be elaborated in the exposure assessment (Chapter 5). For example, the presence of fat component of chocolate protects *Salmonella* against thermal inactivation. The transmission and fate of a hazard may be influenced by the complex interaction between the hazard and various intermediate vectors. For example, bacterial pathogens from food-producing animals may reach the human population directly through the consumption of contaminated animal foods or indirectly through the consumption of crop products contaminated due to the land application of animal wastes.

Sometimes evidence clearly identifies the significance of foodborne transmission for specific microbiological hazards and which foods are implicated before a microbiological risk assessment is conducted. In this situation, less effort can be expected in the investigation of the causal relationship between the occurrence of adverse health outcomes and the exposure to the foodborne hazard. Conversely, emerging hazards are continually being identified through the mechanism of acquiring new traits. Through vertical or horizontal transfer of genetic traits among microorganisms, newer pathogenic or opportunistic strains can be consistently produced, which could result in new microbiological hazards with higher virulence and/or persistence to various environmental conditions. In this situation, when a particular food is suspected, more thorough investigation is needed to indicate whether the hazard is likely associated with the food product of interest.

4.3 Data sources for hazard identification

A large amount of relevant evidence-based information needs to be collected, appraised and interpreted in hazard identification. The main types of data sources providing useful information to the hazard identification process are as discussed in Chapter 10.

Epidemiologic data from disease monitoring programs, or investigations of foodborne outbreaks are often the first well documented indication of a food safety problem with adverse effects associated with a pathogen. Food contamination surveillance data, together with product/process evaluations can aid the identification of hazard-food combinations. Evidence from these sources is usually quantitative (i.e. includes information about the concentration or number of units of the hazard in the food), which may also provide information, particularly feeding into other steps of microbiological risk assessment such as exposure assessment and/or the establishment of dose-response relationship. Whole genome sequencing (WGS) is being used increasingly for foodborne pathogen surveillance, outbreak investigation and contamination source tracking throughout food supply chains (Rantsiou *et al.*, 2018, WHO, 2018). Clinical research usually provides qualitative data, highlighting the mode of action with which the hazard affects the host, such as through the action of toxins, either in the food or, alternatively, through infectious mechanisms. Inferences from microbiological and clinical studies can be used to support the epidemiological and observational evidence. More details regarding the strength and limitation of different data sources can be found in Chapter 10.

5. Exposure Assessment

5.1 The Process of Exposure Assessment

Codex defines exposure assessment as "the qualitative and/or quantitative evaluation of the likely intake of biological, chemical, and physical agents via food as well as exposures from other sources if relevant." (CAC, 1999). Consequently, exposure assessments are often specific to the production, processing and consumption patterns within a country or region.

Exposure assessment may be undertaken as part of a risk assessment, or it can be a stand-alone process, such as when there are not enough data or information available to undertake a dose-response assessment (i.e. a Hazard Characterization) or when the risk management question only involves quantifying or seeking ways to minimize exposure. The process of exposure assessment can be, and usually is, iterative. Discussions between risk managers and risk assessors may lead to a refinement of the initial question or problem statement to be addressed in the risk assessment, or consultation with other parties may result in the availability of new information, that can in turn lead to revision of assumptions or to further analysis. Also, non-governmental bodies such as food industry may use exposure assessment as a stand-alone process or as part of an MRA approach to assess the safety of their food products, specifically as part of food innovation research and before putting products on market (van Gerwen and Gorris, 2004; Membré and Boué, 2018; Pujol *et al.*, 2013).

The goal of an exposure assessment may be to provide an estimate of the level of exposure to a hazard in a given population but may also be limited to evaluation of one or a few processing steps. The risk manager may also wish to limit the scope to specific regions, or populations, or periods of time. This again reinforces the need for the risk managers to clearly articulate their needs to the assessors, including the level of detail required in the exposure assessment, and any constraints that would limit the range of management options. For example, when a comparison of potential mitigations is requested, the managers should provide an indication of the measures they would consider or have available for the reduction of exposure from a particular source, as well as any other sources, that would not be acceptable under any circumstances.

Once there is a clear understanding of the requirements of the exposure assessment in relation to risk management, the next step is to consider the factors that have a direct effect on consumer exposure to the hazard. These including frequency of consumption of the product or commodity; pathway and frequency and levels of contamination with the hazard; the range of doses; and factors that affect it (potential for microbial growth, inactivation during cooking (or other processes), meal size, seasonal and regional influences, etc.).

In addition, the exposure assessment should describe the relevant pathways of exposure. Scenarios can be constructed to predict the range of possible exposures. For example, if the purpose of the risk assessment is to identify and compare different mitigation strategies to be used from production to consumption, then the entire production-to-consumption pathway has to be addressed (Figure 5). In other cases, only the pathways from retail to consumers may be relevant, thus if the purpose of the exposure assessment were to reach a decision on the maximum tolerable level of a pathogen in a ready-to-eat product at the point of sale, the exposure assessment would be used to determine the potential for further increase or decrease in exposure due to normal consumer handling, such as time and temperature of storage, effect of cooking or other food preparation steps, potential for cross-contamination in the home, etc.

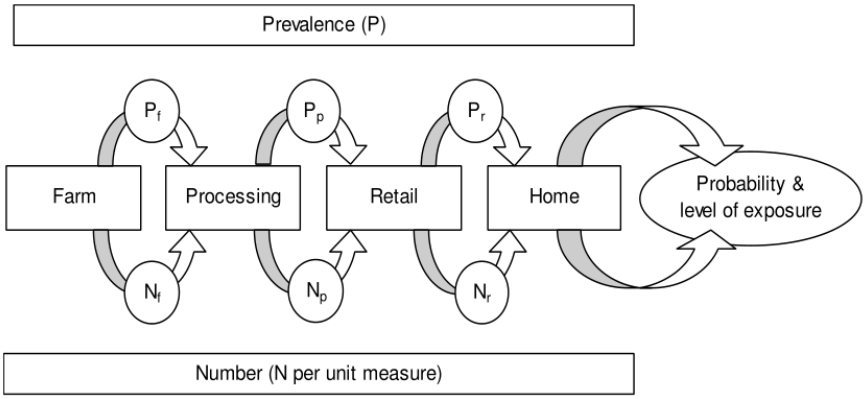


Figure 5: An example of an overview of the conceptual model to describe the exposure pathway for a production-to-consumption exposure assessment. To assess exposure, it is necessary to consider both the probability that a unit of food is contaminated with the hazard (denoted P, for 'prevalence'), and the level, or number, of that hazard in the food (denoted N) at the time of consumption. For microbial hazards, in particular, both prevalence and number can change as the commodity is further processed, and as time elapses before the product is finally consumed.

The level of detail required in the different pathways reflects the question asked and the information needed by the risk managers and may be modified based on the information available. If it has been shown, for instance, that the prevalence and/or numbers of a specific pathogen differs within a specific commodity according to the type of abattoir, type of processing, type of storage at retail, etc., such information might influence the level of detail required and the selection of pathways in the exposure assessment. Food supply pathways can be multiple and complex, for example, 'ready-to-eat' meals are a synthesis of food components (e.g. meat, vegetable and dressing) that arise from different pathways.

Risk managers may have specific questions concerning specific processes, such as organic farming, logistic slaughtering, i.e. order in which animals are slaughtered (e.g. Nauta *et al.*, 2009), or imported foods (e.g. Skjerve, 1999) that they want to be addressed. Accordingly, these specific interests would need to be taken into account in selecting the pathways to be considered or modelled and the types of data to be included.

5.2 Modelling Approaches

5.2.1 *Introduction*

The goal of exposure assessment is to deduce, from the available information, the probability and magnitude of exposure to the hazard. Detailed exposure data, characterizing the extent of microbiological hazards present in foods at the time of consumption, are usually not available. Thus, exposure assessment will often rely on a model, encompassing knowledge of the factors and their interactions that affect the number and distribution of the hazard in foods, to estimate exposure at consumption. This chapter is primarily concerned with development and application of models used as part of the exposure assessment. General data needs and sources are considered in greater detail in Chapter 10.

A model can be defined as 'the description of a system, theory, or phenomenon that accounts for its known or inferred properties and may be used for further study of its characteristics' (McMeekin *et al.*, 2008). Often the model is a simplified description of some more complex system or phenomenon. Models are also used to communicate an understanding, or hypothesis, concerning some aspect of reality that may or may not be able to be directly observed. Thus, another description is that a model is 'a hypothesis or system of beliefs about how a system works or

responds to changes in its inputs' (Cullen and Frey, 1999). That hypothesis or description can be expressed in words or 'as a system of postulates, data, and inferences presented as a mathematical description of that entity or state of affairs'.[6] When developing a model – whether it is a full risk assessment or any part thereof – it is important to ensure that the model is fit-for-purpose. As a result, a model should be as simple as possible, but as complex as necessary.[7]

Among the benefits of a model is that it can be used to predict the outcome of events that have not occurred, or have not been observed, e.g. the probability of infection from low doses. However, a fundamental rule of modelling is that no possibility should be modelled that could not actually occur (Vose, 2008). In the context of exposure assessment, the models synthesize data and knowledge from other observations about the pathways of exposure, the behaviour of microbial hazards in foods, patterns of consumption, and so on, to infer what would, or could, happen in other circumstances of interest. Models can be used to interpolate among discrete values of observed data and, in some circumstances, to extrapolate beyond the range of observations. In either case, the validity of the interpolation or extrapolation depends on validation of the model (see Sections 16.2).

There is a spectrum of approaches available for exposure assessment, ranging from qualitative to fully quantitative in nature. Quantitative exposure assessments may, in turn, be deterministic or stochastic, with the later encompassing and representing variability and uncertainty in the data and knowledge as fully as possible (see Chapter 14).

Although qualitative exposure assessments lack numerical precision, they are still valuable and may, in some circumstances, provide all the decision support needed by the risk manager. Also, as an example, a qualitative assessment may be undertaken as part of a Risk Profile, to determine if the risk is significant enough to warrant a more detailed analysis. This again highlights that risk assessments tend to be, and frequently are, iterative. If a more detailed analysis is needed to answer the risk question and to provide the needed decision support for the risk manager, then a fully quantitative assessment is usually the preferred approach if data, time and resources are available to support it.

5.2.2 *Qualitative and semi-quantitative exposure assessment*

A qualitative assessment may be developed by assigning descriptive ratings of probability and severity such as 'negligible', 'low', 'medium' or 'high' to the exposure factors (ACMSF, 2012; Fazil, 2005).

As noted in Section 3.5, semi-quantitative exposure assessment provides an intermediary level between qualitative and quantitative exposure assessment. It does not require the same mathematical rigor as quantitative exposure assessment, nor does it require the same amount of data, which means it can be applied to exposure and exposure minimisation strategies where precise data are missing. See also Sections 9.1 and 9.2 for more detailed discussion of these qualitative and semi-quantitative risk assessment approaches. Examples of semi-quantitative risk assessment approaches, including for exposure assessment, being used to make risk management decisions (Cardoen *et al.*, 2009; Hald *et al.*, 2006; Omurtag *et al.*, 2013; Sumner and Ross, 2002).

[6] https://www.merriam-webster.com/dictionary/model accessed 26 Nov 2018

[7] A rephrasing of Einstein's principle "A scientific theory should be as simple as possible, but no simpler."

5.2.3 *Quantitative exposure assessment*

As noted above, quantitative exposure assessments provide numerical estimates of exposure. They require models to be developed, in which all relationships between factors affecting exposure are described mathematically.

As well as mechanistic or empirical, quantitative models can be divided into two categories (Bassett *et al.*, 2012):

1. *Deterministic*, sometimes also referred to as 'fixed-value' or 'point-estimate' and which in some situations can be solved analytically, and
2. *Stochastic*, sometimes also referred to as 'probabilistic'. In some limited circumstance, these models may be able to be evaluated analytically, though most are more likely to need to be evaluated using 'Monte Carlo simulation', requiring computers and software.

In a mathematical model, 'input' variables are those that determine the type and magnitude of the response, or 'output', variables. The output variables in exposure assessment are the frequency and magnitude of exposure of consumers to the microbiological hazard in the food of interest. Depending on how much of the food supply chain is included in the exposure assessment, input variables could include factors such as time, temperature, production volume and dilution during processing (see data sources in Chapter 10). If a modular process framework is utilised for the exposure assessment (e.g. Figure 5), then outputs from one module are the inputs for the next module. 'Parameters' quantify the input variables and can be fixed values or distributions. For example, while bacterial growth may be proportional to temperature, a mathematical model is needed to relate growth rate and temperature (see Chapter 11). The parameters of that model could be fixed for a specific strain of a hazard but will differ between species and perhaps even for different strains of the same species. In the latter situation the between-strain variability in growth rates, as a function of temperature, could be described by a distribution.

Stepwise approach to quantitative risk assessment

As described above, exposure assessments often involve description of very complex systems, where each variable may not contribute equally to exposure and where not all the desired data may be available. In the context of MRA, van Gerwen *et al.* (2000) suggested that, under such conditions, it could be beneficial to conduct an exposure assessment in a series of stages of increasing complexity/sophistication. Similar approaches have been suggested by the US EPA (2006) and Cullen and Frey (1999) and may be particularly useful when there is an urgent need for an estimate of exposure or risk. A rough estimate is first made of the order of magnitude that individual factors or parameters may contribute to exposure or consequent risk. This could be considered as part of a risk profile. For those factors that contribute most significantly, a more detailed assessment is performed, or more data are gathered and combined in, for instance, a deterministic approach. Where relevant, an even higher level of detail can be achieved using a stochastic approach. Van Gerwen *et al.* (2000) propose that, when using a stepwise approach, both efforts and resources are focused where they add most to reducing uncertainty in the exposure estimate.

5.2.4 *Modelling the production-to-consumption pathway*

Introduction

As noted above, the methods by which exposure is estimated depends on the combination of risk management questions being addressed and the amount of data and other resources available, such as expertise and time. An exposure assessment that considers the events from agricultural

production through to consumption will demand the most time and resources. Such an exhaustive approach may be appropriate if:

- the risk management questions require consideration of all stages, e.g. the effectiveness or feasibility of mitigation at the farm, estimates of exposure in final product as consumed, and
- there are sufficient data, knowledge, time and expertise to enable consideration of each stage.

A generic full production-to-consumption pathway is outlined in Figure 5. Various approaches for modelling of this pathway are outlined below. It is important to emphasise that the final approach utilized depends on the risk management questions being addressed and is therefore assessment-specific, thus the following should be viewed as guidelines, or examples, rather than as being prescriptive.

Model development

'Conceptual model' is a term used to describe the understanding of the routes by which the population of interest is exposed to the hazard of concern, including all the factors and their interactions that affect the probability and level of exposure. The conceptual model may be expressed in text, diagrams, as a mathematical model or a combination of these. There is no preferred method to develop and describe the conceptual model. Rather, whatever form the conceptual model takes, it should adhere to the principles and guidelines for the conduct of microbiological risk assessment (CAC, 1999). For the purposes of communication of the conceptual model to non-mathematicians, a diagrammatic representation may be useful and more readily understood than a text-only description, or the mathematical model alone.

Different approaches can be used to develop the conceptual model. The *Event Tree* approach describes a scenario from a contamination event to a defined end-point of the assessment (Roberts, Ahl and McDowell, 1995), e.g. consumption. This approach serves to describe or identify the most likely pathways that lead to contamination and subsequent disease and may identify variables in need of further data or modelling. Conversely, the *Fault Tree* approach begins with the occurrence of a hazard and from there describes the events that must have occurred for the hazard to be present (Roberts, Ahl and McDowell, 1995). This approach can provide a framework to analyse the likelihood of an event by determining the complete set of underlying conditions or events that would allow the given event to occur (Jaykus, 1996).

Additional approaches to modelling used in assessments of microbial food hazards include the *Dynamic Flow Tree* model (Marks *et al.*, 1998) and the *Process Risk Model* (PRM) (Cassin, Paoli and Lammerding, 1998). The former emphasizes the dynamic nature of bacterial growth and incorporates predictive microbiology using statistical analysis of data, whereas the latter focuses on the integration of predictive microbiology and scenario analysis to provide an assessment of the hygienic characteristics of a manufacturing process.

A general framework is the *Modular Process Risk Model* (MPRM) (Nauta, 2001, 2008; Nauta *et al.*, 2001), which can be thought of as an extension of the PRM approach (Cassin, Paoli and Lammerding, 1998). The fundamental assumption of the MPRM approach is that at each of the steps or key activities in the various intermediary stages from production to consumption, at least one of several processes can be assigned. These processes can be divided into microbial and product handling processes. The microbial processes include growth and inactivation, and the food and product handling processes include mixing of units, partitioning of units, removal of parts of units and cross-contamination of organisms among units. The transmission of infection among live animals during

primary production could be viewed as an additional biological process, which provides the starting estimates of prevalence in a full production-to-consumption model.

When developing mathematical models, the model structure can facilitate or hinder probabilistic (stochastic) analysis and sensitivity analysis. It is recommended that the models should be formulated such that independent variables affecting exposure are clearly specified and in such a way that paired data for each iteration of the model can be stored for all inputs and outputs for which sensitivity analysis is required. Depending on the modelling approach selected, a one-to-one relationship may not be possible when partitioning or combining of units is included (e.g. Kiermeier, Jenson and Sumner, 2014).

The definition of 'unit' is crucial when modelling the processes from production to consumption. A unit is defined as a physically separated quantity of product in the process, for example an animal, a (part of a) carcass, or a package of ground beef, a milk tank or a bottle of milk. It may be that one unit from primary production is also the consumer package (e.g. an egg or whole chicken), but most examples are more complex, e.g. beef carcass transformed to ground beef burger. In this case, units have to be redefined at each partitioning or mixing stage. Both the number of organisms (N) and the prevalence (P) (see Figure 5) should be treated as uncertain and variable throughout the model. This makes it possible to assess the uncertainty and variability in the final exposure, and thus the uncertainty in the final risk estimate.

It should also be noted that prevalence and concentration are related. If the (mean) concentration of the pathogen in a batch of food were low (e.g. 1 cell per 5 kg) the prevalence of contamination will depend on the size of the unit of food. If the unit size were 100 g, then it would be expected that one in 50 units would contain a pathogen, i.e. the prevalence would be 2%. But if the unit size were 500 g, then it would be expected that one unit in 10, on average, would contain a pathogen, i.e. the prevalence would be 10%. If the unit size were 5 kg, then it would be expected that the prevalence would be 100%. However, in practice, because the cells would not be expected to be perfectly evenly distributed, the prevalence would be less than 100%, because some units would contain more than one cell and, consequently, some others would contain none. It is possible to estimate the concentration in a batch from the prevalence and size of positive samples, provided that not all samples of that size are 'positive', and this approach based on the same statistical principles as the 'most probable number' technique used in microbiology (Cochran, 1950). For a good exploration of the distribution of microbes in food (Bassett *et al.*, 2010).

Approaches to mathematical modelling of microbial growth and inactivation and their application are outlined in Sections 12.1 and 12.2. It is difficult to suggest a general model framework for cross-contamination but useful discussion of this topic can be found in Schaffner (2003, 2004).

As noted above, different modelling approaches have been proposed and used. The approach used therefore depends on the perspective of the assessor and on the problem being modelled, as indicated by the risk question. Discussion of modelling strategies for the stages from production to consumption is presented below; which stages to include will depend on the scope and purpose of the risk assessment.

Primary production (farm)

The main focus of the primary production or "farm" stage of the exposure assessment is to estimate the prevalence and concentration of the microbiological hazard in the population or crop or product of interest; the same approach applies for wild capture or harvest situations. For example, this might be prevalence and contamination levels per live cow, per bird, per homestead, per kg of lettuce

leaves, per apple or per vat of raw milk. Within the model for animal products, it is important to differentiate infection and colonization from contamination of skin surfaces. These may of course be dependent on each other, such as where excretion by infected or colonized animals may result in contamination of that animal as well as any other animals in the group.

Recognizing and incorporating dependencies between variables in a risk assessment model is an important aspect of constructing robust and logical models. This is particularly important when constructing stochastic models in which the variables in the model are described as a distributions of possible values, because the values are selected randomly from each variable's distribution. Thus, it is can occur that impossible outcomes can be modelled if a value is selected from one distribution that could never occur with a value selected for another variable. Such model iterations can greatly distort the results of stochastic models, unless the dependencies between variables are explicitly recognised and included in the modelling. These issues are further exemplified in Section 12.2.

The level of detail required in the farm model depends on the risk questions being addressed and specifically if on-farm control is of relevance or possible. This detail will relate to whether or not transmission of infection or contamination is included. The model of Hartnett *et al.* (2001), for example, considers transmission on farm while the models of Cassin *et al.* (1998) and USDA/FSIS (2001) do not. Similarly, FAO/WHO (2009c, 2009d) concerning the risk to human health from *Campylobacter* in broiler chickens included on-farm modelling of infection and transmission from fomites, contaminated water, other birds, etc. Conversely, FAO/WHO (2002a) were unable to usefully model pathways of transmission of *Salmonella* on farms.

It must be remembered that animals or plants harvested for food may become contaminated/ infected from many sources including irrigation/drinking water, contaminated feed, vermin and feral animals, bird faeces, etc. or from the water itself in the case of fish and especially shellfish.

Transport to processing plants

Transport from primary production to processing can also be included in the exposure assessment, because cross-contamination of primary production units can occur, or infection can spread between units in close proximity, and can cause an increase in overall microbial load. Stress during transport of animals can lead to increased faecal shedding and dissemination of pathogens to uninfected animals. Microbial loads on produce can also increase due to microbial growth during transport (Arthur *et al.*, 2007; FSIS, 2001).

Processing

The stages in processing need to be defined before a model can be constructed to describe the changes in prevalence (see also comments above about the interplay between prevalence, sample size and contamination level) and in the numbers of organism. There can be many stages in food processing though not all will necessarily have a strong influence on the ultimate risk to human health. Cassin *et al.* (1998), for example, identified 36 distinct processing operations during the slaughter of beef cattle. It is unlikely that all these stages will be followed by all processors, and an added difficulty is elaborating processing scenarios that are both representative of the majority of processors, yet take into account differences between processors. Flow diagrams developed for HACCP systems can be a useful source of information on process steps and conditions.

Modelling of processing involves:

- Considering the way in which the unit size changes from stage to stage and how this affects prevalence and concentration of organisms;

- Considering changes as a result of cross-contamination, without unit size changing; and
- Considering changes due to microbial growth or inactivation.

Much effort is expended during food processing operations to minimize microbial growth and/or to maximize microbial inactivation (e.g. using heat), or to prevent cross-contamination from other material or the processing environment through cleaning and sanitation. Important factors controlling the extent of growth and inactivation are the duration of conditions and severity of treatment (particularly temperature) prevailing during the process. The MPRM methodologies for mixing, partitioning and removal can be used to model the effects of changes to unit size (Bassett *et al.*, 2010; Nauta, 2008).

Studies of the effects of some processing steps on the levels of microbiological hazards often report on the result of analysis of 'before and after' samples, such as the number of organisms contaminating a broiler carcass before and after a stage, e.g. defeathering. Dogan *et al*. (2019) evaluated the effectiveness of intervention strategies in processing plants to protect the safety of chicken consumers, through the development of quantitative exposure assessment models. The same approach was applied by Smith *et al*. (2013) to evaluate the relative effects of pre-harvest and processing interventions on public health risk for the consumption of ground beef and beef cuts contaminated with *Escherichia coli* O157:H7 in Canada. When the process is not relevant to the decision, then detailed modelling is not needed or desired. The reduction (or increase) in numbers is, thus, sometimes modelled using a 'black box' approach whereby the changes are modelled, without attempting to describe any of the underlying microbial processes. Alternatively, mechanisms of recontamination of products in factory environments are discussed in den Aantrekker *et al.* (2003). Similarly, where changes are due to growth or inactivation, the effects of process duration and conditions on microbial numbers can be estimated using well-established predictive models (Tenenhaus-Aziza and Ellouze, 2015; e.g. Zwietering and Hasting, 1997a, 1997b).

Normally, results from 'before' and 'after' samples are reported in terms of $\log_{10}$ populations. Caution is needed, however, when modelling cross-contamination when the initial contamination levels are reported as $\log_{10}$ populations. For example, if a cross-contamination event adds 1,000 organisms per unit (i.e. 3 $\log_{10}$) to a unit containing 100 organisms (i.e. 2 $\log_{10}$) it is incorrect to conclude 2 $\log_{10}$ + 3 $\log_{10}$ = 5 $\log_{10}$ (or 100,000 organisms per unit). The correct calculation involves converting the log counts to their arithmetic value and then adding the total numbers, i.e. 100 + 1,000 = 1,100, which means the final contamination is 3.04 $\log_{10}$ organisms per unit, from the original 2 $\log_{10}$. This is because contamination is an additive process. In contrast, microbial growth is a multiplicative process because growth is exponential, *i.e.* where the increase is based on the initial number of organisms in the product and numbers change exponentially over time (such as microbial growth or inactivation). In those cases, the log values can be added, e.g. 2 $\log_{10}$ initial plus 3 $\log_{10}$ growth = 5 $\log_{10}$ at the end of growth, because *every* cell initially present increased in number by 1000-fold. These are examples where errors would result in causal relationships that are incorrect and thus resulting in a flawed assessment; such errors should clearly be avoided.

The variation and uncertainty associated with modelling the change in numbers should also be given careful consideration. When choosing the approach, careful thought should be given to what the data represent (variation, uncertainty or both) and how representative they are. For example, a problem with modelling the results of carcass samples is ensuring that the sampled portion is representative of the entire carcass. An example of a remedy to this challenge is to estimate the magnitude of the bias in a separate study and include this in the model. A practical corollary of this is that if contamination on the carcases is unevenly distributed, then when the carcase is broken down

into smaller pieces, not all will carry the same level of contamination. This is a good example of the consequence of partitioning and where contamination on each smaller unit may differ. Consequently, the prevalence and distribution of contamination levels on sub-units would need to be described.

During processing, formulation of products can be altered. Such alterations may change the potential for microbial growth, e.g. adding growth inhibiting compounds (e.g. salt or organic acids) to processed food, drying/water removal leading to reduction of water activity, acidification during fermentation, addition of water, etc. Similarly, packaging can influence the potential for microbial growth, or inactivation, or cross-contamination. Thus, changes in the condition of the product over time have to be modelled as part of exposure assessment.

Processing often involves steps designed to reduce or eliminate microbial loads so that not only the expected magnitude of the reductions due to these steps, but also their uncertainty/variability, will need to be modelled Also, if the initial contamination levels are low, and a typical unit size is small, then not all units will contain the hazard so that increased risk (in the absence of cross-contamination) can only come from growth in the units that *do* contain a viable infectious unit.

Post-Processing

The post-processing environment includes storage and transport/distribution, retail display and handling, food service operations and home kitchens. These steps can allow microbial growth, cross-contamination, but also hazard reduction through cooking, physical removal of contamination, etc. Table 1 lists some of the factors of the post-food-processing environment that could influence hazard frequency and level of exposure.

While some of these environments may differ in some respects, there are often important similarities and some data collected in one environment may be suitable surrogates for assessing changes in exposure in other environments (e.g. cross-contamination from cutting boards).

Table 1: Examples of factors of importance when determining the impact of the post-processing environment on the level of exposure.

Factor	Example
Temperature	
Static (though variable)	Refrigerated storage temperature
Dynamic	Cooling times and temperatures for cooked food
Product formulation	pH and water activity of the food, preservative compounds (sorbate, lactate, nitrite, nisin, etc.)
Biotic factors in food (inter-species competition)	Relative level of spoilage or other microorganisms on the product compared to pathogens, e.g. fermented food, lactic acid bacteria in vacuum-packed foods.
Time	Time on a salad bar, time between cleaning the blade of a processed meat slicer
Cross-contamination	
Foods	*Salmonella* transfer from chicken
Surfaces	
Food contact surface	*Campylobacter* transfer to cutting board
Hand contact surface	*Listeria* transfer to refrigerator door
Cleaning (sponge, cloth)	*E. coli* survival on sponge

Factor	Example
Hands	*Staphylococcus* transfer from hands
Bodily orifices	Hepatitis A virus from diarrhoea via hands, fomites
Survival on surfaces	*Shigella* survival on stainless steel
Cleaning	
Washing	Effect of washing, soap and water for 20 seconds
Sanitizing	Effect of 200 ppm chlorine
Discards	Decision to use lunch meat beyond its use-by date

Transport and storage post-processing can include:

- Transport from the processor to a food service establishment or retail outlet, possibly via a distribution centre, and subsequent storage
- Warehousing
- Retail storage and retail display
- Storage and handing in food service
- Transport from retail to the home by the consumer and subsequent home storage; this type of transport and storage is likely to be less well controlled: most consumers do not have refrigerated vehicle and frequent access to domestic upright domestic refrigerators means frequent loss of temperature control

Transport and storage conditions may also be less-well controlled in different regions, e.g. in countries where street food vending is common, street vendors often lack the facilities for proper temperature control, or insect or vermin control. In addition, farmers markets may pose additional challenges in terms of temperature control during transport, storage and retail (Young *et al.*, 2017b).

In general, relatively little information is available in the published literature on transport temperature and durations. With respect to transport between processor and retailers (or further processing), information on durations is likely known by the processors, indicating the need for good risk communication and involvement of stakeholders early in the risk assessment process. However, less is known about the temperature profile during transport, although the increasing availability of relatively cheap data loggers, possibly GPS enabled, are helping to remedy this situation (e.g. Sumner, 2016). Similarly, not many published research articles exist about retail or food service storage. An example of temperature data collection is provided by Ecosure (2008), who collected data on cold temperature storage of products in various areas of retail stores (which is available in raw spreadsheet format).

Less is known about the treatment of food during transport to the home, likely related to the logistical difficulties of obtaining such data. Ecosure (2008), however, also collected data from consumer volunteers on transport to the home. The volunteers also reported how product was transported, the temperature in the part of the vehicle where product was located as well as the outside temperature, and time between purchase and placing each product into the refrigerator/freezer at home. Similarly, Kim *et al.* (2013) reported on temperature profiles of various food products during transport to the home.

Using information about duration and temperature at each stage during post processing, predictive microbiology models may be used to predict the growth and inactivation of the hazard. Depending on the hazard and the durations involved, care may be needed to include the effects of shelf life

(limit on total duration between production and consumption) and competing and spoilage bacteria, where possible (Section 12.2).

Cross-contamination

Post-processing environments can be much more complex than processing environments because of the variety of foods involved (restaurant menus, for example, may have dozens of items, and a cafeteria may have hundreds); the complexity of food preparation operations (highly non-linear when compared with food processing operations); differences in preparation setting (home *vs* food service); differences between operations in terms of physical layout (one kitchen *vs* another); and level of training (new worker *vs* highly experienced). The need to evaluate how microorganisms are transmitted along the food chain has motivated the study of other phenomena besides growth and death. Cross-contamination has been recognized as an important factor directly related to outbreaks of food-borne diseases and food spoilage and therefore may need to be included in the exposure assessments (Possas *et al.*, 2017).

The potential complexity involved in modelling cross-contamination during food preparation is shown in Figure 6 for the act of preparing a cooked chicken product and a lettuce salad.

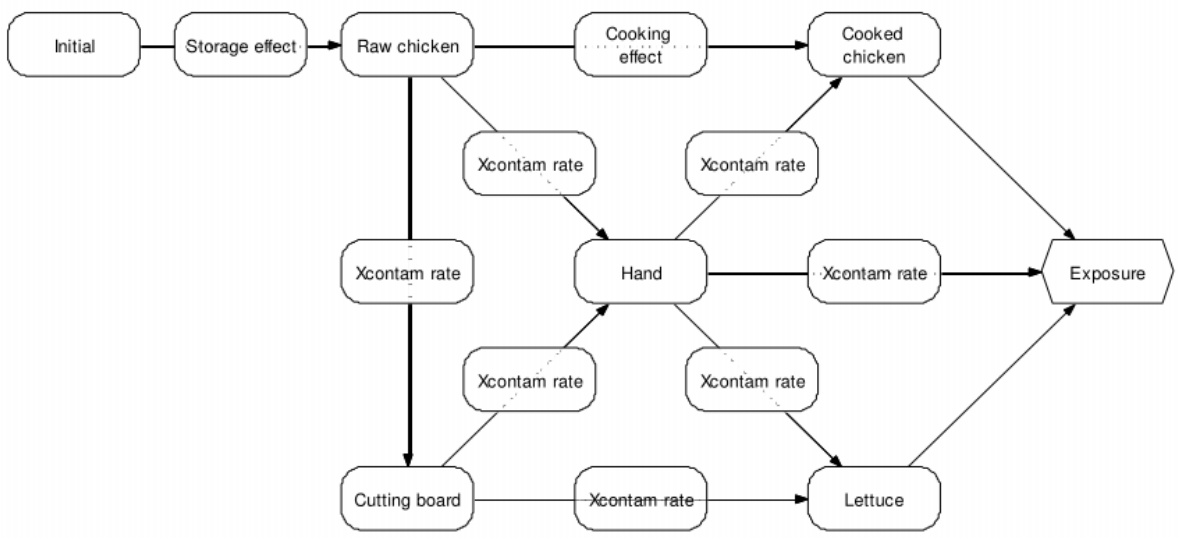


Figure 6: An example 'influence diagram' of a model of a cross-contamination pathway for the preparation of cooked chicken and lettuce salad. (Xcontam = cross-contamination).

Despite its complexity, a number of simplifying assumptions are made in Figure 6:

- The lettuce and the individual preparing the food do not contribute any microbiological hazard to the exposure except for cross-contamination originally arising from the chicken;
- Hands and cutting board are the only cross-contamination vehicles, and other kitchen surfaces (knives, plates, sponges, towels, aprons, counter-tops, etc.) do not contribute to exposure;
- No changes in microbial numbers occur during any step except storage and cooking (e.g. bacterial populations on cutting board do not change); and
- The frequency at which each event occurs is not specified, and in fact multiple contamination events may occur in any food preparation procedure.

Some of the simplifying assumptions listed above can be shown to be false in many situations. One simplifying assumption is that no changes in microbial numbers occur during any step except storage

and cooking, but growth on contact surfaces does occur and may be important. The rate of potential growth on contact surfaces can be used to dictate the minimum time interval between successive cleanings of equipment in contact with raw product. Surfaces that become contaminated with films of nutrient-rich liquids from raw product may contain bacterial pathogens which could grow in the film. This surface is then replenished with new material from each subsequent unit and can promote cross-contamination to other units. Consider that a work-shift may be 4 to 8 hours in duration and that the working environment is maintained at 10-15°C (such temperatures are maintained in some food processing operations because at lower temperatures workers became less dextrous and are more likely to have accidents and injuries). Based on estimates from published predictive models, pathogens could increase by 10- to 1000-fold in some products, e.g. *Vibrio parahaemolyticus* on fish and shellfish (100- to 1000-fold), *Listeria monocytogenes* on smoked fish (10-fold) and *E. coli* on raw meat (10-fold). Predicted increases may be quite different under processing settings where food products are moved on and off the preparation surface throughout the shift, each potentially depositing and/or removing some of the contamination.

Another difficulty in populating the diagram in Figure 6 with real numbers and mathematical relationships is a lack of published data on many consumer storage practices and on cross-contamination rates. The large uncertainty and variability associated with preparation and cooking practices has been recognized in national and international reports of exposure assessments. The FAO/WHO exposure assessment models for *Salmonella* spp. and *Campylobacter* spp. in broilers suggest that cross-contamination during preparation and cooking can affect exposure (FAO, 2001; FAO/WHO, 2002a; WHO, 2001).

Despite the large number of studies reviewed by Pérez-Rodríguez *et al.* (2008) the authors concluded that: “The main objective and challenge when modelling bacterial transfer is to develop reliable mathematical models … However, with today’s knowledge, such models are a Utopia, since information is imprecise and scarce, and data show major experimental errors.” Possas *et al.* (2017) have updated the available cross-contamination modelling approaches in foods as well as the available evaluation methods for model robustness.

Given the limited amount of reliable data available for quantifying the effects of cross-contamination, most exposure assessments have considered this event in a simplistic manner, for example, by including a limited number of pathways, and by estimating both the probability of transfer and the numbers of organisms transferred (e.g. Hartnett, 2002). Other approaches have also been adopted including the Health Canada *Campylobacter* risk assessment, where the transfer of organisms in the drip fluid was also considered (Fazil *et al.*, 1999). Schaffner (2004) modelled the cross-contamination of *Listeria* species using a quantitative mathematical model using Monte Carlo simulation techniques. Chen *et al.* (2001) quantified the probability of bacterial transfer associated with various steps in the food preparation process and provided a scientific basis to include cross-contamination in the exposure assessment with the aim to support risk management strategies to reduce or prevent the cross-contamination in the kitchen. Zilelidou *et al.* (2015) evaluated the cross-contamination phenomena that might take place between cutting equipment and leafy vegetables in common households or in food preparation environments and provided quantitative data regarding the transfer rate of *E. coli* O157:H7 and *L. monocytogenes* from contaminated lettuce to kitchen knives and subsequent transmission to fresh lettuce. Other studies have evaluated the cross-contamination rates of *L. monocytogenes* (Gallagher *et al.*, 2016), *Salmonella* (Smid *et al.*, 2013), *Campylobacter* (Hayama *et al.*, 2011; Moore, Sheldon and Jaykus, 2003; Mylius, Nauta and Havelaar, 2007), and *E. coli* O157:H7 (Jensen *et al.*, 2015; Pérez-Rodríguez *et al.*, 2011).

In summary, post-process food preparation is a highly complex, and poorly characterized, part of the production-to-consumption food chain. Limited data are available, and numerous data gaps have been identified. Given the complexity of this part of the food chain, research to better understand and describe these processes is ongoing. Publication of the results of that research will contribute to improved exposure assessment where cross-contamination may be an important route of exposure. However, cross-contamination is initially a *redistribution* process and, unless that redistribution alters the fate of the hazard, that is, either due to growth or reduction the benefits of cross-contamination modelling, prediction the risk to consumers, or elucidating practical risk management options, should be carefully considered.

5.2.5 *Consumption*

To characterize the risk from exposure to microbiological hazards in food, it is necessary to know the amount of food consumed and how often it is consumed and by whom, and the form in which it is consumed (raw or cooked) because susceptibility is variable and some groups (e.g. very old, very young) are more likely to develop illness from food-borne hazards.

The specific characterization of food consumption patterns used in the MRA depends on the question to be answered by the assessment, as well as the food consumption data that are available to the risk assessor (Chapter 10). The data collated and published by WHO through the GEMS cluster diets[8] may be useful when no other data are available. However, care needs to be taken, as for any consumption data, to ensure correct interpretation (see below).

Modelling the amount of food consumed

When modelling food consumption, it is important for risk assessors to understand the specifics of how the food consumption data were collected and analysed, and to clearly describe how these data were used in the model, including any assumptions used in arriving at the estimates.

The important aspects of calculating the amount of food consumed, particularly when using results from food consumption surveys, include:

- the population divisor, *i.e.* whether the total consumption amount is divided by the total population (amount per capita) or only those who consumed the food (amount per consumer);
- the frequency of consumption (per day/week/month/year); and
- the amount consumed per consumption event.

These are discussed below.

Amount per capita vs per consumer

The per capita amount is calculated by dividing the total amount of a food by the total number of people in the population. The per consumer amount is calculated by dividing the total amount of food only by the number of people who actually consumed the food.

For foods that are consumed regularly by the majority of the population (e.g. bread), the per capita and per-consumer amounts will be nearly equal. For foods that are consumed by fewer individuals (e.g. raw oysters), the per capita and per-consumer amounts will be quite different.

[8] http://www.who.int/nutrition/landscape_analysis/nlis_gem_food/en/ accessed 29 Nov 2018

For example, consider that 10 million kg of a food are consumed by 10% of the population, which consists of 10 million people. The average consumption per capita equals 1 kg, while the average consumption per consumer equals 10 kg.

Amount per year, per day or per eating occasion

Consumption may be calculated as the amount per time-period (e.g. year, month, week or day) or per eating occasion. Definition of the consumption period is particularly important in MRAs because acute, rather than chronic, exposure is of concern. In contrast, chronic exposure may be relevant for some microbial toxins that are released into foods before consumption, e.g. mycotoxins, and in such situations chemical risk assessment approaches are appropriate ((e.g. see FAO/WHO, 2009e)). Often, the dose of microbial toxins is stoichiometrically related to the level of contamination of the food by the toxigenic organism.

National food production statistics (e.g. FAOSTAT[9]) generally report an amount of food produced per year. Care needs to be taken to fully understand the values. For example, if the amount of fish caught is reported, does the amount relate to whole fish landed, or does it relate to the amount after gilling and gutting? Clearly, amounts ultimately consumed need to be adjusted to remove inedible parts of the food and any losses incurred during processes. Similarly, food wastage in the supply chain due to spoilage or other reasons needs to be accounted for if possible. For highly perishable products (meat, fish, fruits, salad vegetables, etc.), this may be as high as 20 to 25% of production (Gustavsson, Cederberg and Sonesson, 2011).

A consumption amount may be estimated by dividing the total annual amount (per capita or per consumer) by the average number of eating occasions. Returning to the example above, if the food product is thought to be consumed daily then the average amount would equal 10kg divided by 365 days, or about 27.4g per day. This amount may be too small to be realistic and hence the data and assumptions for the calculations need be re-assessed and adjusted, if necessary. For example, it may be that a typical amount consumed in a meal is closer to 100g and hence this would imply that the food is consumed about 100 times per year, or approximately once every 3-4 days, or that not all members of the population eat that food. Meal size and consumption data may be available from surveys for some countries.

Food consumption surveys of individuals allow much more flexibility in estimating the consumption amount. Survey results are frequently summarized and reported on the basis of daily consumption. If the raw data from the survey are available, then it may also be possible to calculate the amount of food consumed per eating occasion (depends on coding system and questions in the questionnaire) and the frequency of consumption. The basis for consumption is particularly important when considering foods that may be consumed more than once in a single day. For example, if a person drinks a 250-ml glass of milk at each of three meals, the amount per meal would be 250 ml, whereas the amount per day would be 750 ml.

When calculating daily food consumption from food consumption survey data, it is important to note whether the amount was calculated as an average over all days of the survey or for only the days on which a food was consumed. As an example, in one study, five days of dietary records were collected for individuals participating in the survey. From those data, consumption could be calculated as consumption on the days the food was actually consumed or as the average, or total, over five days for which each person participated in the survey. Of course, different people will consumer different amounts per meal, e.g. young children or the elderly might have smaller portion

[9] http://www.fao.org/faostat/ accessed 29 November 2018

sizes than young adults. In this case, serving size can be modelled as a distribution, if the data are available. In general, all other things being equal, larger serving sizes would be correlated with slightly higher risk of illness. If there is a correlation between serving size and particular consumer characteristics, these correlations can also be modelled to reflect the differential risk to different consumers.

Importance of characterizing the distribution of contamination

The importance of modelling the distribution of the number of organisms in a food will depend on the dose-response relationship for that organism. If a high level of growth occurs in a single unit of food prior to consumption, only one person is likely to be affected because that single unit of food will be consumed by one person. Assuming that there are more than enough cells of the hazard present to cause infection in most individuals, if that same dose were spread equally over 100 servings, then the same dose might be enough to infect many of the 100 consumers (assuming a pathogen with a high probability of infection per infectious particle, e.g. norovirus). Conversely, for a pathogen with a very low probability of infection per cell (e.g. *Listeria monocytogenes*), the predicted risk to the entire population from the exposure is largely independent of the distribution of doses among units of food and is effectively estimated from the average dose. This is because there is, effectively, a direct proportionality between the dose and probability of infection for all realistic doses (see Chapter 6) and for those realistic doses the probability of infection is much less than one. In this situation, there is less need to characterize the distribution of the pathogen among different servings. Nauta (2000) provides advice on modelling distribution among individual servings. However, the risk to an individual is dependent on the dose ingested which, in turn, is dependent on the serving size.

Consumption frequency

The frequency of consumption refers to how often an individual consumes a food in a specific period. In MRAs (e.g. FAO/WHO, 2002a; USDA-FSIS, 2001; USFDA/FSIS, 2003; USFDA, 2005), frequency of consumption has been expressed in a variety of ways:

- Number of days per year on which the food is consumed.
- Number of eating occasions over a year:
    - annual number of meals,
    - number of times the food is consumed per year, or
    - number of 100-g portions consumed in a year.

The number of days of consumption during the consumption survey period can be determined directly from the survey results; from that, an annual number of days of consumption may be extrapolated.

The number of meals, eating occasions or individual food items may be calculated directly from the survey results, if the survey covers more than one day per individual. Alternatively, data from single 24-hour recall surveys can be combined with information from food frequency surveys on the proportion of the population who 'usually' consume a food in a given period to estimate the annual number of consumption days.

It may be possible to refine or verify the estimated frequency of consumption by combining food consumption data with other industry information, such as annual sales volume or market share information (Chapter 10). For example, if the food consumption data report the frequency of consumption of a broad category such as cheese, market share data may be used to predict the frequency of consuming a particular type of cheese (e.g. Camembert). Note that it might be

reasonable to assume that the amount of cheese consumed is similar across types of cheese although the frequency differs by cheese type. As noted above, consideration should be given to the proportion of production that is never consumed due to spoilage, not sold by specified 'use-by' or 'best-before' date, or due to other forms of 'wastage'.

A useful 'reality check' is to combine food consumption amounts with frequency of consumption, and number of consumers to calculate approximate production volumes, taking into account wastage, imports and exports, etc. These estimates should be comparable to actual production volumes and big discrepancies may indicate that some of the estimates or assumptions are not valid.

Considerations and challenges in modelling food consumption

There are a number of aspects of food consumption data that should be considered when developing the food consumption model.

Extrapolating data from results of food consumption surveys

Food consumption surveys generally collect information from a subset of the population (e.g. van Rossum *et al.*, 2011). If the sample is representative of the total population and statistical weights developed for the survey are used in the data analyses, survey results may be used to predict food consumption patterns for the population as a whole.

For MRAs, it may be important to estimate the consumption by sensitive population groups, such as the elderly or the immunocompromised. In the absence of specific data for these groups, it is usually assumed that their consumption patterns are the same as the normal, healthy population of the same age and gender.

Infrequently consumed foods

Estimates of consumption based on a small number of observations (i.e. small number of food consumption records) will be less reliable than estimates based on larger samples. For this reason, care should be taken when interpreting and extrapolating survey results for infrequently consumed foods, even if the overall survey size was large and survey weights are used in the data analysis.

If the survey data are used to model consumption for an infrequently consumed food, it is important that the consumption amount be calculated from the day or eating occasion on which the food was consumed, rather than as the average over all survey days.

Food consumed as discrete items vs components of mixed dishes

Some foods may be consumed both as discrete items and as components of combination foods or food mixtures. For example, milk may be consumed as a beverage, but also as an ingredient (often in small amounts) in many food items. The normal usage of those foods can also affect hazard levels, e.g. milk consumed in meals may be heated which could reduce pathogen numbers compared to milk consumed as part of a cold milk drink. When modelling food consumption, it is important to know whether the consumption estimate includes all sources of the food or only the amount of food consumed as a discrete item. If the consumption estimate includes consumption of the food from all sources, it may be necessary to consider the 'recipes' for foods containing that ingredient. This will not only allow estimation of the total consumption from all sources, but also the form in which the food is eaten, including the effects (if any) of food preparation steps for combination foods that might affect the risk. Similarly, it may be necessary to estimate from the total consumption only that proportion consumed in a form in which the hazard could be present, such as unpasteurized juice or milk, or hot dogs eaten without reheating. As another example of the effect of mixing and partitioning, while consumption data for shell eggs may indicate that a person eats 60 g of shell egg per day, in some situations the serving may have been made from many eggs combined, such as

scrambled eggs in an institutional setting. In such a case, many consumers might be exposed to a single contaminated egg compared to another situation where a single consumer eats the entire contaminated egg.

Aggregation or grouping of foods

If the risk assessment is focused on food groups rather than individual foods, consideration should be given to the way in which foods are aggregated for estimating consumption. The average consumption amount for a food category is affected by the number of foods it represents and how similar the foods are in terms of the usual amount and frequency of consumption. If the foods are too dissimilar, the average amount and frequency of consumption may be misrepresented. For example, if fluid milk and cheese are grouped together as 'dairy products', the consumption amounts may be quite different, and the average consumption will likely underestimate consumption of milk and overestimate consumption of cheese. Again, if a food category includes seasonal items as well as foods that are available year-round, the frequency of consumption may be under- or over-estimated for the seasonal foods. Some consumption surveys do, however, identify seasonal effects, e.g. by sampling individuals at many times throughout the year.

6. Hazard Characterization

6.1 The Process of Hazard Characterization

Codex defines hazard characterization as "the qualitative and/or quantitative evaluation of the nature of the adverse health effects associated with biological, chemical and physical agents, which may be present in food" (CAC, 1999). Hence, the hazard characterization provides a description of the adverse effects that may result from ingestion of a hazard, whether that is a microorganism or its toxin. Where possible the hazard characterization should include an indication, for the population of interest, of the probability to cause an adverse health effect as a function of dose; this would ideally take the form a dose-response relationship, if available, or using the *Median Dose* or *Infectious Dose 50 (ID_{50})*, the dose at which 50% of consumers become infected (or ill); see Section 6.3 for details. The hazard characterization may also include identification of different adverse effects for different subpopulations, such as neonates or immunocompromised people. Hazard characterizations can be conducted as stand-alone processes or as component of risk assessment.

A hazard characterization for a particular hazard may serve as a common module or building block for risk assessments conducted for a variety of purposes and in an assortment of commodities. A hazard characterization developed in one country may serve the needs of risk managers in another country when combined with an exposure assessment specific to that country. A hazard characterization developed for one specific food product may be adapted to a food exposure scenario for another food product by taking into consideration the food matrix effects, where possible. In general, hazard characterizations are fairly adaptable between risk assessments for the same pathogen. This is because the human response to infection from a specific pathogen are not considered to be based on geography or culture but are about the interaction between the hazard and the host only, recognising that some hosts will be more susceptible than others.

Hazard characterization, either as part of a risk assessment or as a stand-alone process, can be iterative. For well-established hazards, such as *Campylobacter* or *Listeria monocytogenes*, the hazard characterizations tend to be well developed and may not require much revision unless considerable new information is available. However, for emerging hazards the hazard characterization may be less certain due to lack of data and information, and thus may require more frequently updating to reflect the increasing knowledge about the hazard. These guidelines for the characterization of hazards in food and water follow a structured, step-wise approach, as outlined in Figure 7 and described in detail in subsequent chapters.

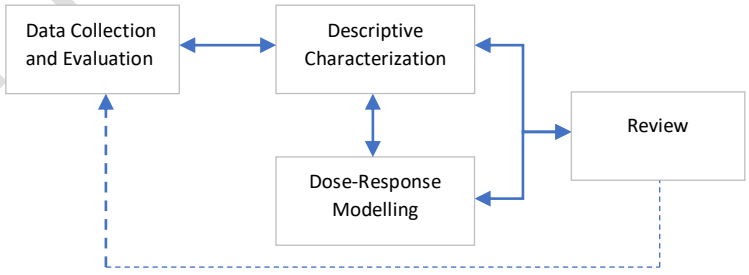


Figure 7: Process flow diagram for hazard characterization of pathogens

6.2 Descriptive Characterization

Descriptive hazard characterization serves to structure and present the available information on the spectrum of human illness associated with a particular hazard, and how this is influenced by the characteristics of the host, the hazard and the matrix, as indicated in Chapter 4. This is based on a qualitative or semi-quantitative analysis of the available evidence and will take the different illness mechanisms into account.

6.2.1 *Information related to the disease process*

When a hazard characterization is being undertaken, one of the initial activities will be to evaluate the weight of evidence for adverse health effects in humans to determine, or confirm, the ability of the hazard to cause disease. The weight of evidence is assessed based on causality inferences appropriately drawn from all available data. This entails examination of the quantity, quality and nature of the results available from clinical, experimental and epidemiological studies; analyses of hazard characteristics; and information on the biological mechanisms involved. When extrapolating from animal or in vitro studies, awareness of the biological mechanisms involved is important with respect to assessment of relevance to humans.

Undertaking hazard characterization for waterborne and foodborne microbial hazards, the biological aspects of the disease process should be considered. Each of these steps is composed of many biological events. Careful attention should be given to the following general points:

- The process as a whole, as well as each of the component steps, will vary by the nature of the hazard.
- Hazards may be grouped in regard to one or more component steps, but this should be done cautiously and transparently.
- The probability of an event at each step may be dependent or independent of other steps.
- The sequence and timing of events are important.

For (toxico-)infectious hazards, it is recommended to consider separately the factors related to infection and those related to illness as a consequence of infection (discussed later, in Section 13.1). While doing so, the following points should be considered when evaluating the available evidence:

- The definition of infection may differ between studies, i.e. is not universally accepted.
- Infection can be measured dichotomously (infection: yes or no), but some aspects can be measured quantitatively.
- Detecting/measuring infection depends on the sensitivity of diagnostic assay.
- Target cells or tissue may be specific (one cell type) or non-specific (many cell types), and local (non-invasive) or invasive or systemic, or a combination.
- The sequence of events and the time required for each may be important and may vary according to the hazard.

The information related to the disease should provide detailed – qualitative or quantitative, or a combination – insights into the disease process. In most cases, this would be based on the available clinical and epidemiological studies. Narrative statements are helpful to summarize the nature of and confidence in the evidence, based on limitations and strengths of the data. Each source of information has its advantages and limitations, but collectively they permit characterization of potential adverse health effects. The analysis should include evaluations of the statistical characteristics of the studies, and appropriate control of possible bias, while identifying what is uncertain and the sources of uncertainty.

Characterization of the adverse human health effects should consider the whole spectrum of possible effects in response to the microbial hazard, including asymptomatic infections and clinical manifestations, whether acute, subacute or chronic (e.g. long-term sequelae), or intermittent (see Table 2). Where clinical manifestations are concerned, the description would include consideration of the diverse clinical forms, together with their severity, which may be variable among strains and among hosts infected with the same strain. Severity may be defined as the degree or extent of clinical disease produced by a microorganism, and may be expressed in a variety of ways, most of

which include consideration of possible outcomes. For mild gastrointestinal symptoms, severity may be expressed as duration of the illness, or as the proportion of the population affected (morbidity). Where the gravity of the distress requires medical care or includes long-term illness, or both, severity may be expressed in terms of the costs to society, such as the proportion of workdays lost or cost of treatment. Some hazards and the related clinical forms may be associated with a certain degree of mortality and therefore severity may be expressed as mortality rate (e.g. *Vibrio vulnificus* infections and *L. monocytogenes* infections). For hazards that cause chronic illness (i.e. the disease leaves long-term sequelae, e.g. foodborne trematode infections) it may be desirable to include, in the characterization of the human health effects, considerations related to quality of life as it may be affected by the disease. Quality of life may be expressed in a variety of ways, depending on the nature of the illness. For instance, human life expectancy may decrease, chronic debilitation may occur, or quality of life may be affected by episodic bouts of disease. Increasingly, concepts such as Quality Adjusted Life Year (QALY) or Disability Adjusted Life Year (DALY), discussed in Section 7.4.2, are being used to integrate and quantify the effects of different disease end-points on the health of individuals or populations (Batz, Hoffmann and Morris, 2014; e.g. Havelaar *et al.*, 2000; WHO, 2000, 2015).

Table 2: Elements that might be included in characterization of adverse human health effects (Adapted from ILSI, 2000)

Clinical forms
Duration of illness
Severity (morbidity, mortality, sequelae)
Pathophysiology
Epidemiological pattern
Secondary transmission
Quality of life

In addition to a description of the human adverse health effects, information on the disease should include consideration of the epidemiological pattern and indicate whether the disease may be sporadic, endemic or epidemic. The frequency or incidence of the disease or its clinical forms, or both, should be addressed, together with their evolution with time and possible seasonal variations. The description should include consideration of the repartition of clinical forms according to specific groups at risk. Finally, the potential for, extent of or amount of transmission, including asymptomatic carriers, as well as secondary transmission, should also be characterized. Information collected on these aspects is important to guide the risk characterization phase of the risk assessment.

In all cases, and with particular regard to further modelling, it is important that the characterization includes a definition of possible end-points to be considered. Thought needs to be given to the appropriate criteria when defining “infection” of the host by the hazard, and the criteria of what constitutes a clinical “case”. In addition, a definition of the severity scale should be provided, specifying the indicator chosen (e.g. disease end-point or consequences) and how it can be measured. The description should also include information on uncertainties and their sources.

To the extent possible, the characterization should incorporate information on the pathophysiology of the disease, i.e. on the biological mechanisms involved. Depending on the information available, this would include consideration of elements such as:

- the entrance route(s) of a microorganism into a host;

- the effect of growth conditions on expression of virulence by and survival mechanisms of the microbe;
- the influence of the conditions of ingestion, including matrix effects;
- the influence of gastrointestinal status;
- the mechanisms involved in the penetration of the hazard into tissues and cells;
- the status of the hazard relative to non-specific cell-mediated (innate) immunity;
- the status of the hazard relative to humoral defences;
- the effect of intercurrent illnesses and treatments, such as immunosuppressive or antimicrobial therapy;
- the potential for natural elimination; and
- the behaviour of the hazard in a host and its cells.

The "natural history" of the disease needs to be completed by specific consideration of factors related to the microorganism, the host and the food matrix, insofar as they may affect development of health effects, their frequency and severity.

6.2.2 *Information related to the hazard*

Basically, this information is analysed with a view to determining the characteristics of the hazard that affect its ability to cause disease in the host via transmission in food. The analysis will take the biological nature of the hazard (bacterial, viral, parasitic, prion) into account as well as the relevant mechanisms that cause illness (infectious, toxico-infectious, toxigenic, invasive or not, immune-mediated illness, etc.). In principle, the descriptive hazard characterization is applicable to all types of hazards and all associated illnesses. In practice, by nature of the data collected, the focus will be on acute effects, associated with single exposures rather than long-term effects associated with chronic exposure. Note that the possible interaction between repeated exposures (e.g. the development of acquired immunity) is an integral part of the descriptive characterization.

The ability of a hazard to cause disease is influenced by many factors (Table 3). Some of these factors relate to the intrinsic properties of the hazard, such as phenotypic and genetic characteristics that influence virulence and pathogenicity, and host specificity. The characteristics of the hazard that determine its ability to survive and multiply in food and water, based on its resistance to processing conditions, are critical components of MRA, with reference to both exposure assessment and hazard characterization. Ecology, strain variation, infection mechanisms and potential for secondary transmission may also be considered, depending on the biology of the microorganism and on the context of the hazard characterization, such as the scenario that has been delineated during the problem formulation stage of a full risk assessment.

Table 3: Elements that might be included in characterization of the hazard (Adapted from ILSI, 2000)

Intrinsic properties of the hazard (phenotypic and genetic characteristics)
Virulence and pathogenicity mechanisms
Pathological characteristics and disease caused
Host specificity
Infection mechanisms and portals of entry
Potential for secondary spread
Strain variability
Antimicrobial resistance and its effect on severity of disease

If not already included in the characterization of the hazard, then specific consideration should be given to the intrinsic properties of the hazard that influence infectivity, virulence and pathogenicity; their variability; and the factors that may alter the infectivity, virulence or pathogenicity of the microorganism under consideration. As a minimum, elements to be addressed as best as possible in hazard characterization with regard to the hazard are summarized in Table 3.

6.2.3 *Information related to the host*

Host-related factors are the characteristics of the potentially exposed human population that may influence susceptibility to the particular hazard, taking into account host intrinsic and acquired traits that modify the likelihood of infection or, most importantly, the probability of illness and its severity. Host barriers are multiple in number and pre-existing (innate); they are not all equally effective against hazards. Each barrier component may have a range of effects depending on the hazard, and many factors may influence susceptibility and severity. These are identified in Table 4.

Table 4: Factors related to the host that may influence susceptibility and severity (Adapted from ILSI, 2000)

Age
General health status, stress
Immune status
Underlying conditions, concurrent or recent infections
Genetic background
Use of medications
Pertinent surgical procedures
Pregnancy
Breakdown of physiological barriers
Nutritional status, bodyweight
Demographic, social, and behavioural traits

Not all of the factors listed in Table 4 would be relevant, or important, for all hazards. In all cases, however, an important issue in hazard characterization is to provide information on whom is at risk and on the stratification of the exposed population for relevant factors that influence susceptibility and severity.

6.2.4 *Information related to the matrix*

The factors related to the food matrix are principally those that may influence the survival of the hazard through the hostile environment of the stomach. Such effects may be induced by protection of the hazard against physiological challenges, such as gastric acid or bile salts. These are related to the composition and structure of the matrix (e.g. highly buffered foods; entrapment of bacteria in lipid droplets). Alternatively, the conditions in the matrix may phenotypically affect the ability of the hazard to survive the host barriers, such as increased acid tolerance of bacteria following pre-exposure to moderately acidic conditions, or induction of stress-response by starvation in the environment. Stress conditions encountered during the processing or distribution of food and water may alter a hazard's inherent virulence and its ability to resist the body's defence mechanisms. These potential matrix effects can be important elements in hazard characterization. The conditions of ingestion may also influence survival by altering the contact time between hazards and barriers, e.g. initial rapid transit of liquids in an empty stomach. These factors are summarized in Table 5.

Table 5: Elements that may be included in characterization of the effect of the matrix on the hazard-host relationship.

Protection of the hazard against physiological barriers, e.g. fatty foods, ingestion of pathogen in, or after, ingesting a large volume of fluid
Induction of stress response
Effects on transport of hazard through the gastrointestinal tract

6.2.5 *Relationship between the dose and the response*

The final, and essential, element in the descriptive hazard characterization is the relationship, if any, between the ingested dose, infection and the manifestation and magnitude of health effects in exposed individuals. Specific modelling aspects are covered Sections 6.3 and 11.

Description of the dose-response relationship involves consideration of the elements or factors related to the hazard, the host and the matrix, insofar as they may modulate the response to exposure. Where appropriate information is available, it also involves a discussion about the biological mechanisms involved, in particular whether synergistic action of the hazards, may be a plausible mechanism for any harmful effect, or whether a single hazard may cause adverse effects under certain circumstances. Elements to be considered are listed in Table 6.

Table 6: Elements to be considered in describing the dose-response relationship (Adapted from ILSI, 2000)

Organism type and strain
Route of exposure
Level of exposure (the dose)
Adverse effect considered (the response)
Characteristics of the exposed population
Duration – multiplicity of exposure

Where clinical or epidemiological data are available, discussion of the dose-response relationship will generally be based on such data. However, the quality and quantity of data available will affect the characterization. The strengths and limitations of the different types of data are addressed in Chapter 10. A specific difficulty is obtaining data to characterize infection, or to characterize the translation of infection into illness and illness into different outcomes. In many cases, the analysis may only be able to describe a relationship between a dose and clinical illness. Other difficulties arise from several sources of variability, including variation in virulence and pathogenicity of the microorganisms, variation in attack rates, variation in host susceptibility, and type of vehicle, which modulates the ability of hazards to affect the host. Therefore, it is essential that the dose-response analysis clearly identify what information has been utilized and how the information was obtained. In addition, the variability should be clearly acknowledged and the uncertainties and their sources, such as insufficient experimental data, should be thoroughly described.

In cases where a dose-response model cannot be ascertained or is not really needed, such as a qualitative MRA, an indication of the likely dose required to cause a certain probability of infection/illness should still be considered. In particular, the dose that results in infection/illness in 50% of exposed consumers – often referred to the ID_{50} or median dose – may be a simple, yet practical, indicator. However, such a dose should not be interpreted as a threshold or minimal infective dose (see box below). For example, is the hazard highly infective and only a very small dose is required, as is the case for norovirus, for which it has been estimated that the ID_{50} may be as low as 18 viruses (Teunis *et al.*, 2008). Or is a larger dose required to cause 50% illness, as is the likely

case with *Listeria monocytogenes* in the general population (FAO/WHO, 2004; Buchanan *et al.*, 2017)?

It should be recognised that for many organisms a very low dose may cause illness, even though the probability of this happening may be very low. However, often the exposure distributions (i.e. distribution of doses) are highly right-skewed and so most exposures occur at (very) low doses. As a result, these low doses, together with a small probability of illness may still represent a large number of illnesses in a population; such exposures are consistent with the concept of "sporadic" illness.

6.3 Quantifying the Dose-Response Relationship

Illness can be the result of intoxication, toxico-infections or infection processes. In the first case the illness is the result of ingestion of toxins being preformed in the food. The health risks of certain toxins, e.g. cyanobacterial toxins in water or aflatoxins in foods, usually relate to repeated exposures and hence tend to be chronic; these require another approach, which resembles hazard characterization of chemicals. Other toxins have more acute effects like botulinum toxin, *Staphylococcus aureus* enterotoxin or *Bacillus cereus* cereulide. In toxico-infection organisms produce toxins in the intestines that either produce adverse effects there, or are transported in the body and create effects in other places in the human body, and for infections the organisms invade human cells, being the intestinal cells or for certain pathogens even further into the human body.

To determine the probability of adverse effects, a dose response relation is needed to translate the doses resulting from exposure assessment. For this, a mathematical model is needed, as well as the value(s) of its parameter(s), including variability and uncertainty. Attention should be paid to various aspects:

1. The dose ingested is characterized by the multiplication of the concentration and the amount of food (or water) ingested (that are both variable).
2. The definition of the response(s), e.g. infection, disease, sequelae.
3. The specific model used, e.g. exponential, Beta-Poisson.
4. The set of parameters including variability and uncertainty, potentially relevant for a specific population group and/or food commodity and/or organism subgroup

The Minimal Infective Dose (MID) model posits that there is a dose below which there is no risk, and above which infection always occurs. Microbial dose-response models today are based on the single-hit assumption, i.e. each individual cell has a discrete, non-zero probability of establishing infection. Models based on this assumption can be found in numerous peer-reviewed papers and are also recommended in the WHO/FAO Guidelines for Hazard Characterization of Pathogens in Water and Food (FAO/WHO, 2003). Therefore, the MID concept, the words "minimal infective dose", "infectious dose", or statements like the dose response is between 10^4 and 10^5 cells should not be used. It is appropriate to use an infectious dose for a certain (quantitative) response like ID_{50} or ID_{10}, representing the dose at which 50 or 10% respectively of those exposed get infected. This concept holds true for toxico-infectious and infectious organisms. Sometimes the ID_{50} is used or interpreted as a threshold of infection; however, such an interpretation is incorrect and should be avoided. A minimal toxic dose (MTD) might exist for illness cause by food containing preformed toxins (e.g. staphylococcal enterotoxins), where there is a level below which there is no observable response.

Plots of empirical datasets relating the response of a group of exposed individuals to the dose (often expressed as a logarithm) frequently show a sigmoid shape (e.g. Figure 8 left) and a large number of mathematical functions can be used to model the dose-response relationship (Haas, Rose and Gerba, 2014; Teunis, 1997). It is important to also investigate this curve on log-log basis, since the

'low exposure' (X-axis) and 'low probability' (Y-axis) part of the relationship (Figure 8, right) is often of particular relevance (Williams, Ebel and Vose, 2011a) as explained at the end of Section 6.2.5. It should be noted that the uncertainty bounds appear different in width when viewed on the log-log scale compared with the linear scale. When extrapolating outside the region of observed data, different models may predict widely differing results (Coleman and Marks, 1998; Holcomb *et al.*, 1999). It is therefore necessary to select between the many possible dose-response functions and justify the decision. In setting out to generate a dose-response model, the biological aspects of the hazard-host-matrix interaction should be considered carefully (Teunis, 1997).

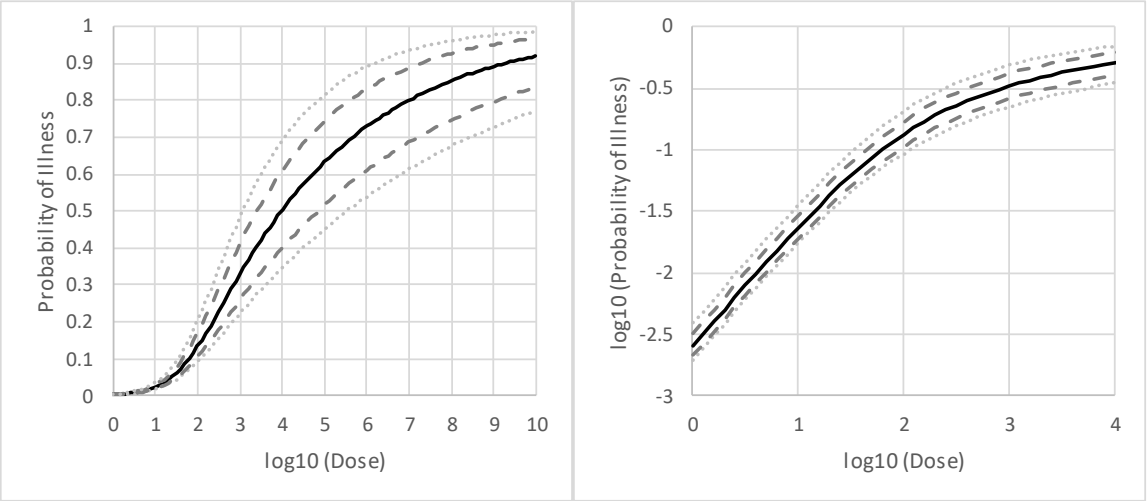


Figure 8: Example Salmonella Dose-Response model, including expected response (solid line), approximate 2.5th and 97.5th uncertainty percentile lines (dashed) and upper and lower uncertainty bounds (dotted) (FAO/WHO, 2002a p. 87) on linear-log scale (left) and on log-log scale (right).

For the use of dose-response models one could use default models and parameter values from other sources (see Table 7). In those cases, relevant assumptions need to be evaluated. It could also be decided to extend the dose-response relation with additional data or derive a fully new dose response model. For deriving new or updated dose response models, guidance is provided in Chapter 13.

1987

1988 *Table 7: Dose-response models and parameter estimates commonly used in QMRA.*

Organism	Reference	Model	Parameters	Lower bound (Percentile)	Upper bound (Percentile)
Salmonella	FAO/WHO (2002a)	Beta-Poisson	α=0.1324 β=51.43	0.0940 (2.5th) 43.75 (2.5th)	0.1817 (97.5th) 56.39 (97.5th)
Listeria monocytogenes [a]	FAO/WHO (2004)	Exponential (susceptible) Exponential (healthy)	r=1.06×10^{-12} r=2.37×10^{-14}	2.47×10^{-13} (5th) 3.55×10^{-15} (5th)	9.32×10^{-12} (95th) 2.70×10^{-13} (95th)
***Campylobacter* spp.**[b]	FAO/WHO (2009d)	Beta-Poisson	α=0.21 β=59.95		
***Shigella dysenteriae/ E. coli* O157**	Cassin *et al*. (1998)	Beta-binomial	α=0.267 β=Lognormal(5.435, 2.47^2)		
Vibrio vulnificus	FAO/WHO (2005)		α=9.3 × 10^{-6} β=110,000		

1989 [a] For *Listeria monocytogenes*, newer animal model data (Roulo *et al.*, 2014; Smith *et al.*, 2003, 2008; Williams *et al.*, 2007, 2009) and outbreak data (Pouillot *et al.*, 2016)
1990 suggest much higher r-values and hence lower ID_{50}s than predicted by this model which was based on the method of Buchanan *et al*. (1997) of matching expected loads of
1991 *L. monocytogenes* across the food supply to the total annual cases in a community, and which relies on many untested assumptions.

1992 [b] The dose response relation is for infection and the conditional probability of disease following infection was 33% (29/89) and can be described by a beta(30,61)

1993

7. Risk Characterization

7.1 The Process of Risk Characterization

Codex defines risk characterization as "the process of determining the qualitative and/or quantitative estimation, including attendant uncertainties, of the probability of occurrence and severity of known or potential adverse health effects in a given population based on hazard identification, hazard characterization and exposure assessment." (CAC, 1999). Hence, the risk characterization integrates the findings from those three components (see Figure 2) to estimate levels of risk, which can subsequently be used to make appropriate risk management decisions.

Risk characterization is the final step in the risk assessment component of risk analysis (Figure 2). The risk assessment process is initiated by risk managers who pose specific questions to be answered by the risk assessment. As noted previously, the questions posed by risk managers are usually revised and refined in an iterative process of discovery, discernment and negotiation with risk assessors. Once answered, the risk managers have the best available science-based information they need to support their decision-making process.

Risk characterization is the risk assessment step in which the risk managers' questions are directly addressed. While 'risk characterization' is the process, the result of the process is the 'risk estimate'. The risk characterization can often include one or more estimates of risk, risk descriptions, and evaluations of risk management options. Those estimates may include economic and other evaluations in addition to estimates of risk attributable to the management options.

Although the Codex risk assessment framework is a common context for undertaking risk characterization, it is by no means the only context. In actual practice an assessment of the risk may include some or all of these steps. The scientific analyses comprising any one of these steps may be sufficient on their own for decision-making. Risk assessments can follow a "bottom-up" or "top-down" approach. A bottom-up approach links knowledge about the prevalence and concentration of a hazard in a food source with knowledge about the causal pathways, transmission routes and dose-response relations. Alternatively, top-down approaches use observational epidemiological information to assess risk, typically making use of statistical regression models (Williams, Ebel and Vose, 2011b). Also, models exist that use elements from both approaches, e.g. for source attribution. These approaches have different starting points, use different types of data and serve different purposes. For example, in Denmark (Hald *et al.*, 2004) and USA (Guo *et al.*, 2011), the number of human cases of salmonellosis attributed to different animal sources was estimated without a precise exposure assessment and without using a dose-response model. A further example is provided by De Knegt *et al.* (2015). Bottom up and top down MRA approaches have been published on aiding risk managers in the use of risk metrics (i.e. ALOP, FSO) with case studies using *Listeria monocytogenes* in deli meats (Gkogka *et al.*, 2013a) and *Salmonella* spp. in raw chicken meat (Gkogka *et al.*, 2013b).

7.2 Qualitative Risk Characterization in Risk Assessment

7.2.1 *Introduction*

The risk characterization generated by a qualitative risk assessment, while ideally based in numerical data for exposure assessment and hazard characterization, will generally be of a descriptive or categorical nature that is not directly tied to a more precisely quantified measure of risk. Qualitative risk assessments are commonly used for screening risks to determine whether they merit further investigation and can be useful in the 'preliminary risk management activities' described in (FAO/WHO, 2002b), but may also provide the needed information and analysis to answer specific risk management questions. The major difference between qualitative and quantitative risk

characterization approaches is in the way the information is synthesized and the communication of the conclusions.

7.2.2 *Performing a qualitative risk characterization*

Qualitative risk characterization requires an overall textual estimate of the risk. This may be based upon a combination of the stepwise assessed risks. This is a complex process as it should still obey basic principles of probability theory when combining probabilities but there are no clear rules to the outcome of the combination of (possibly subjective) textual descriptions of probability. For example, Table 8 illustrates a comparison between the process for computing risk estimates in quantitative versus qualitative risk assessments. When combining the equivalent qualitative statements, the only inference that can be made is that the final risk is either of equal magnitude or lower than the probability at the first stage (P1). This qualitative process can lead to errors in probability logic and may be impossible if there is uncertainty to address or multiple pathways to combine (Wooldridge, 2008). Alternatively, Wooldridge (2008) proposes the risk characterization process consist of a summary of the individual conclusions for each of the steps of the risk assessment (including descriptions of uncertainty).

Table 8: A comparison of the process for computing the final risk estimate in risk characterization in quantitative and qualitative risk assessments. (Table adapted from Table 4 in (Wooldridge, 2008)).

Stage	**Quantitative risk assessment**		**Qualitative risk assessment**	
	Probability	**Computation**	**Probability**	**Computation**
P1	0.1		Low	
P2	0.001	*P2* = *P1* x 0.001=0.0001	Very Low	*P1* x Very Low →Very Low or lower
P3	0.5	*P3* = *P2* x 0.5=0.00005	Medium	*P2* x Medium → further reduction
P4	0.9	*P4* = *P3* x 0.9=0.000045	High	*P3* x High→ further (small) reduction
Risk Estimate	**0.000045**		**Very Low or lower**	

Despite its name, a qualitative risk assessment still relies on as much numerical data as possible to provide inputs. The search for information, and thus for numerical data, should be equally as thorough as for a quantitative risk assessment. Also, where there are crucial numerical data deficiencies, expert opinion must again be utilized. The major difference between qualitative and quantitative risk assessment approaches lies in how the data and expert opinion is treated and combined once obtained.

Transparency in reaching conclusions

A qualitative risk characterization should show clearly how each of the risk estimates is reached. The precise way of doing this will vary depending in part on the complexity of the risk assessment, and in part on the risk assessor(s) preferences. Methods used include:

- a tabular format, with data presented in the left-hand column, and the conclusions on risk in the right column; or
- a 'sectional' format with a summary or conclusions section at the end of each data section.

Examples of these formats that illustrate 'good practice' (i.e. documentation of evidence and logic) are presented in Table 9 and Table 10. The examples are based on particular steps in an overall risk

assessment for which the question is: What is the probability of human illness due to microbe 'M', in country 'C', due to the consumption of meat from livestock species 'S' infected with microbe M?

Table 9: Example of a possible tabular format for presenting data linked to risk estimates and conclusions.

Step being estimated: **'What is the probability of a randomly selected example of species S in country C being infected with microbe M?**	
Data available	**Risk estimate and conclusions**
The prevalence of microbe M in species S in Country C was reported as 35% (Smith & Jones, 1999*). The prevalence of microbe M in region R, a district within country C, was reported as 86% (Brown, 2001*). There are no particular geographical or demographic (with respect to S) differences in region R, compared with the rest of C (Atlas of World Geography, 1995*). The diagnostic test for microbe M, used in the livestock surveillance programme in country C is reported to have a sensitivity of 92% and a specificity of 99% (Potter & Porter, 1982*). **Fictional references for illustrative purposes only*	The studies suggest that the probability of a randomly selected example of species S in country C being infected with microbe M is medium to high. However, the two studies indicate that considerable variability by region is likely. With only two studies available, there is also considerable uncertainty of the actual range of prevalence by region, as well as the probability of infection in a randomly selected example of S. In addition, the timing of these surveys may suggest an increasing prevalence of M in C. The reported parameters for the diagnostic test used do not alter these conclusions.

Table 10: Example of a possible sectional format for presenting data linked to risk estimates and conclusions.

SECTION X. What is the probability of human ill health, given infection with microbe M?
Data available
• No specific dose-response data has been found for microbe M. • Health authorities for country C provide the following data (National Health Reviews, 1999–2002*).   ○ Incidence over the period was reported as 22 cases per million of the population per year (22 per million is 0.000022% of the population per year). • Clinical incidence recording and reporting systems in Country C are considered to be of exceptionally high quality (Bloggs, pers. comm.*). • Experts' opinions indicate that once clinical symptoms appear, cases are likely to consult a medical practitioner (Journal of Microbial Medicine, 1992*). • Cases tend to be seen in the very young or the very old (Journal of Microbial Medicine, 1992*). • A surveillance study undertaken by practice-based serological testing indicated that 35% of the population of C had been exposed to microbe M and had sero-converted (Hunt, Hunt and Seek, 2001*). This was a countrywide, statistically representational study.

*Fictional references for illustrative purposes only
Conclusions
Data suggest a high level of exposure to microbe M in country C, but a very low incidence of clinical disease. Expert opinion indicates under-reporting of clinical disease due to lack of medical practitioner involvement is unlikely to account for this. Overall, therefore, the probability of human ill health, given infection with microbe M, is likely to be low. The level of uncertainty in the data specific to country C appears to be low, making this conclusion reasonably certain. However, data also indicate that there are specific groups at higher risk of clinical illness, specifically the very old and very young. From the data currently available it is not possible to indicate how much higher this risk is likely to be.

Limitations of qualitative risk characterization

It may be difficult to conceive of a fully qualitative risk assessment that will provide useful advice to risk managers, except in a few special cases. In those special cases, the number of factors that could affect the risk may be very low or every factor that affects the risk, may change the risk in the same direction. Since risk managers may make decisions on the basis of economics, qualitative descriptions may be difficult to translate directly to financial benefits and/or costs. In other cases, it may be virtually impossible to assess the combined effect of multiple stages because the relative contributions of factors, expressed in qualitative terms, cannot be logically combined to determine their overall affect. In some cases, a qualitative best-effort may still be needed, and any assumptions and uncertainties need to be clearly explained. Thus, while a fully qualitative risk assessment can identify pathways or scenarios that lead to extremes of risk, the relative risk from all other scenarios cannot be logically differentiated. Logical qualitative reasoning can provide conclusions like 'the risk of X is logically less than that of Y' where Y is another, more precisely quantified, risk that has previously been deemed acceptable. Such reasoning can also provide conclusions like 'the risk of A is logically greater than that of B' where B is another, more precisely quantified, risk that has previously been deemed unacceptable. One can also argue that both of these approaches are forms of best- and worst-case quantitative risk assessment. Cox, Babayev and Huber (2005) discuss these limitations in greater detail and provide examples.

Qualitative analyses often suffer from the inability to determine what pieces of evidence were influential, how they were combined, and ambiguity concerning the meaning of any assigned risk characterization labels. Without explicit criteria identifying what is meant by descriptions such as high, moderate, and low risk, there is little to distinguish the conclusions from arbitrary and possibly value-laden judgements about the level of risk. These shortcomings tend to make qualitative risk characterization unacceptable in many decision-support situations.

Another limitation of qualitative risk assessment may be to blur the lines between risk assessment and risk management. For example, a risk assessment that concludes the level of the risk under consideration to be 'Low', may be perceived to be making a management evaluation of the risk, and therefore confusing the roles of assessor and manager.

It is possible to present an unstructured analysis as a more structured analysis by including standard documentation headings such as exposure assessment, hazard characterization and risk characterization. Examples that illustrate qualitative approaches that do link evidence and conclusion are presented in Section 8.1.

If the risk assessment will be read by a broader audience, assessors should be mindful that interpretation of words or terms used as descriptors might vary between languages or regions. Even when there is a consensus between assessors and managers over the interpretation of the terms used, some limitations of qualitative risk assessment can be identified.

7.3 Semi - Quantitative Risk Characterization

7.3.1 *Introduction*

Semi-quantitative approaches to risk characterization involve assigning numbers to qualitative estimates in the form of probability ranges, weights or scores, and combining them by addition, multiplication, or other mathematical operation with the objective of achieving a greater level of objectivity compared to qualitative approaches. It is the role of risk characterization to provide to management an unbiased estimate of the level of the risk being considered. Semi-quantitative approaches avoid this problem by using a specific, quantitative meaning (instead of a judgemental meaning) rather than terms like 'Low probability'.

Table 11 and Table 12 provide some example definitions for probability, exposure rate and severity categories where probability ranges have been assigned to qualitative descriptions.

Table 11: Example definitions of probability and exposure frequency categorical labels.

Category	Probability range (Probability of event per year)	Category	Exposures per year
Negligible	Indistinguishable from 0	Negligible	Indistinguishable from 0
Very Low	$< 10^{-4}$, (except 0)	Very Low	1-2
Low	10^{-4} to 10^{-3}	Low	3-10
Medium	10^{-3} to 10^{-2}	Medium	11-20
High	10^{-2} to 10^{-1}	High	21-50
Very High	$> 10^{-1}$ (except 1)	Very High	>50
Certain	1		

Table 12: Example definitions of health effect / severity category labels

Category	Severity description
None	No effect
Very low	Feel ill for few days without diarrhoea
Low	Diarrhoeal illness
Medium	Hospitalization
High	Chronic sequelae
Very high	Death

7.3.2 *Performing a semi-quantitative risk characterization*

Semi-quantitative methods require the development of decision rules guiding how the categorical risk levels are combined and that is logical, aligns with general principles of probability, and is transparent in terms of the operations performed. The options to conduct the risk characterization using semi-quantitative methods spans the continuum between qualitative and quantitative approaches with no single approach endorsed as the single "best" approach in all circumstances. Approaches include (but are not limited to) the combination of labels or scores in algebraic form

with a fixed equation (e.g. specifying multiplication or addition of scores), using specified probability ranges/bounds in place of quantitative point estimates of risk, or using a combinatorial risk-matrix. The level of complexity of the approach varies widely as the exact set of rules to combine the categorical risk levels are often designed specifically for the risk assessment being conducted. Examples of the types of approach that may be used include:

Using an algebraic approach: Components of the risk characterization (and overall risk assessment) are assigned numerical values to represent categorical levels and an equation is specified that defines how the scores or weights are combined. An example using an algebraic approach is RiskRanger by Ross & Sumner (2002). The probabilities involved in exposure and impact are converted to scores from 0 to 1, which are combined (usually by multiplication but including additions, e.g. for recontamination) and subject to logical tests in the software (e.g. to prevent unfeasible risk estimates) to define a "comparative risk" and, in conjunction with the number of consumers, a predicted number of cases of illness is obtained. An example of its use is presented in Section 8.1.7.

Using probability bounds: The categorical labels are assigned probability ranges which are then combined. Often, in the course of carrying out a qualitative risk assessment, one can roughly estimate the probability of exposure, etc., from comparison with other, previously quantified risks or from good data pertaining to the problem in hand. If time or the available data are insufficient to carry out a complete quantitative risk assessment, one can use these categorical labels to express the risk level in a more structured way than a simple description of the evidence one has acquired.

However, when terms like "low risk" or "very low risk" are used, it is very important to consider the number itself, but even more so to examine the context to see what the number means. For example, consider where the probability of botulinum toxin in one can of food from a single supplier is 0.0001. This number itself (0.0001) seems "very low". However, since this number refers to only a single can in a potentially very large population of cans, e.g. 10 million, the resulting number of 'toxic cans' equals 0.0001×10,000,000 = 1,000 cans, which would be considered a very large number of toxic cans, given the nature of the illness. On the other hand, if it is considered a probability of one can per year in the entire world containing botulinum toxin to be 0.01, then this value is 100 times larger than the value above (0.0001), but the actual risk is much lower (i.e. one 'toxic can' in 100 years) – this risk is actually quite low, considering that the yearly worldwide can use is in the trillions rather than millions. Therefore, the denominator of the probability needs to be clearly defined (per serving, per person per year, over the whole population, etc.) and the probabilities need to be considered in this context (risk per serving, for a person per year or for the whole population), to classify them as 'high' or 'low'. In addition, the severity needs to be considered when moving from probability to risk.

For example, if the qualitative risk assessment has determined that:

- the probability a serving could be contaminated is 'Very High',
- the number of servings a random person consumes is 'Medium' and
- the probability of illness given consumption of the contaminated product is 'Low',

one can conclude the composite probability to be between 'Low' and 'Medium' by multiplying the corresponding bounds from each of the probability ranges, as shown in Table 13, using the example definitions from Table 11 and Table 12.

Table 13: Example of combining category labels.

Component	Category	Numerical range
Probability that serving is contaminated	Very High	10^{-1}-1
Number of servings in a year	Medium	10-20
Probability of illness from a contaminated serving	Low	10^{-4}-10^{-3}
Probability of illness in a year	Low to Medium	10^{-4}-2×10^{-2}

This approach enables people to make more consistent, logical conclusions: a 'Low' exposure probability per serving and a 'High' probability of illness given exposure cannot, for example, be categorized as a 'Very High' probability of illness per serving.

It is possible to use categorical labels to perform some rudimentary type of probability manipulation. For example, by carefully defining the ranges assigned to each term, it is possible to combine a 'Low' exposure with a 'High' probability of subsequent health effect (the hazard characterization, or dose-response component) to determine the appropriate categorization for the total risk. It is only possible to maintain consistency and transparency in combining categorical labelling of elements of a risk assessment if numerical ranges have been defined for each label. Combining categorical labelling nonetheless should still be approached with some considerable caution (see Chapter 9).

Using a risk matrix: A risk matrix uses combination rules to combine categorical labels; an example of such a matrix is show in Table 14. This approach has been adopted for many years in other areas of risk assessment but has also received criticism because of the difficulties of defining a robust, defensible treatment of risk characterization (and risk assessment in general). See Levine (2012) and Cox Jr. (2008) for a discussion of these issues and suggestions for improvement.

Table 14: A hypothetical example of a risk matrix to combine likelihood and severity as could be applicable to risk characterization using probability ratings as presented in Table 15.

		A	B	C	D	E
		Negligible	**Minor**	**Moderate**	**Significant**	**Severe**
E	**Very Likely**	Low Med	Medium	Med Hi	High	High
D	**Likely**	Low	Low Med	Medium	Med Hi	High
C	**Possible**	Low	Low Med	Medium	Med Hi	Med Hi
B	**Unlikely**	Low	Low Med	Low Med	Medium	Med Hi
A	**Very Unlikely**	Low	Low	Low Med	Medium	Medium

Table 15: Semi-quantitative allocation of categorical labels to probability ranges.

Probability	Risk Rating
>70%	Very likely
40% to 70%	Likely
10% to 40%	Possible
1% to 10%	Unlikely
<1%	Very Unlikely

Limitations of semi-quantitative risk characterization

Any semi-quantitative risk characterization has limitations which can result in inaccuracies in risk estimates. These are discussed in more detail in Section 9.2.3, and include:

- Number of categories to use: there is no rule regarding the number of categories that should be used, e.g. 5 or 25 categories of severity
- Granularity of scale: a risk whose probability of occurrence falls just above the boundary between two categories, and for which a risk management strategy reduces that probability by a small amount, it could be dropped down one category, but which is indistinguishable from reducing the probability by a factor of 10.
- Difficulty combining probability scores: it is not easy to create a rule with scores that replicates the probability rules.

Data requirements

The basic principle of risk assessment is to collect as much data as possible, providing that the inclusion of more data may affect the decision being made. The data collected for a qualitative risk assessment are often sufficient for semi-quantitative risk assessment needs. The difference between the two is that semi-quantitative risk assessment has a greater focus on attempting to evaluate the components of the risk to within defined quantitative bounds. Thus, at times, one may do a statistical analysis on a data set to attempt to more precisely estimate a probability, or the expected impact, providing it will give the assessor more confidence about how to categorize the risk.

Semi-quantitative risk assessment is usually used as a means to compare several risks or risk management strategies. At times there may be sufficient data to be able to perform a full quantitative risk assessment for a select number of risks (e.g. food–pathogen combinations). A quantitative model can provide more information about specific strategies to apply to that particular risk issue, but the quantitative results can also be used to place these more precisely evaluated risks into context with others of concern in a semi-quantitative environment.

Transparency in reaching conclusions

Semi-quantitative risk assessment is a system for sorting out risks, focusing on the big issues, and managing the entire risk portfolio better. The scoring system is inherently imperfect, but so is any other risk evaluation system. If the scoring system being used can be shown to produce important errors in decision logic, then one can use potentially more precise quantitative risk assessment arguments or change the scoring system to something more precise.

Semi-quantitative risk assessment may offer some advantages in achieving transparency. No sophisticated mathematical model is necessary, for example, which is appealing to the lay person. However, the use of mathematical models as an obstacle to transparency may be overemphasized. Most food safety risk assessments require understanding of complex microbiological information and a reasonable understanding of human medicine and of epidemiological principles, which tend to be postgraduate topics. In contrast, quantitative risk assessment uses mathematics that are generally covered at an undergraduate level. The main obstacle to transparency of quantitative models is that there are only a few people who have specialized in the field.

The key transparency issue with semi-quantitative risk assessment arises from the granularity of the scales used in scoring. The usually rather broad categories mean that lose any distinction between risks which can be considerably different in probability and/or impact magnitude. This means, for example, that one food industry could be unfairly penalized because its product lies just above a category bound, or that industry or regulator only have the incentive to push a risk just over, or below, a category boundary.

7.4 Quantitative Risk Characterization

7.4.1 *Introduction*

As described in Section 5.2.3, quantitative assessment can be either deterministic (where single values, like means or percentiles, are used as model input variables), or probabilistic (stochastic) where probability distributions are the model input variables. Most of the literature, guidance and the best-known examples in QMRA are probabilistic quantitative microbial risk assessments. This approach offers many advantages over deterministic risk assessment, and these are described at length in Chapter 11. Examples of deterministic quantitative risk assessment can be found most readily in the food additive safety assessment (also known as chemical risk assessment) literature. FAO and WHO have produced numerous examples of probabilistic risk assessments, through the Microbiological Risk Assessment Series, as have food safety authorities around the world; some examples are provided in Section 8.2

Quantitative risk characterization addresses risk management questions at a finer level of detail than a qualitative or semi-quantitative risk characterization and facilitates a more precise comparison between risks and between risk management options. This extra level of detail can be at the expense of a far greater time to completion, a reduction in scope and a greater difficulty in understanding the model. Probabilistic techniques are more complex and therefore introduce a greater likelihood of error or misunderstanding. Quantitative risk assessments may also rely on subjective quantitative assumptions (WHO/OECD, 2003), and the mathematical precision of these quantitative results can inadvertently give a false impression of the degree of accuracy in characterizing risk. This has been recognized for a long time in the risk analysis community, e.g. Whittemore (1983) noted: “Quantitative risk analyses produce numbers that, out of context, take on lives of their own, free of qualifiers, caveats and assumptions that created them”.

7.4.2 *Quantitative risk measures*

Quantitative measures of risk must combine the two quantitative components of risk: (a) a measure of the probability/amount of the hazard occurring (i.e. exposure) and (b) the severity of the health effect should that hazard occur (Kaplan and Garrick, 1981).

Measure of exposure

The probability of exposure in microbiological food safety risk assessment must relate to a specified level of exposure, which is the result of the exposure assessment component (Chapter 5). The subsequent probability measures of risk are expressed generally as risk of an outcome (e.g. risk of illness per serving) or as population risk (e.g. risk of the population experiencing more than 10 illnesses per year).

There are advantages and disadvantages in selecting each probability measure. The first option underlines the probabilistic content of the risk measure, while the second can be misread to make one believe that the risk event will occur deterministically with the specified frequency; though explicit identification of the distribution of the risk measure, or associated probability intervals helps to counter that perception.

The choice of probability measure needs to be made carefully and in collaboration with the risk managers, to make any explanation of the risk assessment results as clear as possible to the intended audience.

Measure of health effect

There are different ways of expressing risk (EFSA, 2012). Codex Alimentarius defines risk as “a function of the probability of an adverse health effect and the severity of that effect, consequential

to a hazard(s) in food". There are different metrics that have been developed to characterize and compare risk including the number of an adverse outcome, the Quality-Adjusted Life Year (QALY), the Disability-Adjusted Life Year (DALY) as well as metrics for monetary valuation of public health. Each of these metrics has some pros and cons, and there is no preferred choice for all scenarios. Each individual metric provides a different perspective on the public health risk of foodborne pathogens and the choice should be based on the purpose and scope of the risk assessment. The selected measure(s) of health effect will reflect what the risk manager cares about.

There are many potential adverse health effects that a risk manager might be interested in, in addition to those about which the affected individual is directly concerned. This, in turn, means that there are many possible ways to measure and express the magnitude of the risk (sometimes called the '*risk metric*') that might be selected as the required output from a risk assessment. The selection of a particular measure of risk is therefore not necessarily straightforward, and must be discussed between the risk manager, the risk assessor, and other interested stakeholders. In addition, for quantitative modelling, the unit or units required must be defined whilst considering the practical aspects of modelling so that the outputs can be produced and reported in those units.

A) Number of adverse outcomes: The number of adverse outcomes (e.g. illnesses, hospitalisations, deaths) is the simplest metric that can be used in risk assessment. This number (or the probability) of adverse outcomes can be estimated as "per serving" or "per annum" and standardised for population size (e.g. per 100,000 per year)". In general, the per annum relative risks inherently have a greater degree of uncertainty than the corresponding per serving relative risk because of the additional uncertainty associated with the number of annual servings. Another factor that affects relative risk on a per annum basis is the size of the susceptible subpopulations, in proportion to the total population which are substantially different, e.g. YOPIs (young, old, pregnant, immunocompromised). Note that not all subpopulations may be equally susceptible to all hazards, e.g. susceptibility to infection may differ from susceptibility to microbial toxins produced in the food prior to consumption.

- **Risk of some outcome per serving**: requires that a serving be defined (e.g. 100 g of cooked chicken, 150 ml of orange juice, or use of a serving size probability distribution). The risk of some outcome per serving measure provides an easy comparison of the risk from direct consumption of different food products. It can also be helpful in establishing cost-benefit type arguments where, for example, one is looking for the lowest risk for a given nutrition requirement.
- **Individual risk**: can be specified for a random individual within the population of concern, or for a random consumer of the product. If a random consumer of the product is assumed this presupposes that there are no significant secondary infections or cross-contamination effects. Random individuals can be assumed to be part of various subpopulations if one wishes to explore the risk to different subpopulations. Examples of different individual risk estimates include:
    i. The probability per year that a random individual will suffer illness X from exposure to bacteria Y in food Z;
    ii. The probability per year that a random individual will suffer any deterioration in health X from exposure to bacteria Y in food type Z;
    iii. The probability that a person will suffer some adverse health effect in their lifetime from exposure to bacteria Y in foods;
    iv. The expected number of foodborne-related adverse health events for a random individual from consuming food type Z in a year;

v. The distribution of the number of foodborne-related adverse health events for a random individual from consuming food type Z in a year;
vi. The per capita (or per kg consumed, or per kg produced, by the nation) expected incidence of health impact X from food type Z.

This risk per person is very often a very low number (e.g. 0.000013 expected illnesses per person per year), making it difficult to understand and compare. These values can be made more useable by considering the risk over a large number of people (e.g. 1.3 expected illnesses per 100,000 people per year).

- **Population-level risk**: this estimation considers the risk distributed over the population or subpopulation of interest and might also look at the risk burden to the whole population. It may not distinguish between subgroups within that population, such as by region, ethnicity, age or health status. The following are some examples of population-level risk estimates:
  i. Uncertainty about the total expected number of cases of foodborne illness within the population in a year;
  ii. Expected number of hospital bed-days taken up per year as a result of a particular foodborne pathogen;
  iii. Probability that there will be at least one outbreak (or one death, one illness, etc.) in the population in a year;
  iv. Probability that there will be more than 10,000 illnesses in the population in a year.

  These estimates can be produced for separate subpopulations if required and aggregated to a single measure for the whole population.

B) Health adjusted life years (Burden of disease). Summary measures of public health can characterize and compare the health effect of diverse risks and health outcomes. These are particularly useful when a risk assessment is considering or comparing different pathogens. For example, deciding between risk management options that pertain to two different pathogens requires a method that accounts for the differences in severity between those pathogens. In contrast, if a risk assessment is concerned with a particular product-hazard pairing, and the severity of outcomes is independent of exposure pathway, then these summary metrics are less critical. For example, deciding between risk management options that pertain to controlling illnesses for a particular product-hazard pair is less dependent on the differences in severity between the options (because this is the same).

Different methods have been developed that provide a common metric for more fully valuing and comparing health risks. Health-adjusted life years (HALYs) are non-monetary health indices and are summary measures of population health permitting morbidity and mortality to be simultaneously described within a single number (Gold, Stevenson and Fryback, 2002). HALYs are used in economic cost-effectiveness analyses, also sometimes referred in the literature as cost-utility analysis or weighted cost-effectiveness analysis (Mangen *et al.*, 2010). The two most prominent HALYs are Quality-Adjusted Life Years (QALYs) and Disability Adjusted Life Years (DALYs).

The DALY is based on the amount of life quality lost multiplied by the duration of that health state (Van der Fels-Klerx *et al.*, 2018). They are useful for overall estimates of burden of disease, comparisons of the relative impact of specific illnesses and conditions on communities, and in economic analyses. The DALY method presumes perfect health for the entire life span, and therefore measures the loss due to ill health. The QALY concept is analogous, but measures the increase in quality of life, and its duration, as a result of an actual or putative intervention.

The DALY approach has been used by WHO to quantify the global burden of foodborne disease as it incorporates life years lost through specific types of disability, pain or other reduced quality of life, including premature mortality. This allows the comparison of one health state with another, and with mortality itself. Integrated health measures provide information to put diverse risks into context. The WHO Initiative to Estimate the Global Burden of Foodborne Diseases (WHO, 2015) provides an estimation of global foodborne disease incidence, mortality, and disease burden in terms of DALYs for thirty-one foodborne hazards (including 11 diarrhoeal disease agents, 7 invasive infectious disease agents, 10 helminths and 3 chemicals).

DALYs lost is the summation of two quantities:

1. YLL: Years of life lost (the difference between the age at death and the life expectancy)

2. YLD: Years lived with a disability (multiplied by the extent of the disability)

Given values of these disability rates, and data on time course (distribution) of severity of outcomes, the DALYs in units of total years of impact in the population under consideration can be computed (Ssemanda *et al.*, 2018). This formulation recognizes that different illnesses will have different patterns of severity and longevity of disability (Haas, Rose and Gerba, 2014). The DALY methodology has been widely used in both national (Lake *et al.*, 2010; Monge *et al.*, 2019; Scallan *et al.*, 2015; Ssemanda *et al.*, 2018) and global (Mangen *et al.*, 2010) disease burden estimations or to compare the burden of disease estimates attributed to different cooking practices (Berjia, Poulsen and Nauta, 2014).

A related approach to integrate the spectrum of health outcomes is the QALY (quality adjusted life year) approach. QALYs differ from DALYs primarily by the nature of the weights used. Rather than using expert-derived “disability weights,” the QALY concept uses “quality weights” which are based on survey or preference data to assess the relative perceived quality of life under certain health impairments. Such an approach allows for the differentiation among subpopulations, socioeconomic conditions, and differences in underlying society (Haas, Rose and Gerba, 2014).

The DALY method is considered by some to be preferable to the QALY method for making societal resource allocation decisions. The QALY method was intended to evaluate the benefit in quality of life improvement through a medical intervention, i.e. compared to the cost, while DALY mostly seeks to quantify the burden of disease due to a particular hazard in a particular context.

A strong point of the HALY approach is that utilities and disability weights are not income constrained. However, HALYs do not capture non-health effects and HALY impacts cannot be compared to other non-health projects (as would be the case if all effects would be expressed in monetary values). HALYs are based upon the assumption that a life-year is the appropriate metric for measuring health; as a result, the valuation of permanent disability and mortality is linearly valued by age of patients. DALYs and QALYs are semi-quantitative estimates based on disability scoring, and their accuracy is highly dependent on the quality of input data and risk assessment models used for estimating the incidences of relevant health outcomes (Van der Fels-Klerx *et al.*, 2018).

C) Monetary risk metrics. The public health impact of foodborne disease can also be characterized using monetary metrics (Mangen *et al.*, 2010). However, health economics is a branch of economics with additional complexities (Arrow, 1963). Factors that distinguish health economics from other areas include extensive government interventions, uncertainty in several dimensions, asymmetric information (the physicians know more than the patients), barriers to entry, externalities

(communicable diseases, fear of catching disease) and the presence of a third-party agent (professional health care provider).

Several different approaches have been developed for the monetary valuation of risk (Mangen *et al.*, 2010). There are three general approaches:

(1) the human capital approach, measuring a person´s production in the marketplace;
(2) cost of illness (COI) methods, and
(3) revealed or stated preferences which also include intangibles (not measurable) factors such as suffering and pain.

With the human capital approach, the benefits of a health program or costs of disease is measured by the impact on a person's productive input. The human capital approach is generally restricted to the impacts on labour productivity (e.g. foregone income) and makes no attempt to include intangible costs. It is therefore not considered a measure of individual or social welfare. Opportunity costs of time or a replacement cost approach are two methods usually used to value the time for non-market activities (e.g. home-keeping).

A second approach to measuring the public health impact of disease is the cost of illness (COI) method. The COI approach does not measure intangible costs but traces the economic flow associated with an adverse health outcome through the quantification of measurable monetary costs. Cost-of-illness (COI) measures include (Mangen *et al.*, 2015):

1) the costs related to the resources used within the healthcare sector;
2) the resources used by patients and their families; and
3) productivity losses and other non-healthcare related resources used that are indirectly related to illness (e.g. special education).

The COI method estimates the money spent on medical expenditures and the value of the productivity of the patient foregone as a result of foodborne illnesses, complications and deaths. It can be applied wherever there are quantitative data relating to the impact of disease and sufficient cost data for calculating resultant treatment costs and loss of income. Subject to data availability, it is possible to compare large numbers of food risks using COI (Van der Fels-Klerx *et al.*, 2018). COI can be applied for comparing diseases (Mangen *et al.*, 2015), for food-disease combinations (Thomsen *et al.*, 2019), for supply chain analysis of a single food-disease combination (Duncan, 2014; McLinden *et al.*, 2014; Monge *et al.*, 2019), and for comparing the cost-effectiveness of different interventions to reduce the foodborne risk (Lawson *et al.*, 2009).

A third approach uses stated preference studies that are based on the presentation of hypothetical scenarios on which to evaluate how much a person would pay for reductions in the risk of death or other adverse health states. Stated preventative studies can be designed for a specific health state, but are based on a hypothetical construction and, therefore, describe the intention of individuals to adopt particular decisions (Mangen *et al.*, 2010).

Matching dose-response endpoints to the risk measure

Exposure to microbiological agents can result in a continuum of responses ranging from asymptomatic carriage to death. Risk characterization needs to consider the reported health outcome used in developing the dose-response relationship and may require estimating the desired risk assessment endpoint(s) from a more or less severe measurement endpoint. A fraction of exposed individuals will become infected. Infection may be measured as the multiplication of organisms within the host, followed by excretion, or a rise in serum antibodies. A fraction of those

infected will exhibit symptomatic illness, known as the *morbidity ratio* (Haas, Rose and Gerba, 2014), as measured by clinical observation or reported by patients or consumer responses. A fraction of those becoming ill will suffer severe symptoms (e.g. bloody diarrhoea), require medical care or hospitalization, or will die, known as the *mortality ratio* or *case-fatality rate* (Haas, Rose and Gerba, 2014). It should also be noted that DALY and QALY are not typically dose-response endpoints; rather, the endpoints are infections, illness, death. A template (e.g. DALY/case) must be used to translate the risk estimate (e.g. cases) from a quantitative microbial risk assessment to DALYs, etc.

In addition, care must be taken to ensure that the implications of the case definition used in a clinical trial or epidemiological investigation are understood. For clinical trials, typical measurement endpoints include infection (e.g. as indicated by a faecal positive) or illness (e.g. as indicated by diarrhoea). Epidemiological surveys may provide information on morbidity and mortality ratios. These ratios might be dose-dependent, but epidemiological data may not indicate this relationship. In some cases, clinical trials have used a continuous dose-response measurement endpoint (e.g. volume of diarrhoea excreted) that might provide some insight about the dose-dependency of outcome severity (Coleman *et al.*, 2004).

Accounting for subpopulations

Subpopulations may vary with respect to susceptibility, exposure, or both. If the risk characterization seeks to distinguish risk by subpopulation (e.g. by age class), then the exposure assessment outputs should be kept separate for each subpopulation to reflect variation in exposure among them (e.g. the frequency, size and preparation of servings consumed by members of each age class). Even where separate dose-response relationship by subpopulation cannot be specified, it may be informative to characterize risk by subpopulation.

The subpopulations of interest to the risk managers (e.g. susceptible consumers) may not correspond directly to easily identified categories (e.g. age classes). There should be a reasoned basis for classifying consumers as members of different subpopulations, and that subpopulation definitions are consistent between the exposure and dose-response analyses.

7.4.3 *Integration of hazard characterization and exposure assessment*

Codex guidelines describe the need to assess exposure to a hazard and assess the level of risk (dose-response relationship) that the exposure represents. Most quantitative risk assessments will implement the exposure and dose-response models separately, and risk characterization will connect these to estimate the risk. This need for connection should be included in the planning stage of the modelling whenever possible, to avoid having to adjust the output of exposure or the input of the dose response to achieve consistency.

When there is a logical separation between variability and uncertainty in either the exposure assessment or hazard characterization, this distinction should be propagated through the process of integration to determine both the variability and uncertainty in the relevant measures of risks that are the focus of the assessment. Failure to maintain separation between variability and uncertainty can profoundly affect the risk characterization (Nauta, 2000). Additionally, assumptions implicit to specific dose-response models or potential biases associated with estimation of the dose-response can limit how exposure and dose-response can be combined.

In the section below the dose concepts as formulated above are briefly reviewed and suggestions are offered to address the issues of maintaining consistency of units, dose-response model rationales and reducing biases when integrating potentially inconsistent exposure and hazard characterizations.

Units of dose in exposure assessment

According to Codex (CAC, 1999) the output of the exposure assessment is defined as an estimate, with associated uncertainty, of the likelihood and level of a pathogen in a specified consumer portion of food. This exposure estimate is commonly represented by a distribution of the probability that a randomly selected portion of food is contaminated with the pathogen, combined with a probability distribution representing the numbers (or concentration) of pathogens in those portions of food that are contaminated (i.e. contain one or more cells of the pathogen).

Whether the level of contamination is expressed as a concentration (CFU per gram or per ml) or a number (CFU) is important when linking this exposure output to a dose-response model. Numbers of CFU potentially ingested are necessarily positive integers, so a discrete distribution may be the most natural choice for the estimated exposure. The use of a continuous distribution for modelling of individual exposures would be most appropriate when pathogen concentrations are relatively high but can always be converted back to a discrete distribution with some rounding function. Continuous distributions are often used for bacterial counts because they are more flexible and easier to manipulate than discrete distributions. If a concentration is used to express the level of exposure, the concentration has to be multiplied by the amount of food ingested to determine the individual exposure. If the concentration being modelled is in the form of a probabilistic mean, then one needs to use dose-response functions for which inputs are probabilistic (usually, Poisson) mean doses rather than dose-response functions whose input is an actual dose (Haas, 2002; Pouillot, Chen and Hoelzer, 2015).

Units of dose in dose-response assessment

Dose-response models in microbiological risk assessment typically apply the concepts of non-threshold mechanisms, independent action and the particulate nature of the inoculum (Chapter 11). This results in the application of single-hit models like the exponential model, the Beta-Poisson model, the Weibull-Gamma model and the hypergeometric model (Haas, 1983; Teunis and Havelaar, 2000). These models assume each ingested cell acts independently, and all cells have the same probability of causing infection. The non-threshold assumption implies the existence of some level of risk for any dose greater than zero.

A review of dose-response models is provided Chapter 11. The two principle types of data useful for developing a dose-response assessment are clinical feeding trial studies with human volunteers and epidemiological outbreak data and data on disease incidence associated with foodborne exposure. These different types of human data have varying strengths and weaknesses, as discussed in Chapter 10.

Combining exposure and dose-response assessments

Consistency is important when combining exposure and dose-response assessments. The exposure assessment and hazard characterization should be applicable to the same hazard and the same population (e.g. one might mistakenly use a dose-response relationship estimated using data from young healthy volunteers to a less homogenous population that includes susceptible individuals). Such extrapolations should be avoided by looking at alternative modelling approaches. However, if extrapolation is done, then it should be clearly stated, and the potential biases and uncertainties of such extrapolation should be incorporated as part of the assessment.

The output of the exposure assessment should be in units of ingested organisms (CFU, cells, virus particles, etc.) per individual and usually on a per-exposure event basis. In contrast, the input of the dose-response may not be on a per-individual level. For example, the exposure may be expressed as

a mean or other summary of a distribution of exposures over a group of individuals (e.g. Teunis *et al.*, 2010), though this should be avoided if at all possible. Differences between individual- and group-level exposure summaries in a hazard characterization may create problems of consistency when combining the two assessments for the purpose of risk characterization.

Exposure assessment and hazard characterization can be combined in a Monte Carlo simulation by calculating a probability of infection (or illness) associated with each sample from the exposure distribution. For a given sample containing a known number of cells from the exposure distribution, the probability of infection from the specified dose, would then be calculated based on the dose-response relationship. Exposure and risk predictions will generally be uncertain due to the uncertainty associated with alternative models of the exposure distribution and the risk of illness at any specified dose level. These uncertainties extend to predictions of risk when the exposure and dose-response are combined and should be properly represented in the output of the assessment.

Limitations of quantitative risk characterization

Just as with qualitative and semi quantitative risk characterization, there are limitations of quantitative risk characterization as well. These primarily stem from its advantages and are related to the potential need for large quantities of data, as well as the use of complex models. Because of the data and modelling needs, some multi-disciplinary teams tasked with performing quantitative risk characterization can be quite large, and thus costly and time-consuming. The complex nature of the models often makes the review of such models limited to select experts, as well as time consuming. This complexity can also provide a challenge to transparency as complex models may not be easily interpreted by non-experts.

8. Examples

The examples below are provided to give a perspective on the breadth and depth of published risk assessments. Some were done at the country level, others in larger or smaller regions. Some were done in the early days of risk assessment and others more recently. Some were done by federal employees, while other were done in partnership with academic experts. Some focus on a particular food, while others focus on large food categories. Some are for a single pathogen, while others focus on two or more. Some are "farm to fork" while others focus on a specific part of the food chain. Most focus on infectious pathogens, but one focuses on a toxin(histamine) produced by microbial action. Some of the examples are qualitative, others semi-quantitative (Section 8.1), while others are quantitative (Section 8.2).

8.1 Examples of qualitative – semi-quantitative risk assessments

8.1.1 *Risk assessment for main determinants of antibiotic resistance in South East Asia*

The emergence of antibiotic resistant bacteria and genes has been observed in the environment, driven by the indiscriminate use of antibiotics in human and veterinary medicine and food production. A qualitative risk assessment was conducted to evaluate the relative effects of the main determinants of antibiotic resistance, and to estimate the risk of the emergence and spread of antibiotic resistance among humans in the WHO South East Asia region (Chereau *et al.*, 2017). Factors were examined at the policy level (e.g. scope of policies and guidelines), system level (e.g. implementation of healthcare, wastewater, or agriculture and livestock management options), and at individual level (e.g. human behaviour).

The region considered includes 11 countries (Bangladesh, Bhutan, Democratic People's Republic of Korea, India, Indonesia, Maldives, Myanmar, Nepal, Sri Lanka, Thailand, and Timor-Leste).

Hazard Identification: Seven bacteria with high levels of antibiotic resistance were identified and the study focused on those causing infections with high mortality (extended spectrum β-lactamase and carbapenemase producing Enterobacteriaceae and meticillin resistant *Staphylococcus aureus* (MRSA).

Exposure Assessment: the process leading to the acquisition, selection, and spread of the resistant bacteria and genes in humans was described, including the reservoirs, transmission routes, and biological determinants of the emergence and transmission of resistance. Exposure routes considered included the release from human and animal waste, aquaculture, and pharmaceutical industry, ingestion of contaminated food and water, direct contact with reservoirs (animals, soil, water), and human-to-human transmission (including health case workers).

A context assessment was also conducted which looks at the environment in which the event is taking place considering socioeconomic, ecological, other factors that may affect the exposure and/or risk.

Risk Characterization: the likelihood of occurrence of each event was rated using a qualitative approach using:

- *Negligible*: the event occurs under exceptional circumstances
- *Low*: the event occurs some of the time
- *Moderate*: the event occurs regularly
- *High*: the event occurs in most circumstances.

The events in the chain were chronologically integrated leading to transmission of antibiotic resistance in the human population using a matrix to calculate the risks from two consecutive, and dependant events. When multiple independent events contributed to the estimation of risk, the highest risk was used. The risk matrix used was from Wieland *et al.*, (2011), and is designed to combine two risk estimates based on the assumption that the second event is fully conditional on the previous event, and is shown in Table 16.

The risk assessment concluded that South East Asia is at high risk of the emergence and spread of antibiotic resistance in humans. The assessment provides an overall picture of the factors affecting the emergence of antibiotic resistance emergence in humans in the WHO South East Asia Region, and highlights the limited benefit of interventions that are sector specific as opposed to an overall holistic 'One Health' approach.

Table 16: Risk matrix used to combine two consecutive, and dependant events (adapted from Wieland et al., 2011)

Event 2 / Event 1	Negligible	Low	Moderate	High
Negligible	Negligible	Negligible	Negligible	Negligible
Low	Negligible	Low	Low	Low
Moderate	Low	Low	Moderate	Moderate
High	Low	Moderate	Moderate	High

8.1.2 *Faecal pollution and water quality, WHO*

The 'Annapolis Protocol' (WHO, 1999) was developed in response to concerns regarding the adequacy and effectiveness of approaches to monitoring and management of faecal-polluted recreational waters. One of the most important changes recommended in the Annapolis Protocol was a move away from sole reliance on 'guideline' values of faecal indicator bacteria to the use of a qualitative ranking of faecal loading in recreational-water environments. The protocol was tested in several countries, and an expert consultation was convened by WHO. A revised Chapter 4 in Volume 1 of the guidelines was produced from the expert consultation, which described a suitable approach to risk assessment and risk management (WHO, 2003). Tables were produced for water bodies affected by three different sources of human faecal contamination: sewage outfalls, riverine discharges and bather shedding. The tables were based on qualitative assessment of risk of exposure under 'normal' conditions of sewage operation, water levels, etc, and classified the potential human risk. Table 17 reproduces the classification for sewage outfalls.

Table 17: Relative risk potential to human health through exposure to sewage through outfalls (reproduced from WHO, 2003).

		Discharge type	
Treatment	**Directly on beach**	**Short outfall[a]**	**Effective outfall[b]**
None[c]	Very High	High	NA[d]
Preliminary	Very High	High	Low
Primary (including septic tank)	Very High	High	Low
Secondary	High	High	Low
Secondary plus disinfection[e]	Moderate	Moderate	Very Low
Tertiary	Moderate	Moderate	Very Low
Tertiary plus disinfection	Very Low	Very Low	Very Low
Lagoons	High	High	Low

Notes: (a) The relative risk is modified by population size. Relative risk is increased for discharges from large populations and decreased for discharges from small populations. (b) This assumes that the design capacity has not been exceeded and that climatic and oceanic extreme

conditions are considered in the design objective (i.e. no sewage on the beach zone). (c) Includes combined sewer overflows. (d) NA = not applicable. (e) Additional investigations recommended to account for the likely lack of prediction with faecal index organisms

8.1.3 *Drinking Water Guidelines, Australian National Health and Medical Research Council*

As part of Australia's National Water Quality Management Strategy the Australian National Health and Medical Research Council produced the Australian Drinking Water Guidelines (NHMRC, 2018) as a framework for good management of drinking water supplies. The guidelines are not mandatory standards but are designed to provide an authoritative reference document and framework for good management of drinking water supplies to assure safety at point of use by consumers in all parts of Australia. The guidelines consider that the greatest risks to consumers of drinking water are pathogenic microorganisms, and as such covers similar issues for water that microbiological food safety risk assessment covers for food. However, it should be noted that the issues of microbiological growth and inactivation are likely to play a much larger role in microbiological food safety risk assessment because of the greater potential for microbial growth in foods, and the application of strong inactivation processes that do not occur in water in nature. The extensive guidelines document includes a qualitative method for assessing human health risks and recommends that risks should be assessed at two levels:

- **Maximum risk** in the absence of preventive measures; and
- **Residual risk** after consideration of existing preventive measures.

The level of risk of each hazard (pathogen, or hazardous event) is qualitatively assessed by combining a qualitative assessment of the likelihood of the hazard occurring, and the severity of the consequences if it were to occur, according to Table 18,Table 19 and Table 20 (Tables 3.1, 3.2 and 3.3 in the original document), which were developed from the Australian/New Zealand risk analysis standard 'AS/NZS 4360:1999 Risk management', which has since been superseded by AZ/NZS ISO 31000. The guidelines document also includes what are essentially qualitative hazard identification and hazard characterizations for a wide range of water-borne hazards that can be used to assist in the application of the risk matrices. The stated aim of the methodology is "to distinguish between very high and low risks" (NHMRC, 2018).

Table 18: Qualitative measures of likelihood.

Level	Descriptor	Example description
A	Almost certain	Is expected to occur in most circumstances
B	Likely	Will probably occur in most circumstances
C	Possible	Might occur or should occur at some time
D	Unlikely	Could occur at some time
E	Rare	May occur only in exceptional circumstances

Table 19: Qualitative measures of consequence or impact.

Level	Descriptor	Example description
1	Insignificant	Insignificant impact; little disruption to normal operation; low increase in normal operation costs
2	Minor	Minor impact for small population; some manageable operation disruption; some increase in operating costs
3	Moderate	Minor impact for large population; significant modification to normal operation but manageable; operation costs increased; increased monitoring

4	Major	Major impact for small population; systems significantly compromised and abnormal operation, if at all; high level of monitoring required
5	Catastrophic	Major impact for large population; complete failure of systems

Table 20: Qualitative risk analysis matrix: level of risk.

	Consequences				
Likelihood	1 Insignificant	2 Minor	3 Moderate	4 Major	5 Catastrophic
A (almost certain)	Moderate	High	Very high	Very high	Very high
B (likely)	Moderate	High	High	Very high	Very high
C (possible)	Low	Moderate	High	Very high	Very high
D (unlikely)	Low	Low	Moderate	High	Very high
E (rare)	Low	Low	Moderate	High	High

8.1.4 *BSE/TSE risk assessment of goat milk and milk-derived products, EFSA*

A research group in France found a suspected case of Bovine Spongiform Encephalopathy (BSE) infection in a slaughtered goat in 2002. As a result, the European Commission (EC) requested advice from the European Food Safety Authority (EFSA) on the safety of milk and meat in relation to Transmissible Spongiform Encephalopathy (TSE) in goats and sheep. EFSA (2004a) published the following preliminary statement:

> *"From the limited data available today it is concluded that in the light of current scientific knowledge and irrespective of their geographical origin, milk and milk derivatives (e.g. lactoferrin, lactose) from small ruminants **are unlikely to present any risk** of TSE contamination provided that milk is sourced from clinically healthy animals. Exclusion of animals with mastitis is considered to reduce the potential risk. Further assurance of healthy milk could include milk tests for total somatic cell counts indicative of inflammation." [Emphasis added].*

EFSA also commented in a press release:

> *"A comprehensive and quantitative assessment of the risks involved in the consumption of goat meat, milk and dairy products will only be possible if more scientific research data on the occurrence of TSE in small ruminants can be obtained. Such a quantitative risk assessment, if feasible, will take considerably more time."*

It is extremely difficult to assess the risk of BSE-contaminated product because there is no means to measure the number of prions present in a food product, and no human dose-response relationship for prion levels. EFSA nonetheless needed to provide comment on the level of the above risk and relied on an expert panel to review the available data.

8.1.5 *Geographical BSE cattle risk assessment, EFSA*

In 2003, EFSA was requested by the European Commission (EC) to re-assess geographical BSE risk (GBR) and concluded the following (EFSA, 2004b):

> *"The Geographical BSE-Risk (GBR) is a qualitative indicator of the likelihood of the presence of one or more cattle being infected with BSE, pre-clinically as well as clinically, at a given point in time, in a country. Where its presence is confirmed, the GBR gives an indication of the level of infection.*

The GBR assessments are based on information submitted by countries concerned in response to a European Commission recommendation in 1998 setting out the information requirements for such an assessment. The information concerns in particular imports of bovines and meat and bone meal (MBM) from the United Kingdom and other BSE-risk countries, rendering standards for animal by-products, use of so called Specified Risk Materials (SRMs), feeding of MBM to ruminants, etcetera.

Table 3.5 [Table 21] shows the current GBR levels of the seven countries assessed by EFSA so far, as well as their former classification where available."

Table 21: Geographical BSE Risk (GBR) in 2003 in seven countries as assessed by EFSA (2004b; Table 3.5). Earlier assessed levels are also shown.

GBR level	Presence of one or more cattle clinically or preclinically infected with the BSE agent in a geographical region or country	GBR of the country or region Current status (status before)
I	Highly unlikely	Australia (I)
II	Unlikely but not excluded	Norway (I), Sweden (II)
III	Likely but not confirmed or confirmed at a lower level	Canada (II), Mexico (N/A), South Africa (N/A), USA (II)
IV	Confirmed at a higher level	none

NOTES: N/A = not applicable, i.e. not assessed before"

8.1.6 *Risk profile of Mycobacterium bovis in milk, New Zealand Food Safety Authority*

The New Zealand Food Safety Authority commissioned the New Zealand Institute of Environmental Science & Research Ltd (ESR) to provide a 'Risk profile' of *Mycobacterium bovis* in milk (Lake *et al.*, 2009).

The analysis took the form of a 'Risk Profile' which is used in the New Zealand food safety system to rank food safety issues for risk management. It forms an early part of their risk evaluation process, which comprises:

- identification of the food safety issue;
- establishment of a risk profile;
- ranking of the food safety issue for risk management;
- establishment of risk assessment policy;
- commissioning of a risk assessment; and
- consideration of the results of risk assessment.

The pathogen was selected for assessment because

"although it is likely to have minimal public health significance, demonstration of the safety of New Zealand produced food with respect to this pathogen may have trade implications. The food most commonly associated with transmission to humans is cow's milk."

The system for assignment of a category for a food/hazard combination uses two criteria: incidence (rate) and severity assigning categories to the estimate of each. A four-category scoring system was proposed for the rate (see Table 22), based on foodborne disease rates experienced in New Zealand (Lake *et al.*, 2005). Note that this is a generic scoring system that would be adapted to *Mycobacterium bovis* in milk.

A three-category scoring system was proposed for the severity (see Table 23), based on a comparison of the proportion of New Zealand foodborne cases that result in severe outcomes (long-term illness or death) (Lake *et al.*, 2005). Note that this is a generic scoring system that would be adapted to *Mycobacterium bovis* in milk.

Table 22: The four generic categories proposed in New Zealand for the incidence (rate) with examples (Appendix 1 in Lake et al., 2005).

Rate Category	Rate range (per 100 000 per year)	Examples of food hazard combinations
1	>100	Significant contributor to foodborne campylobacteriosis
2	10–100	Major contributor to foodborne salmonellosis Significant contributor to foodborne noroviruses
3	1–10	Major contributor to foodborne yersiniosis, shigellosis
4	<1	Major contributor to foodborne listeriosis

Table 23: The three generic categories proposed in New Zealand for severity with examples (Appendix 1 in Lake et al., 2005).

Severity Category	**Fraction of cases that experience severe outcomes**	**Examples**
1	5%	Listeriosis; STEC; hepatitis A; typhoid
2	0.5-5%	Salmonellosis; shigellosis
3	<0.5%	Campylobacteriosis; yersiniosis; noroviruses; toxins

Analysis for *Mycobacterium bovis* in milk was hampered by a complete lack of prevalence information, so it was considered impossible to make even qualitative statements of exposure. The only available dose-response data were from animal experiments from 1934 and earlier, making it meaningless to consider a usual food safety risk assessment of exposure and hazard characterization. The risk profile method is based solely on epidemiological data in an attempt to inform decision-makers of how important the issue is among other food safety issues that need to be managed. The analysis discussed the available evidence and gave the following scores:

- **Severity**: 1 (>5% serious outcomes)
- **Incidence**: 4 (<1 per 100 000 people per year)
- **Trade importance**: high

Note that the risk assessment titles described these as 'qualitative' risk assessments. However, the numerical definitions of the broad category bands would place these risk assessments within the range of semi-quantitative risk assessments as discussed in this document.

8.1.7 *Seafood safety using RiskRanger, Australia*

Sumner *et al.* (2004) discuss the continuum between qualitative and quantitative risk assessment for seafood, and introduce a semi-quantitative risk assessment method that has been coded into a decision support software tool called RiskRanger (Ross and Sumner, 2002; Sumner and Ross, 2002),

which is freely-available[10]. The tool requires answers to 11 questions, which describe the factors throughout the food chain that affect the food safety risk. The questions can be answered in either qualitative (with predetermined categories) or quantitative terms. Qualitative answers are converted to quantitative values according to sets of tables.

The model is intended to be population specific, so key inputs like total and/or region population size are required to be predefined, although user-defined values can also be input. A score is then calculated from the inputs, allowing the ranking of various food–pathogen combinations. The scoring system is designed to have a scale of 0 to 100, where 100 represents the worst imaginable scenario, i.e. that every member of the population consumes a lethal dose every day. A 0 score was arbitrarily set to equate to one mild diarrhoeal case per 100 billion people per hundred years, the logic being that the Earth's population is significantly less than 100 billion, so one would not expect to see an occurrence of the risk anywhere within a person's lifetime. The chosen range extends over 17.6 orders of magnitude, which equates to 100/17.6 ≈ 6 'risk ranking' units for each factor of 10 between risks.

The method has been designed to screen risks and to screen major categories of risk management options. The spreadsheet interface allows a risk manager to instantaneously consider what-if scenarios that can stimulate discussion of possible risk management strategies. The simplicity and generic nature of the model means that its results remain fairly crude. It also means that the questions that are posed are of a very general nature. The authors go into considerable detail to warn the reader of these limitations. There is, for example, no incorporation of uncertainty and variability in the model, though this could be added into the spreadsheet model using Monte Carlo simulation.

The tool was then used to evaluate 10 Australian seafood hazard+product combinations, and considered different consuming subpopulations in Australia, with the results shown in

[10] Available from http://www.foodsafetycentre.com.au/riskranger.php or through https://www.cbpremium.org/; accessed 6 December 2018

2787 Table 24 (from Sumner and Ross, 2002).

2788 The authors compared the ranked risks against observations in Australia. There had been no
2789 documented cases in Australia for risks with a score <32. All risks with scores between 32 and 48 (a
2790 range of three orders of magnitude) had caused several outbreaks of foodborne illness in Australia,
2791 with the exception of *Vibrio cholera*. Risks with scores >48 had all caused outbreaks of large
2792 numbers, some in specific regions.

2793

Table 24: Result of using RiskRanger to evaluate hazard+product combinations for various subpopulations in Australia (from Sumner and Ross, 2002).

Hazard+product pairing	Selected population	Risk ranking
Ciguatera in reef fish	General Australian population	45
Ciguatera in reef fish	Recreational fishers, Queensland	60
Scombrotoxicosis	General Australian population	40
Algal biotoxin in shellfish – controlled waters	General Australian population	31
Algal biotoxin — during an algal bloom	Recreational gatherers	72
Mercury in predaceous fish	General Australian population	24
Viruses in oysters — contaminated waters	General Australian population	67
Viruses in oysters — uncontaminated waters	General Australian population	31
Vibrio parahaemolyticus in cooked prawns	General Australian population	37
Vibrio cholerae in cooked prawns	General Australian population	37
Vibrio vulnificus in oysters	General Australian population	41
Listeria monocytogenes in cold-smoked seafoods	General Australian population	39
Listeria monocytogenes in cold-smoked seafoods	Susceptible (aged, pregnant, etc.)	45
Listeria monocytogenes in cold-smoked seafoods	Extremely susceptible (AIDS, cancer)	47
Clostridium botulinum in canned fish	General Australian population	25
Clostridium botulinum in vacuum packed smoked fish	General Australian population	28
Parasites in sushi or sashimi	General Australian population	31
Enteric bacteria in imported cooked shrimp	General Australian population	31
Enteric bacteria in imported cooked shrimp	Susceptible (aged, pregnant, etc.)	48

Key among the cautions the authors cite are that they have not been able to systematically and objectively evaluate the model's performance because there are few data sets describing exposure and foodborne disease incidence. That caution, however, is also evidence that full quantitative models would also not have been possible.

The authors also found that the model was a powerful tool for teaching the principles of risk analysis.

8.1.8 *Animal and animal product import-risk assessment methodology, Biosecurity Australia*

In 1998, a trade dispute between Canada and Australia over Australia's 24-year ban of uncooked salmon went to the WTO court (WTO, 1998). The Australia Quarantine Inspection Service (now Department of Agriculture and Water Resources) had produced a qualitative risk assessment analysing the disease threat in 1995, and another in 1996: the former assessed the risk to be acceptably low; the latter reached the opposite conclusion. The difference in conclusion came about through using a different qualitative risk assessment approach, rather than through the emergence of new information. The WTO Appellate Body came down on Canada's side because, *inter alia*, it considered that Australia had not implemented a proper risk assessment of salmon imports. This highlighted to the risk analysis community the potential problems of relying on a purely qualitative risk assessment methodology, especially in an adversarial environment.

Australia's regulatory body assessing import risk was re-structured, and it now falls under the responsibility of Biosecurity Australia. They have developed a semi-quantitative approach to assessing import risk (Biosecurity Australia, 2016). The risk evaluation is based on placing the estimated risk in a risk matrix. The band of cells marked 'very low risk' represents Australia's Appropriate Level of Protection (ALOP), or tolerance of loss.

The guidelines describe qualitative (e.g. low, medium, high), semi-quantitative (e.g. 0 → 0.0001; 0.0001 → 0.001; 0.001 → 0.01; 0.01 → 1) and quantitative (exact probability calculation) evaluation of likelihood of entry of an exotic disease into Australia. This has the potential advantage of using one environment to incorporate risk assessments along the qualitative to quantitative continuum. Qualitative evaluations of steps in a sequence that results in exotic disease entry are allowed through a matrix rule for combining such qualitative probabilities.

The consequence assessment component of the risk estimate for an exotic disease import risk is generally considered far more difficult than evaluating the probability of disease entry. This is because imports are regulated and fairly simple to model, and their probabilities are well understood, whereas there are no data on the spread of disease in the naïve country, and disease spread, is anyway, extremely complex to model.

Biosecurity Australia aimed to evaluate the probability and magnitude of a variety of impacts should the disease enter the country. They devised a series of rules that allowed the incorporation of the geographical extent of the consequence (local, district, regional, national), and the level to which the consequence would be felt at that scale. Other rules combined the (necessarily qualitative or semi-quantitative) estimates of likelihood of these consequences (given the disease has entered Australia) to allow a placement of the unrestricted risk estimate in the table (Table 25).

If the unrestricted risk (i.e. the risk from a product where no specific controls are in place to protect against the pathogen in question) estimate fell into an acceptable region, the import would be allowed without any restrictions. If not, restrictions (testing, heat treatment, evisceration, etc.) would be evaluated to determine the least trade-restrictive option that would allow the import product to meet Australia's ALOP.

Whichever approach (or combination of approaches) is chosen, the guidelines state that the approach should provide for the following:

- an assessment based on sound science;
- an assessment that is structured and transparent;
- an assessment that is internally consistent, and that can be repeated (with the same or a similar outcome) by another operator using the same framework and data;
- an outcome that will support the estimation of 'risk' (a combination of likelihood and consequences);
- an outcome that will enable risk to be evaluated against the importing country's ALOP, or 'tolerance for loss'; and
- a framework within which the efficacy of risk management and the acceptability of a mitigated risk can be evaluated.

Table 25: Tabulation of risk as a combination of likelihood and consequence (Biosecurity Australia, 2016).

Likelihood of pest entry, establishment and spread	Consequence of pest entry, establishment and spread					
	Negligible	Very Low	Low	Moderate	High	Extreme
High	Negligible risk	Very low risk	Low risk	Moderate risk	High risk	Extreme risk
Moderate	Negligible risk	Very low risk	Low risk	Moderate risk	High risk	Extreme risk

Low	Negligible risk	Negligible risk	Very low risk	Low risk	Moderate risk	High risk
Very Low	Negligible risk	Negligible risk	Negligible risk	Very low risk	Low risk	Moderate risk
Extremely Low	Negligible risk	Negligible risk	Negligible risk	Negligible risk	Very low risk	Low risk
Negligible	Negligible risk	Negligible risk	Negligible risk	Negligible risk	Negligible risk	Very low risk

8.1.9 *Multicriteria-based ranking for risk management of food-borne parasites, FAO/WHO*

FAO and WHO were asked to review the current status of knowledge on parasites in food and their public health and trade impact (FAO/WHO, 2014). This was done in order to provide the Codex Committee on Food Hygiene with advice and guidance on the parasite-commodity combinations of concern, issues that need to be addressed by risk managers, and the options available to them. As part of this charge some work was undertaken to develop a quantitative ranking tool using expert opinion.

The experts defined global criteria for evaluating the 24 food-borne parasites and rated each parasite along these criteria. The criteria were: (1) number of global illnesses; (2) global distribution; (3) acute morbidity; (4) chronic morbidity; (5) percentage chronic; (6) mortality; (7) increasing illness potential; (8) trade relevance; and (9) socio-economic impact. Each criterion was then weighted by the experts in importance. The three criteria for disease severity (3, 4 and 5) were combined into one criterion, giving a total of 7 criteria weights, reflecting the relative importance of each criterion to the overall score. The overall score for each parasite was calculated by normalized parasite criteria scores multiplied by fractional weights and summed. The resulting tool was able to give a global ranking of food-borne parasites by "importance" and their primary food vehicle.

Mean of elicited criteria weights used in the multi-criteria ranking are shown in Table 26 below. The overall score for each parasite is given by the following equation:

$$\text{Score} = C1*W1+C2*W2+\{C3*(1-C5)+C4*C5\}*W345+C6*W6+C7*W7+C8*W8+C9*W9$$

Table 26: Mean of elicited criteria weights used in the multi-criteria ranking (Table 3 from FAO/WHO, 2014).

Scoring Criterion		Criterion Weight
W1	Number of global food-borne illnesses	0.22
W2	Global distribution	0.14
W345	Morbidity severity	0.22
W6	Case-fatality ratio	0.15
W7	Increased illness potential	0.07
W8	Trade relevance	0.10
W9	Impacts on economically vulnerable communities	0.10

8.2 Examples of quantitative risk assessments

8.2.1 E. coli *O157:H7 in tenderized vs. non-tenderized beef, USDA-FSIS*

Mechanical tenderization, performed using stainless steel blades or needles, translocates pathogens from the surface of intact beef cuts to beneath the surface thereby potentially shielding those pathogens from the lethal effects of heat during cooking.

USDA FSIS aimed to estimate whether blade-tenderized steak posed a significantly greater risk than its equivalent non-tenderized steak (USDA-FSIS, 2002). They created a quantitative simulation model that predicted the change in survival of bacteria due to the extra protection that was afforded by being embedded in the meat through the tenderizing process. They estimated the bacterial load on steaks post-cooking and used this concentration as input into a dose-response model to estimate risk.

FSIS concluded that the probability of *E. coli* O157:H7 surviving typical cooking practices in either tenderized or not-tenderized steaks is minuscule and that differences in bacterial dose after cooking attributable to either type of steak were minimal. They predicted seven additional illnesses due to tenderization for every billion steak servings. This can be seen from Figure 9 below, where the dotted and solid lines for tenderized and non-tenderized steaks are virtually indistinguishable.

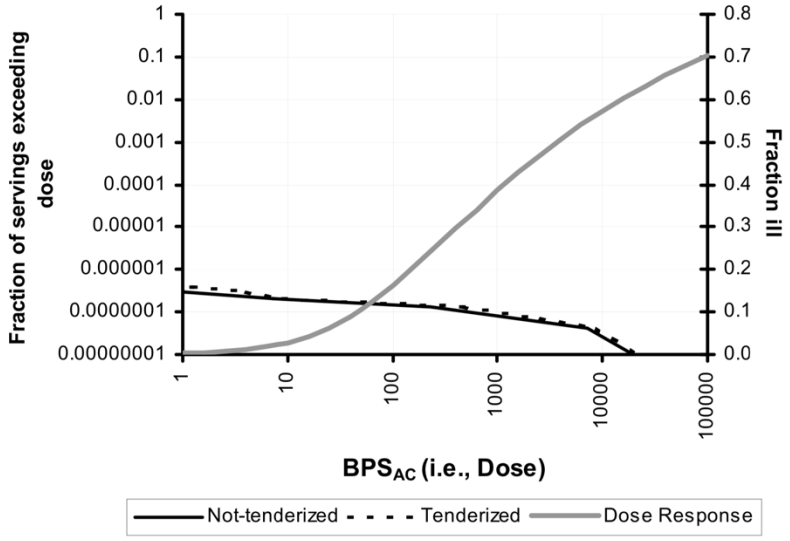


Figure 9: Model output showing predicted bacteria per serving after cooking (Dose) and corresponding frequency of illness (Dose Response).

This was a comparative risk assessment, so the model contained only the elements that were necessary to make the comparison. Thus, the model began with the distribution of bacteria on steak prior to tenderizing, and then looked at the difference in human health risk posed by the same steak under different processing. Consequently, there was no need to consider any factors involved in the rearing and slaughtering of the animal.

8.2.2 Listeria monocytogenes *in ready-to-eat foods, FAO/WHO*

FAO/WHO convened a drafting group to address three questions relating to *Listeria monocytogenes* that were posed by the Codex Committee on Food Hygiene (CAC, 2000).

Those questions were to (i) Estimate the risk of serious illness from *L. monocytogenes* in food when the number of organisms ranges from absence in 25 grams to 1,000 colony forming units (CFU) per gram or millilitre or does not exceed specified levels at the point of consumption; (ii) Estimate the risk of serious illness for consumers in different susceptible population groups (elderly, infants, pregnant women and immuno-compromised patients) relative to the general population; and (iii) Estimate the risk of serious illness from *L. monocytogenes* in foods that support its growth and foods that do not support its growth at specific storage and shelf life conditions.

The risk assessment (FAO/WHO, 2004) did not need to complete a full farm-to-fork model to answer these questions. The questions are also not specific to a particular country or product, which would require defining the scope of the model. The team decided to focus on the level of *Listeria monocytogenes* at retail; model the growth and inactivation from retail to consumption; and use a fitted dose-response function to estimate the subsequent risk.

The team selected four ready-to-eat foods to be reasonably representative of the many different foods available. The quantitative analysis produced the results shown in Table 27.

Table 27: Estimated risk from Listeria monocytogenes as used in the risk assessment (FAO/WHO, 2004).

Food	Cases of listeriosis per 10^9 people per year	Cases of listeriosis per 10^9 servings
Milk	910	0.5
Ice cream	1.2	0.0014
Smoked fish	46	2.1
Fermented meats	0.066	0.00025

The risk assessment report provides a very detailed explanation of the important limitations of the quantitative analysis, and, in particular, the need to rely on mostly European quantitative data on contamination, and on multiple sources for the prevalence estimates. Consumption data were mainly from North America, and the dose-response relationship was derived from epidemiological data from the United States of America. The summary response to the three Codex questions recognizes the caution that should be applied in interpreting the quantitative figures, by providing qualitative context.

> The report notes that the risk assessment demonstrates that most cases of listeriosis result from the consumption of high numbers of *Listeria*. Those cases arise from foods where the *L. monocytogenes* level exceeds the criteria (either 0.04 or 100 CFU/g). The model predicts that consumption of low numbers of *L. monocytogenes* has a low probability of illness. Eliminating higher levels of *L. monocytogenes* at the time of consumption has a large impact on the predicted number of illnesses. *(FAO/WHO, 2004):*

8.2.3 *Shiga-toxin-producing* E. coli *O157 in steak tartare patties, Netherlands*

Nauta *et al.* (2001) simulated the exposure the population in the Netherlands to Shiga-toxin-producing *E. coli* O157 in steak tartare, using a farm-to-fork Monte Carlo model. This risk assessment provided an example of integration of exposure assessment and hazard characterization with a low-level dose and an individual-level dose-response relation. The baseline model predicted 0.29% contaminated tartare patties and a mean dose of 190 CFU per contaminated patty, as shown in Table 28.

Table 28: Baseline risk model results at the stage of raw steak tartare patties, for different routes of exposure and the means for the Netherlands (NL). (Pos. tartare = STEC O157 contaminated steak tartare patty), where the column headers refer to specific segments of the Dutch industry (article 10 slaughter with 'industrial' butcher, article 10 slaughter with 'traditional' butcher and article 4 slaughter).

	Art 10, ind.	Art 10, trad.	Art 4	NL
Prevalence	0.29%	0.30%	0.21%	0.29%
Mean cfu/pos. tartare	3.4	670	1700	190

Pos. tartare with one cfu STEC O157	72%	38%	36%	64%

The dose-response model developed for the hazard characterization was based on a well-documented outbreak in a primary school in Japan (Shinagawa, Hu and Yoshida, 1997). An exponential model was fitted separately to the data for children and adults, resulting in point estimates for the probability of infection by a single cell of r = 0.0093 for children and r = 0.0051 for adults.

The exposure distribution was combined with the dose-response model in a Monte Carlo simulation by applying the single-hit model in the form $1-(1-r)^n$, with 'n' a random sample from the exposure distribution. The risk characterization predicted an attack rate of 0.0015% infections per person per year in the Netherlands; or 2,335 infections per 15.6 million people per year. This example incorporated variability but not uncertainty.

8.2.4 *Vibrio vulnificus in raw oysters, FAO/WHO*

An FAO/WHO assessment of the risk of illness due to *Vibrio vulnificus* in raw oysters adapted a risk model previously developed in the United States of America for *V. parahaemolyticus* (FAO/WHO, 2005). A principle objective was to investigate potential effectiveness of mitigations after development of a baseline model. This risk assessment provides an example of integration of exposure assessment and hazard characterization, with different assumptions used in estimating the dose-response.

A dose-response relationship for *V. vulnificus* was obtained by fitting a parametric model (Beta-Poisson) to estimated arithmetic mean risk for the population versus arithmetic mean dose (grouped by month and year). The magnitude of the difference between risk predictions obtained under these two alternative interpretations of the dose response is shown in Table 29. Assuming that the fitted population-level risk versus dose relationship applied at the individual level resulted in predictions of risk that were consistently lower (by up to 75%) than the epidemiological estimates of mean risks. The predictions of risk obtained based on an aggregate-level interpretation of the dose response were more consistent, on average, with the epidemiological estimates of mean risks used to obtain the dose-response fit, so this latter interpretation was used for risk characterization.

Table 29: Mean risk of illness due to Vibrio vulnificus per serving or exposure.

		Fitted as individual-level risk versus dose		**Fitted as mean risk versus mean dose**	
Season	**Estimated data based on case reports and consumption statistics**	**Risk**	**Ratio to Estimated Data**	**Risk**	**Ratio to Estimated Data**
Winter	1.40E-06	5.10E-07	0.36	1.10E-06	0.79
Spring	2.80E-05	1.70E-05	0.61	3.40E-05	1.21
Summer	4.90E-05	2.80E-05	0.57	3.90E-05	0.80
Autumn	1.90E-05	5.10E-06	0.27	2.30E-05	1.21

8.2.5 *Histamine in Fish Sauce, Thailand*

Fish sauce is a fundamental ingredient used in many Southeast Asian dishes and is also used as a dipping condiment. Due to the nature of raw materials and the production methods for traditional fish sauce, highs levels of histamine are found in many samples.

A risk assessment on histamine in Thai fish sauce was undertaken to respond to the request of the Codex Committee on Fish and Fishery products for sound scientific advice as a basis for the development of guidelines for the control of histamine in fish sauce (CCFFP, 2011).

Previous human trials and outbreak data were used to build a histamine dose-response model. The risk of developing histamine poisoning from fish sauce among Thai consumers was estimated. Consumption of fish sauce alone yielded a very small histamine intake to consumers. Different scenarios reflecting the effect of different histamine standards were also evaluated and are shown in the Table 30 below. As the analysis shows, the risk from fish sauce alone is essentially zero, and clearly less than the risk of histamine poisoning from fish alone. When the risk of histamine poisoning from fish plus fish sauce with two different standards was estimated, the risk increased slightly.

Table 30: Risk estimates using probabilistic approach (Table 5 in CCFFP, 2011).

Scenario	Mean risk per meal (SD)[a]
1. Fish sauce alone (a FS daily dose was consumed in 1 meal)	0.00 (0.00)
2. Fish alone[b] (a fish daily dose was consumed in a meal)	8.12×10^{-6} (0.4×10^{-5})
3. Fish + Fish sauce (a FS daily dose was consumed in 1 meal)	
• 200ppm FS standard	8.39×10^{-6} (0.46×10^{-5})
• 400ppm FS standard	8.47×10^{-6} (0.52×10^{-5})

[a] Risk per meal refers to the predicted risk of an individual becoming ill of histamine poisoning when he or she consumes a daily dose of fish sauce (FS) or a daily dose of a scombroid fish or a scombroid fish with fish sauce. The risk was estimated as a probability of the histamine intake to exceed the NOAEL limit of 50mg using Monte-Carlo simulations.

[b] Assumption: a fresh scombroid fish had a lognormal distribution with an average of histamine concentration of 5ppm and standard deviation of 10ppm.

8.2.6 *Pathogens in Fresh Vegetables, Rwanda*

This study analysed the "farm to fork" microbial risk for the fresh vegetable supply chain in Rwanda, (Ssemanda, 2018). One of the major data gaps identified by the authors was that they could not attribute the estimates of food related illnesses to any food vehicle based on the available data. Despite these limitations, the authors were able to evaluate several scenarios related to the distribution chain including: (i) moving all vegetables from farms to food service establishments without going through markets (ii) moving all vegetables from farms via supermarkets (with specialized refrigeration systems) to food service establishments (iii) holding all vegetables under refrigeration (2 and 8°C) from farm to fork and the introduction of a die off model (iv) all vegetables are effectively washed and sanitized, accomplished by increasing the modelled log reduction by washing (v) assuming no contamination and cross contamination occurs between vegetables and other surfaces throughout the chain (vi) assuming that preventive measures and interventions implemented at farm level reduce prevalence and levels of pathogenic *E. coli* by 90% and (vii) finally by assuming that the last three scenarios above are combined.

Simulation of the 7 "what if" scenarios described above resulted in varying fold-changes in the predicted microbial risk **Error! Not a valid bookmark self-reference.**. Improvement in washing and sanitization at food service establishments resulted in less than a 2-fold change in the predicted microbial risk. About a two-fold reduction in risk was observed for the what-if scenario of channelling all vegetables through supermarkets instead of traditional markets. Farm interventions reduced the predicted prevalence and levels of pathogenic *E. coli* in the base line model by 90%, introducing a cold chain and skipping the market step resulted in a tenfold reduction in predicted microbial risk. The what if scenario of avoiding contamination and cross contamination along the

supply chain led to a more than 4000-fold reduction in the predicted microbial risk. Lastly, combining the final three “farm to fork” measures resulted an estimated reduction in risk of 1 million.

Table 31: Number of illnesses per year and probability of illness per serving after 100,000 iterations of the baseline model and the what if scenarios (Table 6.4 in Ssemanda, 2018).

What if scenarios [b]	No. of illnesses per year (in millions)		Probability of illness per serving		Fold change[#]
	Mode	5th, 95th Percentile	Mode	5th, 95th Percentile	
Baseline/Route 1[a]	12.1	6.96, 32.6	0.100	0.0572, 0.169	–
Improving washing and sanitization at FSEs	10.63	2.13, 27.8	0.1039	0.0151, 0.156	1.14
Route 3	6.26	0.828, 17.3	0.0535	0.0395, 0.0057	1.93
Farm Interventions	1.13	0.517, 3.101	0.01029	0.00395, 0.0165	10.71
Introduction of cold chain	0.288	0.218, 15.1	0.00042	0.0015, 0.1016	42.01
Route 2 (market step skipped)	0.139	0.195, 10.87	0.000455	0.0013, 0.0728	87.1
No contamination and cross contamination along the supply chain	0.00272	0.00339, 9.4	0.0000183	0.0002, 0.0564	4,449
Farm to fork measures and interventions	0.00001108	0.0000144,0.694	7.33×10^{-8}	0.000, 0.00494	1.1×10^{6}

[a] Baseline model or Route 1 represents a simulation of the supply chain through which about 90% of the vegetables are channelled from farms via traditional markets to food service establishments (FSEs)

–, not applicable

#, Fold change were calculated by dividing the mode for the numbers of illness per year in the baseline model with the mode for the numbers of illness per year in the what if scenarios.

[b] What if scenarios arranged in descending order of the number of illnesses per year and probability of illness per serving.

8.2.7 *Campylobacter and Salmonella in Chicken Meals, Senegal*

The authors used a QMRA model to describe the risk of *Campylobacter* and *Salmonella* infection linked to chicken meals prepared in households in Dakar, Senegal (Pouillot *et al.*, 2012). The authors note that prevalence and concentration of pathogens in foods available in developing countries are well-known data gaps for risk assessment. They also suggest that more information on home cooking practices, cooking processes, and the length and temperature of food storage before and after preparation are needed. They used data collected specifically for purposes of QMRA, including prevalence and level of bacteria on chickens from local markets, time-temperature profiles of chickens from purchase to consumption, an observational data from meal preparation in kitchens, and data on pathogens prevalence on utensils, equipment and cooks' hands. Their model was developed in R software using the mc2d package for second-order Monte Carlo simulations. The simulation used 10,001 iterations in the variability dimension and 1,001 iterations in the uncertainty dimension. The model predicted that cross contamination led to a high expected frequency of pathogen ingestion, and that significant *Salmonella* growth was predicted during food storage at ambient temperature before and after meal preparation. The model also predicted a significant decrease in risk could be achieved through reducing prevalence of chicken contamination at slaughter, and by using simple hygienic measures in the kitchen. The model indicated that most effective modification to home cooking practices include the use of a new board, knife, and dish when manipulating the cooked chicken, assuming that these objects are bacteria-free. Figure 10 below illustrates the conceptual model used for quantitative exposure assessment for pathogens in households from the study.

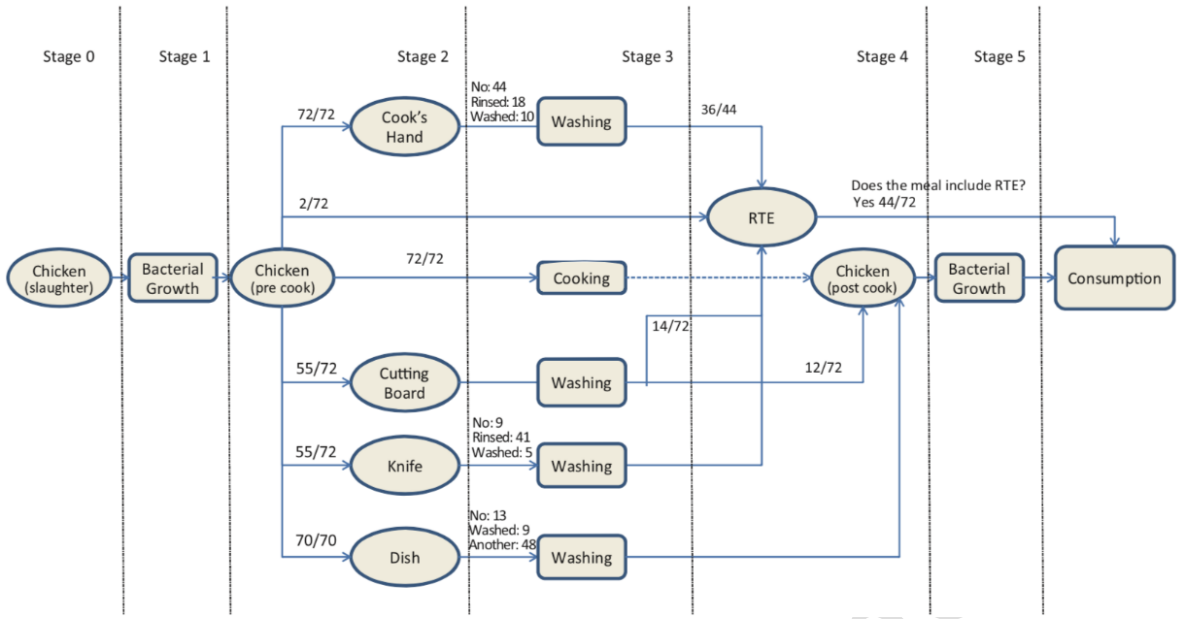


Figure 10: Model diagram of the quantitative exposure assessment for Campylobacter and Salmonella in Dakar households (Figure 1 in Pouillot et al., 2012)..

8.2.8 *Vibrio parahaemolyticus in bloody clams, Thailand*

A microbiological risk assessment of *Vibrio parahaemolyticus* risk from *Anadara granosa* (Bloody clam) was conducted by researchers from Thailand and Japan, who developed two risk assessments (a farm-to-fork model and a fractional change model) based on new data collected primarily from Hat Yai City in southern Thailand, where seafood consumption is popular. The QMRAs were published as part of the FAO/WHO Microbiological risk assessment series in a book entitled " Risk assessment of *Vibrio parahaemolyticus* in seafood (FAO/WHO, 2011a)".

The purpose of the risk assessment was to estimate the risk of *V. parahaemolyticus* infection associated with consumption of one type of seafood in a defined setting and during a limited period. The work documents an example of a case study in a developing country, where scientists were able to conduct a series of clinical and microbiological studies to generate locally relevant data and elaborate a risk assessment model for a non-oyster shellfish species.

The authors report that the study estimated that only a few people per 10,000 people per year acquire *V. parahaemolyticus* infection as a result of consuming the boiled Bloody clam food. The risk estimate does not support the common perception that Bloody clam is a major cause of diarrhoeal illness, including *V. parahaemolyticus* illnesses.

At the same time, the investigators caution that this study may also underestimate the risk of Bloody clam-associated *V. parahaemolyticus* illness due to several critical data gaps. The authors recommended that a case-control study be conducted using patients in Hat Yai City with microbiologically confirmed *V. parahaemolyticus* infections, as this could provide data on various food and environmental exposure paths. These investigations might also provide more realistic evidence of behaviour that reduces or increases the risk of *V. parahaemolyticus* illness. The investigators also suggested that more bacterial data on Bloody clam throughout the food chain should be collected, focusing on detection of virulent strains. Finally, the authors encouraged the collection of more detailed data on behaviour regarding harvesting, storage, cooking and consumption patterns need to be collected.

The figure below shows a representation of the model for a production-to-consumption QMRA for *V. parahaemolyticus* in Bloody clam.

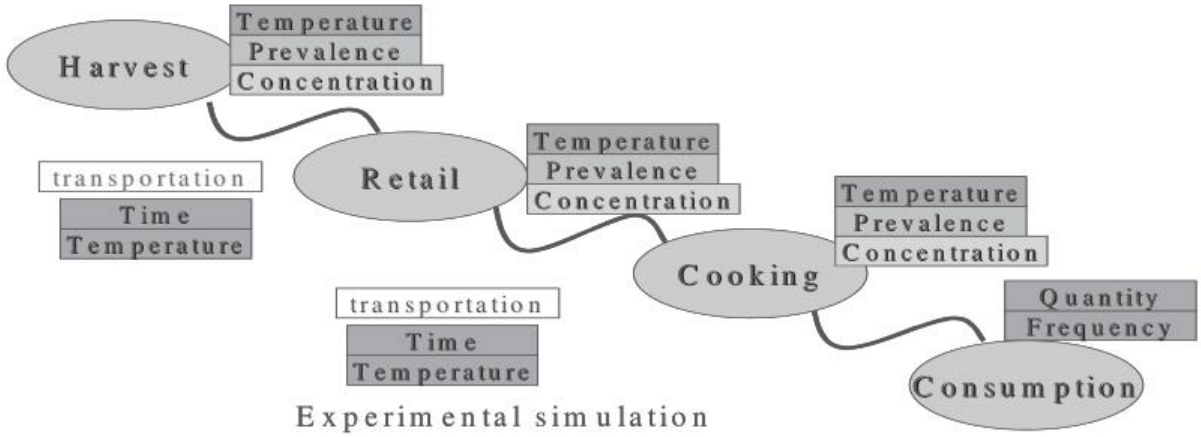


Figure 11: Schematic representation of the model framework for a production-to-consumption risk assessment of V. parahaemolyticus in Bloody clam (Figure II-6 in FAO/WHO, 2011a).

8.2.9 *Salmonella in table eggs, EFSA*

This risk assessment was developed by EFSA, the risk assessor, to answer a European Commission's (EC; the risk manager), question about the risk of *Salmonella* in eggs (EFSA, 2014b). The EC asked EFSA to assess the public health risk posed by *Salmonella* from table eggs and to quantify the relevance of the period of time between laying and consumption and the storage conditions of eggs. The period of time between laying and consumption is related with the "Sell-By date" and the "Best-Before date". The "Sell-By date" applicable to eggs is fixed at 21 days by the EU Hygiene Regulation. This means that table eggs must be delivered to the consumers within of 21 days after laying. The "Best-Before date" applicable to eggs is fixed in Regulation 589/2008 at 28 days from laying.

EFSA applied a quantitative risk assessment model for *S*. Enteritidis in eggs to answer the question. The quantitative model excluded all stages before laying. A baseline scenario was defined according to the current sell-by and best-before dates in the EU. Changes to time and temperature of storage at retail and in the household, were used to assess the impact storage practices as alternative scenarios (Table 32).

Table 32: Dates used in the model for the baseline and alternative scenarios (Table 11 in EFSA, 2014b)

Days post lay / Scenarios	Sell-by date (retail				Best-before date (household/catering)					
	21	28	35	42	28	35	42	56	63	70
Baseline	•				•					
Alternative 1		•			•	•	•	•	•	•
Alternative 2			•			•	•	•	•	•
Alternative 3				•			•	•	•	•
Alternative 4		◊			•	•	•	•	•	•
Alternative 5			◊			•	•	•	•	•
Alternative 6				◊			•	•	•	•
Worst-case scenario				•						•

• Scenarios with egg storage at retail under current conditions

◊ Scenarios with egg storage under refrigeration conditions in all retail establishments

Storage temperature and time were modelled using distributions based on expert opinion. The remaining distributions were adapted from the model using expert opinion distribution or based on scientific literature. Table 33 below shows a summary of time and temperature of storage of eggs in the EU, from farm to retail as derived from industry expert opinion.

Table 33: Summary of time and temperature of storage of eggs in the EU, from the 'on farm' to the 'transport to retail' stages as derived from expert opinion (industry experts) (Table 6 in EFSA, 2014b).

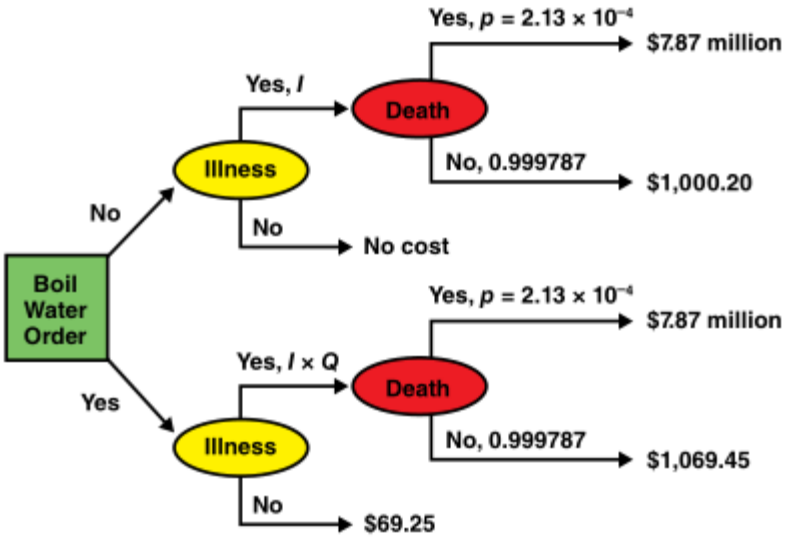
	Time (hours)			Temperature (°C)		
Stage	**Min.**	**Most likely**	**Max.**	**Min.**	**Most likely**	**Max.**
On farm	0	45	168	4	15	30
Transport to grading	0	6	48	4	15	30
Grading	0	18	168	5	15	30
Transport to wholesale	0	5	48	0.1	14	30
Wholesale/ distribution centre	0	23	336	0.1	13	28
Transport to retail	0	7.5	36	0	14	30

Extending the storage time for table eggs resulted in an increase in the number of illnesses, except when eggs are well-cooked. Extending the sell-by date by one week (from 21 to 28 days), but leaving best-before date unchanged, was estimated to result in a relative risk of illness of 1.4 and 1.5 for uncooked and lightly cooked egg meals respectively, compared to the baseline. If the best-before date was also extended by one week (from 28 to 35 days), the relative risk was 1.6 and 1.7. In the worst-case scenario considered in this assessment (sell-by date of 42 days, best before date of 70 days), the risks of illness were 2.9 and 3.5.

EFSA found that the implementation of refrigeration as currently used in the EU during the retail stage (i.e. with temperatures assumed to range from 0 to 12 °C) limited this increase in risk to some extent. The risk was reduced with an extension of up to three weeks in the sell-by date, and one or two weeks of the best-before date for a sell-by date of 35 and 28 days respectively if refrigeration was applied in all retail establishments. If the sell-by date or the best-before date were prolonged beyond three weeks, the risk estimates were greater, even if refrigeration at retail was applied, assuming that the proportion of consumers who do not store their eggs under refrigeration remained unchanged.

8.2.10 Cryptosporidium *in water – a cost-benefit analysis, United States*

The authors developed a simple decision tree (Figure 12) for *Boil Water Order* (BWO), including the effectiveness of the BWO as well as illness and death as possible outcomes (Ryan *et al.*, 2013). For each branch in the decision tree they assigned the relevant probabilities including the probability of illness, probability of death, and probability of the boiling process being ineffective, e.g. due to too short a boiling time or boiled water being transferred to a nondisinfected container, or other factors. Estimates for these probabilities, and for costs of implementation and for the various outcomes were based on published literature, including from the United States Environmental Protection Agency, and the uncertainty in these estimates were evaluated using a Monte-Carlo sensitivity analysis.



***I*—the probability of illness, *Q*—the probability that the boil water order is ineffective, *p*—the probability of death from illness, 0.999787—the probability of no death from illness**

Figure 12: Decision tree for Boil Water Orders for Cryptosporidium *showing the probabilities and estimated costs for illness and death outcomes (Ryan* et al.*, 2013).*

The authors used the decision tree to calculate a threshold value for the oocyst concentration in treated water using an exponential dose response model; this was done by equating the BWO and No BWO branches and solving for the daily dose and associated concentration. The authors concluded that this threshold concentration was equal to 0.046 oocysts/L in treated water or 46 oocysts/L in raw water, which was considered to be more practical to assess using water sampling. These concentrations were estimated to result in 9 illnesses per 10,000 people exposed, given the assumed 3-$\log_{10}$ reduction during water treatment. However, the authors also noted that "many water supplies that exceed this concentration may already be applying additional treatment, given that a concentration of 46 oocysts/L would require treatment beyond the 3-log removal required by the Long Term Enhanced Surface Water Treatment Rule."