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risk assessment in
food processing*

Edited by Martyn Brown and Mike Stringer



Microbiological risk assessment in food processing

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**Edited by
Martyn Brown and Mike Stringer**



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Contents

<i>List of contributors</i>	xi
<i>Preface</i>	xv
1 Introduction	1
<i>M. Brown, Unilever Research, Sharnbrook and M. Stringer, Campden and Chorleywood Food Research Association, Chipping Campden</i>	
1.1 References	4
2 The evolution of microbiological risk assessment	5
<i>S. Notermans and A. W. Barendsz, TNO Nutrition and Food Research Institute, Zeist and F. Rombouts, Wageningen Universiteit</i>	
2.1 Introduction	5
2.2 Historical aspects of safe food production	6
2.3 The evolution of food safety systems	7
2.4 International food safety standards	23
2.5 Present and future uses of microbiological risk assessment ..	29
2.6 List of abbreviations	38
2.7 References	39
Part I The methodology of microbiological risk assessment	45
3 Microbiological risk assessment (MRA): an introduction	47
<i>J. L. Jouve, Ecole Nationale Vétérinaire de Nantes</i>	
3.1 Introduction	47

3.2	Key steps in MRA	49
3.3	Hazard identification	53
3.4	Hazard characterisation/dose–response assessment	54
3.5	Exposure assessment	57
3.6	Risk characterisation	60
3.7	References	63
4	Hazard identification	64
	<i>M. Brown, Unilever Research, Sharnbrook</i>	
4.1	Introduction: the importance of correct hazard identification	64
4.2	What is hazard identification?	64
4.3	What hazard identification should cover and produce as an output	65
4.4	What to do in hazard identification	66
4.5	Key information in hazard identification	67
4.6	Tools in hazard identification	69
4.7	Microbial hazards	70
4.8	Identifying the origin and distribution of microbial hazards	72
4.9	Changes in microbial hazards	73
4.10	Other biological hazards	75
4.11	References	75
5	Hazard characterization/dose–response assessment	77
	<i>S. B. Dennis, M. D. Milotis and R. L. Buchanan, US FDA, College Park</i>	
5.1	Introduction: key issues in hazard characterization	77
5.2	Types of dose–response data	83
5.3	Modeling dose–response relationships	86
5.4	Problems in hazard characterization	90
5.5	Future trends	94
5.6	Sources of further information and advice	96
5.7	References	97
6	Exposure assessment	100
	<i>M. Brown, Unilever Research, Sharnbrook</i>	
6.1	Introduction	100
6.2	The role of exposure assessments in microbiological risk assessment	101
6.3	What’s in an exposure assessment?	105
6.4	Who should do an exposure assessment and when?	109
6.5	Building up supply chain data for an exposure assessment ..	109
6.6	Sources of information	111
6.7	Types of data used in an exposure assessment	114

6.8	The output of an exposure assessment	117
6.9	References	123
7	Risk characterisation	127
	<i>P. Voysey, K. Jewell and M. Stringer, Campden and Chorleywood Food Research Association, Chipping Campden</i>	
7.1	Introduction: key issues in risk characterisation	127
7.2	Risk characterisation requirements	129
7.3	Risk characterisation methods	135
7.4	Quantitative and qualitative outputs	142
7.5	Risk characterisation in practice: some examples	147
7.6	Current problems and future trends	151
7.7	References	153
8	Risk communication	155
	<i>R. Mitchell, Public Health Laboratory Service, London</i>	
8.1	Introduction	155
8.2	The concept of risk	156
8.3	Risk perception	158
8.4	The concept of communication	163
8.5	Risk communication	166
8.6	The future of risk communication	169
8.7	References	170
Part II	Implementing microbiological risk assessments	173
9	Implementing the results of a microbiological risk assessment: pathogen risk assessment	175
	<i>M. Van Schothorst, Wageningen University</i>	
9.1	Introduction	175
9.2	Establishing food safety objectives	177
9.3	Developing food safety management strategies	181
9.4	Establishing microbiological criteria	185
9.5	Problems in implementation	190
9.6	Future trends	191
9.7	References	191
9.8	Acknowledgement	192
10	Tools for microbiological risk assessment	193
	<i>T. Wiltzes, Wiltzes Food Consultancy, Gorinchem</i>	
10.1	Introduction	193
10.2	Qualitative tools for risk assessment	195
10.3	Predictive modelling	196
10.4	Tools for modelling, prediction and validation	203
10.5	Future trends	209

10.6	Sources of further information and advice	210
10.7	References	211
11	Microbiological criteria and microbiological risk assessment	214
	<i>T. Ross, University of Tasmania, and C. Chan, Safe Food Production NSW, Sydney</i>	
11.1	Introduction	214
11.2	Types of criteria	215
11.3	Key issues in the use of microbiological criteria	217
11.4	Dealing with variability, uncertainty and hazard severity: sampling plans	221
11.5	Microbiological criteria and food safety assurance: food safety objectives	226
11.6	Using microbiological risk assessments: to set microbiological criteria	228
11.7	Using microbiological risk assessments to develop performance and process criteria	231
11.8	Using microbiological risk assessments to prioritise risk management actions	236
11.9	Using criteria in risk assessments	237
11.10	Future trends	239
11.11	Further reading	240
11.12	References	241
	Appendix	246
12	HACCP systems and microbiological risk assessment	248
	<i>R. Gaze, R. Betts and M. Stringer, Campden and Chorleywood Food Research Association, Chipping Campden</i>	
12.1	Introduction	248
12.2	Legal requirements for HACCP systems	249
12.3	International guidance on HACCP implementation	250
12.4	Problems in HACCP implementation	256
12.5	The interaction between HACCP systems and microbiological risk assessment (MRA)	258
12.6	The future relationship of HACCP systems and MRA	261
12.7	References	263
13	The future of microbiological risk assessment	266
	<i>M. Brown, Unilever Research, Sharnbrook and M. Stringer, Campden and Chorleywood Food Research Association, Chipping Campden</i>	
13.1	Introduction	266
13.2	Information needs for risk assessment	269
13.3	How should risk assessment processes develop?	278

13.4	Key steps in risk assessment	280
13.5	Risk acceptance	284
13.6	The outputs of risk assessment: risk management and communication	289
13.7	Conclusion	292
13.8	References	292
<i>Index</i>		293

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Preface

Complete elimination of risk from food manufacture and consumption is an impossible goal, but risk reduction is an essential part of every food producer's responsibility to protect both its customers and its business. Risk reduction is necessary because the term risk is never applied to good events. This book presents microbiological risk analysis (MRA) concepts, principles and techniques to help the reader understand and use them for managing food safety.

Theoretical studies and research work in the area of risk have provided powerful analytical tools for dealing with microbiological and epidemiological information, reaching and communicating decisions and then taking preventative actions that are appropriate to the hazard, consumers and the intended use of the product. The use of a range of indirect assessment tools as explained in the chapters of this book is necessary because risk cannot be directly measured; it can only be calculated, based on data indicating probability and type of hazard. Many of the techniques available have their roots in risk assessment in other fields; the chapter authors have refined their application to microbiological risk assessment. Similarly many international organisations (e.g. World Health Organisation, Codex Alimentarius, International Life Sciences Institute and the International Commission on Microbiological Specifications for Foods) are also focussing these tools on microbiological hazards, whilst also trying to maintain uniformity in risk-based approaches to protecting all aspects of public health, so that it is evident to consumers that chemical and microbiological hazards are assessed in the same way.

The performance of MRA will always be limited by the availability of data. In spite of this, informal risk assessments leading to management actions are taken every day based on expert opinion and assumptions that cannot be validated. Part of the function of this book is to highlight the benefits of formal

risk analysis systems and encourage risk managers to ensure that transparent and unbiased risk assessment processes and the best available data are used for decision making. As part of this process, uncertainties and variability or imperfections in data should be clearly identified and taken into account by decisions. Methods for doing this are explained. Potential users of MRA rightly expect the technique to produce results that they can use to suggest controls and improvements at costs that their products can bear and their consumers accept. Use of formal MRA systems will increase the chances of achieving this; but performance will always be limited by the availability of information for the risk assessment. It should be within the capabilities of anyone undertaking a risk assessment to identify hazards and generate reliable supply chain data for the exposure assessment, the weak link may lie in providing hazard characterisations appropriate to consumers. As foods and drinks are increasingly 'tailored' for specific consumer groups it is important that we have a better knowledge of the relationship between exposure to a particular hazard and the severity of any associated adverse health effects.

Governmental management of food safety is changing on a global basis to meet the challenge of changing patterns in the food trade, such as globalisation of the food supply. In the near future, there is the challenge of how MRA will lead to the establishment of food safety objectives, providing an appropriate level of protection and how this will impinge on industrial food safety management practices such as HACCP. Independent, consumer focussed national (e.g. UK Food Standards Agency) and regional authorities (e.g. European Food Safety Authority) have been established and they are seeking common ways of working. Never before has the requirement for absolute transparency in the decision-making process behind food safety management policy been so necessary. The three components of risk analysis suggested by Codex Alimentarius – assessment, communication and management are now accepted tools for reaching supportable decisions on public health policy, risk management strategies and preventative measures. To be credible, such decision making has to be based on the available science and take account of political, economic and other factors that may alter local perception of a risk. Additionally the techniques have far wider application at the food production level. For communicating and managing risks at the plant level by providing material for improved hazard analyses and providing information to help trading partners and consumers make informed choices.

The topic of risk is frequently examined by the media, who often dwell on knowledge of a new hazard or a change in risk to the extent that many consumers feel that they face more risks from food today than in the past and producers feel that changes in the trading environment and consumer preference introduce new hazards and increased levels of risk. This book only deals with the technical analysis of risk; the topics of risk perception and acceptable risk are not covered because expertise in MRA does not yet exist to address these issues. The best that can be produced by risk assessors is a technically justifiable evaluation of real (rather than perceived) risks, with uncertainty and variability

clearly explained. Microbiologists cannot handle perceived risks because every consumer is different and each one perceives hazards and risks differently, making it difficult to reach valid conclusions. Risk assessment can however improve the performance of risk management tools, such as HACCP, and this is well illustrated by the chapters.

Risk analysis is focused on microbiological safety because injuries and deaths caused by food have the most serious implications possible for a country or business (e.g. BSE), it is very difficult to fully quantify the costs of consumer compensation or liability in defining the implications of safety management failures. Often these costs are borne centrally, whereas risk management decisions are made at the local level. Closer commercial links between suppliers and retailers and users of products has resulted in a need for much closer control and management of food hygiene and safety. This book is aimed at helping risk managers take a wider view of systems and techniques, so that they can directly contribute to the success of their business or agency. Different products have different hazards and different consumers different sensitivities and this must be considered by risk assessor and risk manager in developing risk cost effective management procedures.

The most serious long-term consequence of a safety failure for a food business is a decision by consumers to change their eating habits; risk modification is an action everybody takes to some extent. An unpredictable change in eating habits, because of unidentified or uncontrolled hazards can destroy the value of a business. Therefore decisions between course of action available to a risk manager, including providing information to consumers must be guided by the best information (risk assessment) and the most transparent procedures available – risk management and communication. A comprehensive MRA provides a framework from which the potential effectiveness of different intervention or mitigation strategies for risk management can be assessed, thus enabling more scientifically robust decision making. Users of this book need to remember that risk analysis deals with real events and real consequences and that people (e.g. consumers and plant staff and management) are an integral part of the process of assessment and management. MRA should be used for decision making or trade-offs, limited by acceptable risk on one hand and consumer preference on the other. No magic words or infallible techniques exist in this area, this book only provides access to the existing tools and sources of information.

Martyn Brown and Mike Stringer

1

Introduction

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Attempts to assess the nature of the risks posed by foodborne pathogens to consumers have long been undertaken by the food industry as a means of ensuring safe food. However, the 1990s in particular have seen growing government and industry commitment towards developing an internationally-accepted methodology for assessing the importance of microbiological risks. A number of factors have driven this process. Serious and well-publicised outbreaks of foodborne disease in the US and Europe have highlighted the need to improve the identification of new hazards, the assessment and management of existing microbiological food safety risks, and the need for dialogue with consumers about microbiological safety (Pennington, 1997; Tuttle *et al.*, 1999). At the same time, developments in risk assessment methodology, better microbiological data and greater computing power have made it possible to develop more sophisticated and meaningful risk assessments (Tennant, 1997; Benford, 2001; Morgan, 1993).

Further impetus has been provided by the continued globalisation of the food supply, and renewed attempts to harmonise food safety principles and practice in international trade. In 1993 the Uruguay Round of the General Agreement on Tariffs and Trade (GATT) resolved that barriers to international trade in food, including those designed to protect public health, could only be science-based. In response, member countries of the World Trade Organisation (WTO) concluded the sanitary and phytosanitary (SPS) agreement (Anon, 1995a and b). The SPS agreement proposed the key requirements necessary to demonstrate equivalent levels of safety in foods originating in different nations, produced by different manufacturing systems and complying with differing regulatory requirements. The agreement requires that food safety measures taken by individual countries are:

2 Microbiological risk assessment in food processing

- applied only to the extent required to protect human health
- based on scientific principles
- not maintained without scientific evidence
- based on an assessment of the risk to health that is appropriate to the circumstance

The WTO turned for guidance on defining suitable criteria to the Codex Committee on Food Hygiene of the Codex Alimentarius Commission (CAC), the body set up by the WTO and the Food and Agriculture Organisation (FAO) of the United Nations to develop benchmark standards and procedures for international food safety management. The CAC subsequently developed principles and guidelines to define the nature of, and provide a methodology for, assessing the risks to human health from pathogens in foods (Anon., 1996; Anon., 1999). These guidelines provide the foundation for a common methodology for microbiological risk assessment and management by WTO countries.

The CAC defines microbiological risk assessment as a scientifically-based process involving four key steps which are designed to produce a risk estimate:

1. hazard identification
2. hazard characterisation
3. exposure assessment
4. risk characterisation

Hazard identification identifies the causal relationship between a pathogenic agent, an illness and a food as one vector of a specified illness. Hazard characterisation, or dose-response characterisation as this stage is also known, attempts to relate the probability and severity of illness to the dose of the pathogen (or toxin) ingested by the consumer. Exposure assessment seeks to estimate the scale of exposure by assessing how much and how often consumers are exposed to a hazardous agent in food as a result of contamination levels and the effects of processing, distribution and consumer use. Finally, risk characterisation synthesises the output of the previous stages to provide an estimate (qualitative or quantitative) of the level of risk for a defined group of consumers from the identified pathogen in a particular food product.

This introduction shows that microbiological risk assessment is still a relatively new and emerging discipline. Relatively few formal microbiological risk assessments have been completed, in part because of the resources required and the relative paucity of information in some areas. In particular, few formal assessments have been undertaken by the food industry to form the basis for risk management decisions. As a result, much remains to be discovered in the light of practical experience (some of these completed assessments are discussed in Chapter 7). A number of immediate challenges have been identified by individual formal assessments. These challenges include (Anon., 2000a and b; Ross and McMeekin, 2002):

- problems in the quantity and quality of suitable and relevant data
- issues in the handling of variability and uncertainty

- the limited availability of trained personnel
- debates over methodology, for example how best to model the inputs of the hazard to the supply chain and the resulting outputs with the product, and how to model dose-response data
- how to express the output of a risk assessment in a way that is both accurate and meaningful to food safety managers and consumers

This book is the first comprehensive review not only of the methodology of microbiological risk assessment in the light of experience, but also of the range of problems encountered in practice and how these might be addressed. Two initial chapters set the scene. The first (Chapter 2) puts microbiological risk assessment in the context of the broader development of international food safety standards, whilst Chapter 3 introduces basic microbiological risk assessment methodology. These chapters are followed by authoritative coverage of the four key stages in microbiological risk assessment (Chapters 4 to 7), explaining and reviewing the individual steps which underpin each stage, the problems involved in a practical study and how they might be overcome or, their effects at least, minimised. A subsequent chapter (Chapter 10) reviews the range of qualitative, quantitative and computational tools (such as predictive modelling) available to support each of these stages in an assessment.

The CAC has placed risk assessment as the first step within a broader framework of risk analysis consisting of:

- risk assessment
- risk communication
- risk management

As its name suggests, risk assessment provides a formal, validated and transparent estimate of the level of risk which can be communicated to key groups, such as policy and decision makers, QA professionals and consumers. Such assessments provide a basis for making decisions, setting priorities and adopting appropriate procedures for food safety management. The book therefore includes a chapter on the challenge of risk communication (Chapter 8). There is also a detailed introduction to the issues involved in using risk assessment as a basis for the effective management of pathogen risks related to food production (Chapter 9). Chapter 11 discusses how such assessments can be used to establish microbiological criteria (for specifications) and food safety objectives (FSOs). The chapter shows how these can be used as inputs into food safety management tools such as hazard analysis and critical control point (HACCP) systems, or as benchmarks for establishing equivalence between food safety management or regulatory regimes. Chapter 12 considers in detail the critical relationship between microbiological risk assessment and food safety management systems such as HACCP systems. The concluding chapter looks at the future of microbiological risk assessment, including developments in methodology, risk communication and management, and the acceptance of risk by consumers.

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2

The evolution of microbiological risk assessment

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2.1 Introduction

Microbial risk assessment (MRA) is a relatively new tool in the quest for a better means of ensuring the production of safe food. As stated in Chapter 1, MRA comprises four successive key steps: (i) hazard identification, (ii) hazard characterisation, (iii) exposure assessment and (iv) risk characterisation. The use of risk assessment ensures that control of food safety is based on a logical and scientific approach to the problems involved. In practice, elements of MRA have been utilised for many years, although, in earlier times, they were not formally recognised as such. Hazard identification, for example, began at the end of the nineteenth century when the work of van Ermengem served to clarify the etiology of botulism in humans (Van Ermengem, 1896). Later milestones in this category included the recognition of *Clostridium perfringens* as a foodborne pathogen in 1943 (McClane, 1979) and *Bacillus cereus* in the 1950s (Granum, 1997). Human infections with *Listeria monocytogenes* were well known by the 1940s and foodborne transmission was suspected (Rocourt and Cossart, 1997), but it was not until the occurrence of an outbreak in Canada in 1981 that conclusive evidence was obtained. In this case, illness followed the consumption of contaminated coleslaw (Farber and Peterkin, 2000). Since then, numerous foodborne outbreaks have been reported in different countries, and prevention of listeriosis has become a major challenge for the food industry.

Regarding hazard characterisation, data have been obtained from the analysis of many incidents of foodborne disease. Although such information is not sufficient to establish dose–response relationships, some outbreaks have yielded useful data on attack rates and exposure levels for particular pathogens.

6 Microbiological risk assessment in food processing

Even in the distant past, there was evidence of a rational approach to the control of food safety. Therefore, the evaluation of MRA in this chapter begins with some historical aspects of safe food production, followed by discussion of food control systems that have been developed and applied in the past, with special reference to MRA principles. Section 2.4 deals with the establishment of international food safety standards based on the use of risk assessment. In Section 2.5, consideration is given to the ways in which MRA is becoming integrated in food industry practices and some examples of beneficial applications are included. Finally, current issues in MRA are discussed.

2.2 Historical aspects of safe food production

The need to produce safe food has a long history. Problems with foodborne diseases must have been a continuous preoccupation of early humans once they began their hunting and food-gathering activities, and domestic production of food animals and crops. Although the exact timing is uncertain, organised food production probably started between 18 300 and 17 000 years ago, when barley production is said to have flourished in the Egyptian Nile Valley (Wendorf *et al.*, 1979). During that time, there was a need to preserve the grain and keeping it in a dry condition was an obvious precaution. Attempts to preserve other foods were based mainly on experience gained in associating the spoilage of a food with the manner in which it had been prepared and stored. The same would be true for keeping food safe. Increasingly, it became clear that a safe condition could only be maintained if the product was kept dry and away from contact with air. Some foods were treated with honey and later with olive oil (Toussaint-Samat, 1992). This led to the development of additional preservative measures, such as heating and salting. Once salt had been found to have a preservative capability, its value increased, since it was not available in sufficient quantity to meet the demand. According to Toussaint-Samat (1992), the large amount of salt in the Dead Sea was one of the reasons for the interest of the Romans in Palestine.

Over many millennia, humans have learned how to select edible plant and animal species, and how to produce, harvest and prepare them for food purposes. This was mostly done on the basis of trial and error and from long experience. Many of the lessons learned, especially those relating to adverse effects on human health, are reflected in various religious taboos, which include a ban on eating specific items, such as pork, in the Jewish and Muslim religions (Tannahill, 1973). Other taboos showed a more general appreciation of food hygiene. In India, for example, religious laws prohibited the consumption of certain 'unclean' foods, such as meat cut with a sword, or sniffed by a dog or cat, and meat obtained from carnivorous animals (Tannahill, 1973). Most of these food safety requirements were established thousands of years ago when religious laws were likely to have been the only ones in existence. The introduction of control measures in civil law came much later.

Because the underlying causes of foodborne illness were unknown, microbial food poisoning was recurrent. However, the situation changed after 1795, when the French government, driven by war, offered a substantial reward for anyone developing a new method of preserving food. It was Nicholas Appert, a Parisian confectioner, who accepted the challenge and developed a wide-mouth glass bottle that was filled with food, corked and heated in boiling water for about six hours. In 1810, Durand in England patented the use of tin cans for thermal processing of foods, but neither Appert nor Durand understood why thermally processed foods did not spoil (Hartman, 1997), despite the fact that in 1677 van Leeuwenhoek had discovered 'his little heat-sensitive animalcules' (Dobell, 1960).

Louis Pasteur provided the scientific basis for heat preservation in the period 1854–1864. During this time, he showed that certain bacteria were either associated with food spoilage or caused specific diseases. Based on Pasteur's findings, commercial heat treatment of wine was first introduced in 1867 to destroy any undesirable microorganisms, and the process was described as 'pasteurisation'. Another important development occurred in Germany, when Robert Koch introduced a method of growing microorganisms in pure culture and, with colleagues, first isolated the *vibrio cholerae* bacterium in 1884, during a worldwide pandemic (Chung *et al.*, 1995). Over the next 100 years or more, laboratory isolation and study of pure cultures of microbes remained among the predominant activities of food microbiologists (Hartman, 1997).

2.3 The evolution of food safety systems

When it was accepted that people could contract disease from contaminated food, hygiene control laws were introduced and examples can be seen in old legal records. Table 2.1 gives an overview of the more important milestones in developing food safety systems. In the absence of knowledge about the causes of serious foodborne diseases and their etiology, use was made of the 'prohibition' principle. This means that it was prohibited to produce and/or to consume certain types of food after it was realised that the foods could be a cause of high mortality. The principle was used particularly to protect special groups of individuals within society, such as soldiers. After the recognition at the end of the nineteenth century that microbial agents were often responsible for foodborne illness, systems for controlling the safety of the food supply began to be introduced.

First, use was made of microbiological testing of foods and this became widely accepted as a means of assessing food safety during the early part of the twentieth century. Eventually, statutory microbiological requirements relating to food safety were established in many parts of the world. Further progress occurred when Esty and Meyer (1922) developed the concept of setting process performance criteria for heat treatment of low-acid canned food products to reduce the risk of botulism. Later, many other foods processed in this way were controlled in a similar manner. An outstanding example is the work of Enright *et*

Table 2.1 Important milestones in the development of food safety systems

Time	Activity
Distant past	Use of 'prohibition' principle to protect special groups within society against foodborne illnesses
1900 to present	Microbiological examination of food
1922	Introduction of process performance criteria by Esty & Meyer for canned, low-acid food products
1930–1960	Use of risk assessment (for different pathogenic organisms) in setting process performance criteria for heat pasteurisation of milk
1960	Introduction of good manufacturing practices
1971	Introduction of formal hazard analysis critical control point system
ca 1978	Start of predictive modelling of bacterial growth in food
1995	Introduction of formal quantitative risk analysis

al. (1956, 1957) who established performance criteria for the pasteurisation of milk that provided an appropriate level of protection against *Coxiella burnetii*, the causative agent of Q fever. Studies for tuberculosis had been carried out earlier. This work is an early example of the use of risk assessment principles in deriving process criteria.

With greater knowledge of the more important foodborne diseases and the establishment of risk factors from analyses of outbreaks came the development of more comprehensive means of controlling food safety in production. These included the elaboration of good manufacturing practice (GMP), which helps to minimise microbial contamination of food from personnel and the production environment, and, ultimately, the hazard analysis critical control point (HACCP) system (Department of Health, Education and Welfare, 1972), in which GMP plays an important part.

The ability of different bacteria to multiply in foods is influenced by several key factors, including pH, water activity and storage temperature. The effects of these factors, both singularly and in combination, have been studied extensively in laboratory media and model food systems, and this has led to the development of mathematical models for predicting bacterial growth in commercial food products. Although not a food safety system on its own, predictive modelling is a valuable tool, which has helped to make possible the introduction of quantitative risk assessment (QRA). The latter has been used for many years in other disciplines and its use in food microbiology has been stimulated by the decision of the World Trade Organisation (WTO) to promote free trade in safe food (Anon., 1995). It has been emphasised, however, that control of food safety in this context must be based on the application of sound scientific principles, and risk analysis is seen as the basis for ensuring that the requirement is met.

The next sub-section gives more detailed information on the above-mentioned food safety initiatives, with special reference to risk assessment procedures.

2.3.1 The 'prohibition' principle

As their trade in food increased, the Romans paid greater attention to the question of preventing spoilage, and a new rule emerged: it was prohibited to sell spoiled food of any kind. The *aedilis* (churchwarden) inspected and controlled food markets, and was charged with confiscating any food that had become spoiled. Over the last 2000 years, the 'prohibition' principle has continued to be applied in many societies to protect consumers from both spoiled food and that likely to contain deadly disease agents. Some examples are given below.

Consumption of blood products

In an historical account of food safety measures, Baird-Parker (2000) describes the action taken by Emperor Leo VI of Byzantium (AD 886–911). The Emperor introduced an outright ban on the consumption of blood products as a means of reducing the high incidence of poisoning associated with sausages among his people. The law applied particularly to blood sausages and carried a high penalty if it was disregarded, which indicates the seriousness of the problem. It was stated: 'A person found to have blood prepared as food, whether he buys or sells it, shall have all his property confiscated and, after having been severely scourged and disgracefully shaved, shall be exiled for life.' From the data available and current expert knowledge, it is clear that the 'blood disease' was actually botulism.

Selling of contagious flesh

In a document entitled 'A history of government regulation of adulteration and misbranding of food,' Hutt and Hutt (1984) refer to the English Statute of Pillory and Thumbrell (1266/67). This required the following: 'If any butcher do sell contagious flesh or which has died from the murrain (rinderpest), he must be punished.' The customary punishment was to be placed in the stocks with the offending meat buried underneath.

Unsold fish

In 1319, the municipal authorities in Zurich, Switzerland, issued an ordinance prohibiting the sale of any fish that had been left over from the day before. A similar rule also operated in the city of Basel. However, such fish, could still be sold to strangers (Kampelmacher, 1971).

Eating of pufferfish

In Japan, a dish known as 'fugu' is, historically, one of the most favoured and heraldic forms of fish eating. Nevertheless, consumption of this food has resulted in many deaths, and the problem continues to this day. Consumption of the delicacy was banned in 1550 by the Emperor, after a group of soldiers had died, but the ban was abolished in 1888 when the Japanese Prime Minister tasted a small sample of fugu and survived. This disease is known as blowfish or pufferfish poisoning and is due to the neurotoxic effects of the tetrodotoxin,

10 Microbiological risk assessment in food processing

which occurs in various species of pufferfish. The dish is now prepared only by chefs who have been specially trained and certified by the Japanese government and can be relied upon to free the flesh of the toxic liver, gonads and skin. Despite these precautions, many cases of tetrodotoxin poisoning are reported each year in people consuming fugu (Source: *Medical Journal*, 12 June, 2001, vol. 2, no. 6).

Sale of bongkrek

In the Regency of Banyumas and surrounding areas of Central Java, Indonesia, tempe bongkrek and other coconut-based products are prepared from partly defatted coconut. The raw material for tempe bongkrek is sometimes mixed with the residue obtained from the manufacture of tofu (soybean curd) and allowed to ferment with the mould *Rhizopus oligosporus*. Under certain conditions, a contaminating bacterium, *Burkholderia cocovenans*, is able to grow and produce two distinct toxins: colourless bongkrek acid and yellow-coloured toxoflavin. Bongkrek food poisoning usually has a latency period of 4–6 hours. Typical symptoms include malaise, abdominal pain, dizziness and extensive sweating. The victim becomes fatigued and drowsy and eventually passes into a coma. Death occurs 1–20 hours after the onset of the initial symptoms (Steinkraus, 1996). Because many Banyumas people have died as a result of eating tempe bongkrek, sale of the product is now prohibited.

2.3.2 The ‘precautionary’ principle

Once proper scientific data became available, the principle of prohibition began to be largely replaced by food safety regulations, which included process performance criteria, product specifications and specified storage conditions. The risk of botulism from blood sausages was minimised by introducing both product specifications and requirements for storage. As mentioned previously, the safety of fugu was improved by giving more attention to the training of chefs and ensuring that toxic organs were properly removed from the fish.

Despite these advances, another principle, the ‘precautionary’ principle, is still relevant in some situations, although its application is mainly restricted to certain vulnerable groups of the population, where absolute safety cannot be guaranteed with respect to some foods. For example, senior citizens in the USA are advised not to eat the following types of food (see www.foodsafety.gov/~fsg/sr2.html):

- Raw fin fish and shellfish, including oysters, clams, mussels and scallops.
- Raw or unpasteurised milk or cheese.
- Soft cheese, such as feta, brie, camembert, blue-veined and Mexican-style cheese.
- Raw or lightly cooked eggs or egg products, including salad dressings, cookie or cake batter, sauces and beverages, such as egg nog. (Foods made from commercially pasteurised egg are safe.)

- Raw meat or poultry.
- Raw sprouts (alfalfa, clover and radish).
- Non-pasteurised or untreated fruit or vegetable juice. (These juices will carry a warning label.)

The reason for giving such advice to the elderly is that they are more likely to be affected by any harmful bacteria that are present in the above foods. Once illness occurs, older people face the risk of more serious health problems, even death. With increasing age, natural defences, such as the immune system and production of stomach acid, become weaker. Also, underlying conditions, including diabetes and kidney disease, as well as some cancer treatments, may increase the risk of an individual succumbing to foodborne illness and suffering serious consequences. Other groups within the population may also show greater susceptibility to foodborne illness. These include pregnant women, neonates and patients given immunosuppressive drugs for treatment of diseases such as cancer and rheumatoid arthritis. Here, examples of appropriate precautionary advice include a recommendation to avoid feeding honey to infants below one year of age, because of the risk of botulism (described in detail by Lund and Peck, 2000). Also advice is given in several countries to pregnant women to stop eating certain pates and soft cheeses due to the risk of contracting listeriosis (see Fig. 2.1).

Unfortunately, the warning of vulnerable groups against these particular hazards varies considerably between countries and in some cases is non-existent. At the other end of the 'precautionary' scale is the use of it in risk management when there is a lack of proper scientific evidence or possible legal difficulties. A recent example from the UK was the ban on butchers selling beef-on-the-bone, because of the perceived risk of transmitting to humans the agent of bovine spongiform encephalopathy from bone marrow. Although the risk was considered extremely small, sale of the product was nevertheless prohibited by law.

2.3.3 Establishing process criteria

At the start of the twentieth century, it had already been recognised that protection of the public against foodborne hazards required proper control of heat treatments used commercially in food production. Two examples are presented here: (i) the performance criteria for destroying spores of *Clostridium botulinum* in low-acid, canned foods (Esty and Meyer, 1922) and (ii) the process criteria for *Coxsackie burnetii* in milk pasteurisation, as determined by Enright *et al.* (1957).

Setting of process performance criteria for heat treatment of low-acid canned foods

The first mathematical evaluation of the heat sterilisation process for canned foods was made by Bigelow *et al.* (1920) and later developed by Ball (1923) to



Fig. 2.1 Health advice given to pregnant women by the Health Department of Western Australia 1995.

derive methods for calculating the times necessary to process canned foods at appropriate temperatures. For commercial sterilisation, the goal of thermal processing was to reduce the probability of survival and growth of microorganisms in a particular canned food to an acceptably low level. The starting point for the rationale of what is now termed 'an appropriate level of protection' (ALOP) was the work of Esty and Meyer (1922). They derived process performance criteria for the destruction of spores of proteolytic strains of *Clostridium botulinum* in low-acid canned foods. It was proposed that requirements for sterilisation should be based on (i) the response to heating of the most heat-resistant spores found among strains of *Clostridium botulinum* and

(ii) a reduction in the spore population by a factor of 10^{11} – 10^{12} to ensure the desired level of product safety. For this purpose, heat inactivation trials were carried out on 109 different strains of the test species. The resultant performance criteria, based on the approach outlined above, have been applied over many years and have proved to be sound, with an adequate margin of safety (Pflug and Gould, 2000).

Process performance criteria for heat pasteurisation of milk

The work of Enright *et al.* (1957) led to the development of process standards for controlling *Cox. burnetii* in milk. The heat treatments used initially for milk were designed to inactivate any tubercle bacilli present and these were considered to be the most heat-resistant of the nonsporing pathogenic bacteria likely to occur in the product. The treatments were based on information from many studies on the heat-resistance of both human and bovine strains (*Mycobacterium tuberculosis* and *Myc. bovis* respectively). In the USA, the heating regime adopted in 1924 for the conventional process was 142°F (61.1°C) to 145°F (62.8°C) for 30 min. In 1933 a heating regime was introduced for the high-temperature, short-time (HTST) process: 161°F (71.7°C) for 15 s.

In practice, *Cox. burnetii* appears to be slightly more heat-resistant than the tubercle bacilli and, following recognition that the organism, which causes Q fever in humans, could be transmitted by raw milk, it was necessary to check on the adequacy of existing pasteurisation processes for inactivating the organism. The work undertaken by Enright and colleagues (1956, 1957) fulfilled this requirement and, although no formal MRA was employed, elements of the MRA approach were implicit in their studies. These aspects are discussed below.

- **The organism and the disease it causes:** *Cox. burnetii* is a small, Gram-negative bacterium, originally classified as a rickettsia, that cannot be grown in axenic culture but can now be cultivated *in vitro* in various cell lines (Maurin and Raoult, 1999). Q fever is characterised by fever, chills and muscle pain, with occasional long-term complications. It was first described by Derrick (1937) and is known to occur worldwide. The organism infects many wild and domestic animals, which often remain asymptomatic. Domestic animals, such as cattle, sheep and goats, are considered the main sources of infection for humans (Maurin and Raoult, 1999) and, when shed in milk, *Cox. burnetii* is often present in relatively high numbers.
- **Hazard identification:** contact with infected animals was known to result in transmission of *Cox. burnetii* to people, with subsequent development of illness, and the likelihood of the organism contaminating raw milk was recognised. Early on, there was a lack of epidemiological evidence for transmission via milk, but this was suspected in several outbreaks and there was strong supporting evidence from a UK outbreak in 1967 (Brown *et al.* 1968). Thus, the hazard was the presence of *Cox. burnetii* in milk intended for human consumption.

14 Microbiological risk assessment in food processing

- **Dose response:** there was no information on the dose response in humans, since challenge trials had not been carried out and epidemiological data were lacking.
- **Exposure assessment:** information relevant to this step in MRA was obtained by injecting guinea pigs to determine the presence and titre of *Cox. burnetii* in milk. The organism was found in 33% of 376 samples of raw milk from California, USA. 'The maximum number of *Cox. burnetii* demonstrated in the milk of an infected dairy cow was the number of organisms contained in 10 000 infective guinea pig doses of *Cox. burnetii* per millilitre' (Enright *et al.*, 1957). Similar titres were found in milk that had been frozen and thawed. However, the study did not involve testing of all breeds of dairy cattle, and it is possible that even higher levels of shedding may have occurred in some breeds that were not examined. Nevertheless, it was concluded that the maximum level of consumer exposure would be represented by the highest infective dose demonstrated in this study and that the pasteurisation process should bring about thermal inactivation of such a number (Enright *et al.*, 1957).
- **Risk characterisation:** the risk involved in consuming raw milk could not be estimated because of the absence of dose–response data. The data for the prevalence of contaminated milk, the maximum level of contamination and the fact that milk would have been consumed regularly by the majority of the population were probably implicit factors in an assumption that the risks associated with inadequate heat treatment were high.

The studies of Enright *et al.* (1956, 1957) led to the conclusion that heating at '143 °F for 30 min was wholly inadequate to eliminate viable *Cox. burnetii* from whole, raw milk, while heating at 145 °F ensures elimination of these organisms with a high level of confidence' (Enright *et al.*, 1957). This led to the adoption of the higher temperature for vat pasteurisation in the USA. The work on the HTST process indicated that the recommended standard of 161 °F for 15 s was sufficient for total elimination.

2.3.4 Microbiological examination of food

Microbiological testing, as a means of assessing whether a food product is hazardous due to the presence of pathogens, is of relatively recent origin. It became the vogue only after Robert Koch developed a method for growing microorganisms in pure culture and foodborne organisms capable of causing spoilage or disease were recognised and could be enumerated (Hartman, 1997). Over the last 80 years or so, many different methods have been devised for detecting pathogenic organisms and/or their toxins. Even from the beginning of that period, statutory microbiological requirements relating to food safety were established in many countries and were based on the testing of prepared foods for the organisms or toxins of concern.

A disadvantage was that routine examination of foods for a multiplicity of pathogens and toxins was impractical in most laboratories and an alternative

approach was needed. This led to widespread use of microbial groups or species that were more readily detectable in foods and considered to be indicative of conditions in which the food had been exposed to contamination with pathogens, or been under-processed. Enumeration of the organisms was even used as a measure of the possible growth of pathogens in a food, should these have been present. The bacteria in question were termed 'indicator organisms' and they have value for indirect assessment of both microbiological safety and quality of foods. The use of indicator organisms flourished, especially in the period 1960–1980. During that time, numerous procedures for enumerating bacterial indicators were described (e.g. American Public Health Association, 1966; United States Food and Drug Administration, 1972). Clearly, the main objective of their use was to reveal conditions of food handling that implied a potential hazard. Furthermore, some indicators were proposed as a possible index rather than a mere indication of faecal contamination in food (Mossel, 1982).

Setting criteria

The traditional approach to controlling food safety has been based on education and training of personnel, inspection of production facilities and operations, and microbiological testing of the finished product. Testing of the product is usually an integral part of the overall control programme, and the perceived risk of foodborne illness from the presence of a particular pathogen is reflected in the limit values that are set for the organism in a specific type of food. Where possible, these criteria are based on epidemiological data and are a reflection of the minimum dose expected to cause illness. Table 2.2 gives some values that are essentially derived from analyses of outbreaks of foodborne disease. The data show a clear parallel between limit values and the minimum dose associated with human disease. In general, infective organisms such as *Salmonella* should be absent from food because very low numbers are known to be capable of causing illness (D'Aoust, 1989). On the other hand, toxigenic bacteria, such as *Staphylococcus aureus*, may be acceptable at levels that are well below those causing food to become hazardous. With foodborne intoxications caused by *Staph. aureus*, the numbers present in the food usually exceed 10^7 cfu (colony-forming units) per g (Bergdoll, 1989).

Shortcomings of microbiological testing

Leaving aside questions regarding the accuracy and reproducibility of the methods used, it is clear that microbiological testing of food is of limited value without a sound sampling plan. To overcome the problem, a book on food sampling was produced by the International Commission on Microbiological Specifications for Foods (ICMSF, 1974). The book gives details of statistically based sampling plans for the microbiological examination of different types of food.

Although the book gives an excellent account of the various sampling plans, it also reveals the limitation of testing for pathogenic organisms that may be infrequent, low in number and unevenly distributed throughout the test batch, especially when complete absence is the only acceptable result. Thus, testing to

Table 2.2 Correlation between minimum dose considered to cause disease and criteria set for end-products

Pathogenic organism	Minimum dose considered to cause disease ^a	Probability of infection from exposure to 1 organism ^b	General end-product criteria used ^c
Infectious organism			
<i>Shigella</i>	1	1.0×10^{-3}	Absence/25 gram
<i>Salmonella</i>	1	2.3×10^{-3}	Absence/25 gram
<i>Campylobacter</i>	1–10	7.0×10^{-3}	Absence/25 gram
<i>Listeria monocytogenes</i>	$> 10^3$		$< 100/\text{gram}$
<i>Vibrio parahaemoliticus</i>	$> 10^4$		$< 10^3/\text{gram}$
Toxico-infectious organisms			
<i>Clostridium perfringens</i>	$> 10^6$		$< 10^5 - 10^6/\text{gram}$
<i>Bacillus cereus</i>	$> 10^6$		$< 10^5 - 10^6/\text{gram}$
Organisms causing intoxication			
<i>Staphylococcus aureus</i>	$> 10^6$		$< 10^5 - 10^6/\text{gram}$

^a Based on analysis of foodborne disease outbreaks (presented in Doyle, 1989).

^b Rose and Gerba (1991).

^c Criteria for pathogenic organisms are not yet well established and they may differ from country to country. The validity of the criteria starts mostly after production and ends at the time of consumption.

ensure that the target pathogen is absent from the batch requires uneconomically large numbers of samples, with no guarantee that absence of the organism can be established.

2.3.5 Introduction of GMP and HACCP

GMP

One of the first quality assurance systems developed by the food industry was that involving the application of GMP, as a supplement to end-product testing. GMP has been used for many years to ensure the microbiological safety and quality of food, and it provides a framework for hygienic food production. The establishment of GMP is the outcome of long practical experience and it includes attention to environmental conditions in the food plant, e.g. requirements for plant layout, hygienic design of equipment and control of operational procedures. The GMP concept is largely subjective and qualitative in its benefits. It has no direct relationship with the safety status of the product. For these reasons, the concept has been extended by introducing the HACCP system, which seeks, among other things, to avoid reliance on microbiological testing of the end-product as a means of controlling food safety. Such testing may fail to distinguish between safe and unsafe batches of food and is both time-consuming and relatively costly.

HACCP

The HACCP concept is a systematic approach to the identification, assessment and control of hazards in a particular food operation. It aims to identify problems before they occur and establish measures for their control at stages in production that are critical to ensuring the safety of food. Control is proactive, since remedial action is taken in advance of problems occurring.

In a review of the historical background, Barendsz (1995) and Untermann *et al.* (1996) described the development of the HACCP approach, which began in the 1960s. The concept arose from a collaboration between the Pillsbury Company, the US Army Natick Research and Development Laboratories and the US National Aeronautics and Space Administration. The original purpose was to establish a system of safe food production for use in human space travel. At that time, the limitations of end-product testing were already appreciated and therefore more attention was given to controlling the processes involved in food production and handling. When first introduced at a meeting on food protection (Department of Health, Education and Welfare, 1972), the concept involved three principles: (i) hazard identification and characterisation; (ii) identification of critical control points (CCPs) and (iii) monitoring of the CCPs.

Many large food companies started to apply HACCP principles on a voluntary basis, and in 1985 the US National Academy of Science recommended that the system should be used. Further support came from the ICMSF (1988), which extended the concept to six principles. They added specification of criteria, corrective actions and verification (see Table 2.3). In 1989, the US National Advisory Committee on Microbiological Criteria for Foods (NACMCF) added in a further principle: the establishment of documentation concerning all procedures and records appropriate to the principles and their application. Use of the HACCP system was given an international dimension by the Codex Alimentarius Commission (CAC) which published details of the principles involved in 1991 and their practical application (CAC, Committee on Food Hygiene, 1991). In 1997, the CAC laid down the 'final' set of principles and clarified the precise meaning of the different terms (CAC, Committee on Food Hygiene, 1997):

- General principles of food hygiene (Alinorm 97/13, Appendix II).
- HACCP system and guidelines for its application (Alinorm 97/13A, Appendix II).
- Principles for the establishment and application of microbiological criteria for foods (Alinorm 97/13A, Appendix III).

The full HACCP system, as described in Alinorm 97/13, is shown in Table 2.3. The document also gives guidelines for practical application of the HACCP system. By 1973, the FDA had made the use of HACCP principles mandatory for the production of low-acid canned foods (FDA, 1973) and, in 1993, the system became a legal requirement for all food products in the European Union (Directive 93/43).

Despite widespread usage, the present HACCP concept still has some weak points. One of them is the definition of a hazard. This is not defined as 'an agent

Table 2.3 The seven principles of the HACCP system (CAC, Committee on Food Hygiene, 1997)

Principle	Activity
1 Conduct a hazard analysis	List all potential hazards associated with each step, conduct a hazard analysis, and consider any measures to control identified hazards
2 Determine the critical control points (CCPs)	Determine CCPs
3 Establish critical limit(s)	Establish critical limits for each CCP
4 Establish a system to monitor control of the CCP	Establish a system of monitoring for each CCP
5 Establish corrective actions	Establish the corrective action to be taken when monitoring indicates that a particular CCP is not under control
6 Establish verification procedures	Establish procedures for verification to confirm that the HACCP system is working effectively
7 Establish documentation and record keeping	Establish documentation concerning all procedures and records appropriate to these principles and their application

with the potential to cause an adverse health effect', as in risk assessment, but as 'an unacceptable contamination, growth and/or survival by microorganisms of concern' (ICMSF, 1988), which is more restrictive and does not cover all possible hazards. Another weakness arises from the definition of a CCP. It is stated that a CCP is a location, practice, etc. where hazards can be minimised (ICMSF, 1988; International Association of Milk, Food and Environmental Sanitarians (IAMFES), 1991) or reduced to an acceptable level (Bryan, 1992; Alinorm 97/13). In both cases, these are qualitative objectives and may lead to differing interpretations. It was Notermans *et al.* (1995) who first made a plea to use the principles of quantitative risk assessment for setting critical limits at the CCPs (process performance, product and storage criteria). It was their opinion that only when the critical limits are defined in quantitative terms can the level of control at the CCPs be expressed realistically. At the International Association of Food Protection (IAFP) meeting in 2001, Buchanan *et al.* (2001) also favoured the use of these principles and suggested that food safety objectives should encompass end-product criteria, which are related to the criteria used in processing.

2.3.6 Predictive modelling

Modelling in food microbiology began about 1920, when methods were developed for calculating thermal death times. These models revolutionised the canning industry (Pflug and Gould, 2000). Later, Monod (1949, 1950) developed a model that described the continuous, steady-state culture of

microorganisms and became the basis for continuous fermentation processes. In principle, the model was analogous to that used for chemical processes. The recent resurgence of predictive modelling in relation to microbial growth in food originated in the 1960s and has been reviewed by Ross and MacMeekin (1993). In contrast to the situation studied by Monod, the identities and concentrations of nutrients involved are unknown and the organisms of interest are initially present in low numbers, with growth conditions often being less than optimal. For these reasons, initial attempts at mathematical modelling in food microbiology have been more empirical than was the case for fermentation processes, focusing on batch rather than continuous-culture kinetics. As shown by Whiting and Buchanan (1997), growth data are fitted to equations using interactive least-square computer algorithms. Assumptions about randomness, normal distribution and stochastic specifications are the same as they would be for any statistical application of regression (Ratkowsky, 1993). All models are actually simplifications that represent the complex biochemical processes controlling microbial growth and are limited to the most important input parameters, such as temperature, time, water activity and pH. One of the reasons for simplifying the approach is that knowledge of the complex biochemical processes involved is far from complete. The major advantage is that the current models are easy to handle; however, the outcome should always be used with caution and verification may be necessary in some cases.

Primarily, the development of predictive modelling was driven by the proliferation of refrigerated and limited shelf-life food products. It was recognised that (i) even so-called 'rapid' microbiological methods were too slow to show, within an acceptable period of time, whether microbes in the product grew or died (Spencer and Bains, 1964); (ii) testing of factors in a food product that affect microbial growth and toxin production, whether singularly or in combination, is laborious and time-consuming and (iii) work had been done in Canada to draw together the results of numerous growth experiments on *Clostridium botulinum* (Hauschild, 1982). The mathematical and statistical tools already existed prior to the expansion in modelling activity and the process was favoured by the introduction of powerful personal computers and the availability of user-friendly software.

In the review of Ross and MacMeekin (1993), the main reasons for developing predictive models were summarised as follows:

- To permit predictions of product shelf-life and safety, and the consequences of changes in product formulation or composition; to facilitate a rational design for new processes, etc.; to meet or to obtain an insight into requirements for product safety or shelf-life.
- To allow objective evaluations to be made of processing operations and, from this, an empowering of the HACCP approach.
- To provide an objective evaluation of the consequences of any lapses in process control and subsequent storage of the end-product.

Now that MRA has become established in food microbiology, it is clear that the use of predictive models is essential in risk assessment. This is especially

true for exposure assessment. In many foods, particularly those that are fresh and have a short shelf-life, rapid changes in microbial populations can occur and the models are needed to determine, for example, the necessary storage conditions. The models can also provide information about risk factors in handling the product, which have a considerable influence on human exposure to particular pathogens. They may also help to clarify the effects of different control options. Thus, the modelling approach facilitates control of the most important factors that affect food safety. Without the use of predictive models, a quantitative MRA for assessing food safety would be virtually impossible.

2.3.7 Introduction of QRA

Systematic risk analysis approaches have been used by the Food and Agriculture Organisation of the United Nations (FAO) and the World Health Organisation (WHO) since 1955, when the evaluation of food additives at the international level was initiated as a result of a joint FAO/WHO conference on food additives. The conference recommended to the Directors-General of FAO and WHO that one or more expert committees should be convened to address the technical and administrative aspects of chemical additives and their safety in food. This recommendation provided the basis for setting up the Joint FAO/WHO Expert Committee on Food Additives (JECFA). The JECFA started its meetings in 1956, initially to evaluate the safety of food additives.

Risk assessment has also evolved over the last decade within the CAC. The Commission, which was established in 1962 under the parentage of the FAO and WHO, is an intergovernmental organisation with the responsibility for developing international standards, guidelines or other recommendations for food in order to protect the health of consumers and facilitate international trade. In the course of time, the CAC has enlarged its activities and, in addition to risk evaluation for food additives, chemical contaminants, pesticide residues and veterinary drug residues in foods, the issue of biological hazards in foods is now also being addressed. However, no clear MRA activities were undertaken prior to 1995.

The development of MRA was strongly stimulated when in 1995, at the GATT Uruguay Round, the WTO was established and a free trade in safe food was agreed. In the WTO Agreement on the Application of Sanitary and Phytosanitary Measures, the so-called SPS Agreement (Anon., 1995), requires that countries signatory to the agreement base their laws concerned with protecting human, animal and plant health on a risk analytical basis. Thus, the SPS Agreement requires food safety legislation to be scientifically based and the process of risk assessment to be applied, for example, when introducing microbiological criteria for controlling imported foods. In the pursuance of harmonisation and to avoid the need for all countries and all food producers to carry out a risk assessment on each of their products, the WTO SPS Agreement has chosen the scientifically based international standards, guidelines and recommendations of three organisations, one of which is the CAC, as the

preferred measures for adoption by WTO members. In addition, the SPS Agreement states that countries should take into account the risk assessment technique developed by the relevant international organisations, when undertaking a risk assessment. As a result of this, the FAO and WHO began to organise expert consultations dealing with food safety risk assessment, with the purpose of providing member countries with principles and guidelines for undertaking such an assessment. An overview of the key documents produced is given in Table 2.4.

The first expert consultation was devoted to the application of risk analysis to food safety standards issues. The consultation was convened at the request of the Forty-first Session of the CAC Executive Committee, with the aim of promoting consistency in the use of risk analysis for food safety purposes. The main objective was to provide the FAO, WHO and CAC, as well as member countries, with advice on practical approaches for the application of risk analysis to food standards issues. At that meeting, food safety risk analysis terms were defined. A model for risk assessment was also agreed upon. This comprises the four components: (i) hazard identification, (ii) hazard characterisation, (iii) exposure assessment and (iv) risk characterisation. At that consultation, the estimation of risk from biological agents was considered in detail, since it was the general view of the experts that such risks are in many ways a much larger and more immediate problem to human health than risks associated with chemical contaminants in food.

At an expert consultation in 1997, a risk management framework was set up and general principles of food safety risk management were elaborated. In addition, key risk management terms were defined. The main elements of risk management were identified as (i) risk evaluation, (ii) assessment of risk management options, (iii) implementation of management decisions and (iv) monitoring and review. As far as the general principles are concerned, it was stated that risk management decisions should be transparent, primarily aimed at the protection of human health and should ensure that the scientific integrity of the risk assessment process is maintained.

As a logical continuation, a third expert consultation dealt with the application of risk communication. The main issues addressed at this meeting

Table 2.4 FAO/WHO documents dealing with food-related risk analysis

Year	Risk analysis documents	References
1995	<i>Application of risk analysis to food standards issues</i>	FAO/WHO (1995)
1997	<i>Risk management and food safety</i>	FAO/WHO (1997)
1998	<i>The application of risk communication to food standards and safety matters</i>	FAO/WHO (1998)
1999	<i>Risk assessment of microbiological hazards in foods</i>	FAO/WHO (2000a)
2000	<i>The interaction between assessors and managers of microbiological hazards in food</i>	FAO/WHO (2000b)

were the principles of risk communication and barriers to, and strategies for, making the process effective. It is generally accepted that risk communication is essential throughout the risk analysis process. For successful risk communication, it is important that (i) all interested parties are involved, (ii) use is made of individuals trained in risk communication, (iii) risk communication is received and understood, and (iv) transparency is fostered during the whole process. The nature of the risk and the benefits and uncertainty in risk assessment and assessment of risk management options are regarded as the main elements for effective risk communication. The main barriers in risk communication include differences in perception and receptivity, lack of understanding of the scientific process, and media and social characteristics.

The fourth expert consultation, convened in 1999, was directed specifically at risk assessment of microbiological hazards in foods. The main outcome of this consultation was an outline strategy and mechanism for addressing MRA at the international level. The expert consultation made recommendations regarding the activities required to support MRA and how to improve the necessary capabilities. In addition, it recommended that outcomes of risk assessments should be immediately integrated into HACCP plans, that additional expert meetings should be held and that collaborative studies should be conducted between developing and developed countries.

In 2000, a second specific expert consultation was organised, dealing with the interaction between assessors and managers of microbiological hazards in foods. At this consultation, the linkage between risk assessment and risk management was discussed in more detail, with the aim of providing guidance on how both processes could be improved. Issues addressed ranged from the identification of a food safety problem and the establishment of risk profiles to assessment of the effectiveness of management decisions. The former is of interest in relation to collecting as much information as possible for both risk assessment purposes and effective risk management.

Current microbiological risk assessment activities

In 1999, following the request of the CAC and in order to address the needs of their member countries, the FAO and WHO initiated a series of joint expert consultations to assess risks associated with specific microbiological contaminants in foods. This followed the adoption by the CAC of the Principles and Guidelines for the Conduct of Microbiological Risk Assessment (MRA), elaborated by the Codex Commission for Food Hygiene (CCFH) (CAC/GL 30, 1999).

The aims of these joint expert consultations were to provide a transparent review of scientific data on the state of the art of MRA, and to develop the means of achieving sound quantitative risk assessments for specific pathogen–commodity associations. The work included an evaluation of existing risk assessments, a review of the available data and risk assessment methodologies, highlighting their strengths and weaknesses and how they might be applied,

provision of examples and identification of information needs/gaps. A further aim of these consultations was the development of guidelines relating to the different steps in risk assessment, such as hazard characterisation and exposure assessment. The purpose of such guidelines would be to help the risk assessor, the risk manager and other interested parties to understand the principles and science behind the risk assessment steps.

Three such consultations have already been convened. Two of these, one in July 2000 and one in May 2001 have dealt with the risk assessment of *Salmonella* spp. in broilers, *Salmonella enteritidis* in eggs and *Listeria monocytogenes* in ready-to-eat foods. These assessments are currently near completion. In July 2001 another expert consultation addressed risk assessment of *Campylobacter* spp. in broiler chickens, and *Vibrio* spp. in seafood. Work on these will continue for another year. The work plan and priorities programme for work on MRA are established by FAO and WHO, taking into consideration the needs of the CCFH, as well as the member countries.

2.4 International food safety standards

2.4.1 Setting of current international standards

Based on the SPS Agreement, food safety standards need to be based on sound science and risk assessment. Figure 2.2 shows how these standards are set. The starting point is the relevant food safety policy. By using risk analysis, this policy is transformed into food safety objectives, which equate with an agreed level of consumer protection.

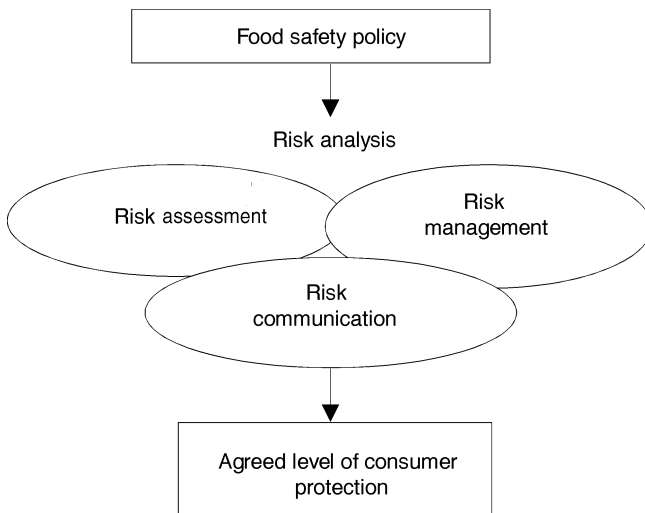


Fig. 2.2 The use of risk analysis to convert a food safety policy into food safety objectives.

Currently, the FAO and WHO are the organisations concerned with food safety at the international level. As far as international food safety standards are concerned, these are established under the Joint FAO/WHO Food Standards Programme by the CAC. This organisation has delegated the development of standards, guidelines and other recommendations to its subsidiary bodies, which are guided by the CAC. Normally, the general subject Codex committees (described as 'horizontal' Codex committees) are more routinely involved in risk management. These include the Codex committees on Food Additives and Contaminants, Pesticide Residues, Residues of Veterinary Drugs in Food, Food Hygiene, General Principles, Food Labelling, and Nutrition and Food for Special Dietary Uses. The tasks of these intergovernmental bodies are to prepare draft standards, guidelines and recommendations for consideration by the CAC.

The process of setting international food safety standards is expressed in Fig. 2.3.

Initiating the process of standard setting

The risk analysis procedure is usually initiated by one of the respective Codex committees, when it proposes setting standards for additives, contaminants, microbiological agents, etc. This process may also be triggered by direct requests to FAO/WHO from member countries. The initiation of the evaluation procedure serves as the hazard identification step.

Risk assessment

The first step in the process of risk analysis is risk assessment, which is carried out by independent expert committees or groups that advise the respective Codex committees. At present, there are two long-standing expert groups that provide advice to Codex, governments and industry. They are the JECFA and the Joint FAO/WHO Meeting on Pesticide Residues (JMPR). In addition, FAO and WHO convene *ad hoc* expert consultations, as required, to address specific issues not covered by JECFA or JMPR. In recent years, several expert consultations have been held on microbiological hazards in food, the risk assessment of foods derived from biotechnology and on animal feeding and food safety. Recently, the CAC, at its Twenty-fourth Session, held in Geneva, Switzerland from 2 to 7 July 2001, requested the FAO and WHO to further strengthen scientific support for science-based decision making. The FAO and WHO, conscious of the importance of this issue, are currently studying the possibility of harmonising the risk assessment procedures used by the various scientific advisory groups and are looking for ways to improve the quality, quantity and time-lines of scientific advice.

The work of the **JECFA** now includes the evaluation of contaminants, naturally occurring toxicants and residues of veterinary drugs in food. For food additives, the JECFA normally establishes so-called acceptable daily intakes (ADIs) on the basis of available toxicological and other relevant information. Specifications for identity and purity are also developed for food additives, which help to ensure that the product in commerce is of appropriate quality, can

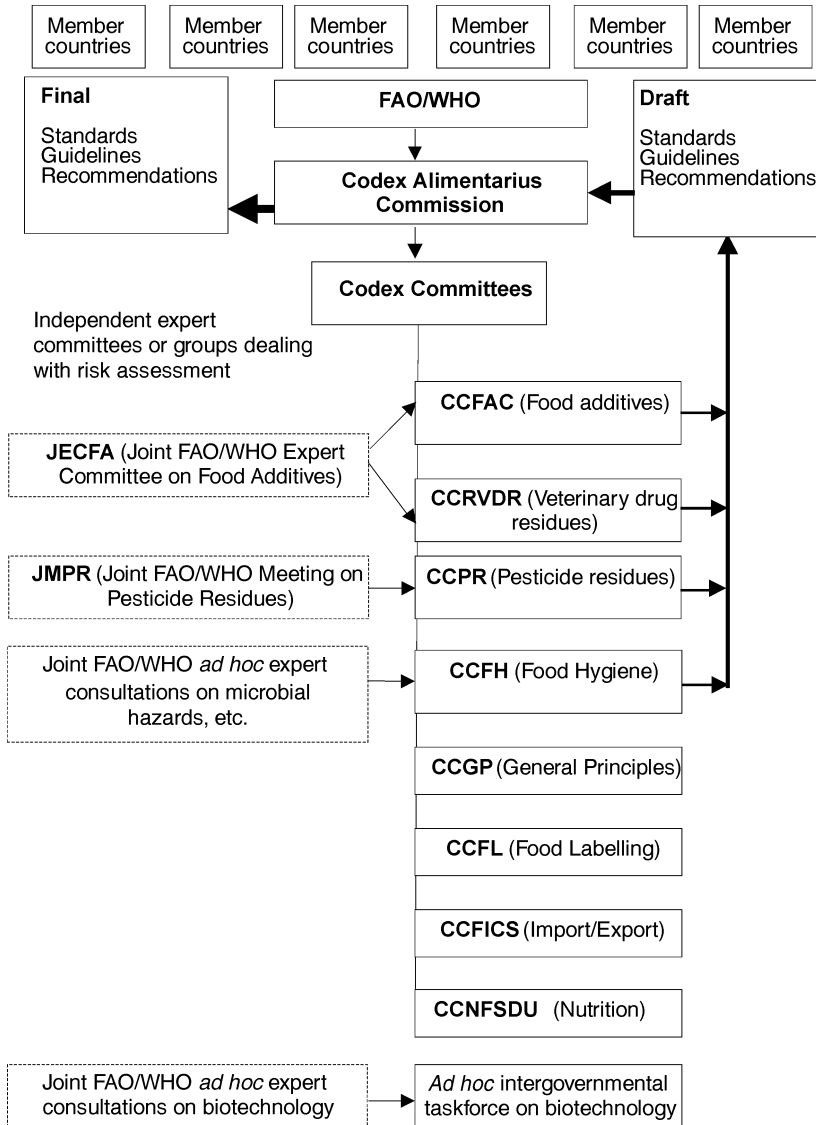


Fig. 2.3 Visualisation of the process of setting international food safety standards.

be manufactured consistently, and is equivalent to the material that was subjected to toxicological testing. For contaminants and naturally occurring toxicants, levels corresponding to ‘tolerable’ intakes, such as the provisional maximum tolerable daily intake (PMTDI) or provisional tolerable weekly intake (PTWI) are normally established when there is an identifiable no-observed effect level. If such a level cannot be identified, the Committee may provide other advice depending on the circumstances. In the case of veterinary drugs,

data on good practice are evaluated and corresponding maximal residue levels (MRLs) in animal tissues, milk or eggs are recommended. Such MRLs are intended to provide assurance that when the drug has been used properly, the intake of any residues of the drug in food is unlikely to exceed the ADI.

The **JMPR** comprises the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and in the Environment and the WHO Core Assessment Group. The JMPR carries out toxicological evaluation of pesticide residues, normally resulting in an estimate of the ADI. In addition, the JMPR proposes MRLs for individual pesticides in or on specific commodities. These MRLs are primarily based on the residue levels estimated in supervised field trials, when the pesticide is used according to good agricultural practices (GAP). In cases where initial estimates indicate that the ADI may be exceeded, more refined intake calculations are performed, using national food consumption data and information from pesticide residue monitoring programmes.

Both the JECFA and JMPR establish chemical safety standards that are based on a review of toxicological studies in the most sensitive test-animal species. They allow for an adequate level of safety, use risk assessment procedures, consider use and consumption patterns and define specifications for the identity and purity of food grade chemicals to be used.

For microbiological hazards, there is currently no JECFA or JMPR-like body. For food safety risk assessment activities, *ad hoc* expert consultations are set up and independent and appropriately qualified experts are invited. A procedure for this process, adopted and in use since 2000, enhances the principles of transparency, equal opportunity, excellence and independence, and seeks to harmonise the working procedures between different expert bodies and between FAO and WHO. Briefly, the procedure involves the following steps:

- An open call for experts is made 6 months prior to each expert meeting.
- Review of candidates by a four-member selection panel.
- Completion of a 'Declaration of Interests' form, indicating institutional affiliation by candidates.
- Secretariat selects appropriate individuals.
- Secretariat notifies governments of the selected experts to obtain their consent.
- Secretariat invites the experts.

Risk management

The risk management activities are carried out by the respective Codex committees, comprising participants from all member countries, including representatives of industry, consumers and governmental bodies. These representatives carry out the risk management part of the standard-setting procedure. Draft standards, guidelines and recommendations are elaborated via an eight-step process (or in some cases a five-step, accelerated process) by the committees. The final decision regarding their adoption is made by the CAC.

2.4.2 International criteria: future trends

The generic frameworks of current food safety systems used for chemicals and microbiological agents show some similarities, but also important differences. The frameworks for both entities are presented in Fig. 2.4, which is based on the paper given by Hathaway at the IAFP congress, held in Minneapolis, 2001 (Hathaway, 2001).

For the setting of international criteria for chemicals, an international food safety policy has been developed. The policy comprises certain general rules. Examples of these are that carcinogens should be absent from food and the aim should be to follow the ALARA principle, which means that, for extraneous chemicals, levels 'as low as reasonably achievable' are required. Also, an appropriate level of protection has been agreed. For most chemicals, levels below the no-effect level, including an uncertainty factor, are considered to provide an appropriate level of protection (ALOP). The risk assessment process

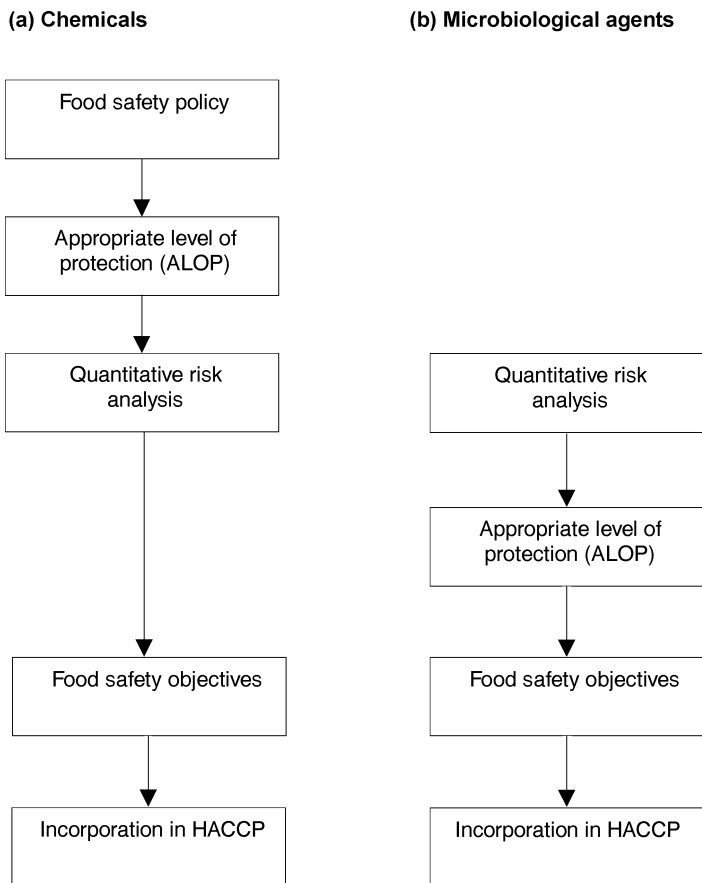


Fig. 2.4 Generic framework of current food safety systems as developed for chemicals (additives, pesticides, etc.) and for microbiological agents (based on Hathaway, 2001).

is primarily directed at assessing the characteristics of potentially hazardous agents and exposure assessment. The risk management process, which is carried out by the relevant Codex Commission, results in the final food safety objectives. These must be incorporated as the required process, product and storage criteria in the HACCP system.

With the passage of time, the system used for chemicals has proved to be very effective in preventing foodborne illness from this source. Actually, with some exceptions, chemical contaminants and residues do not cause overt health problems, and in that respect they are quite different from microbiological agents. Almost all reported foodborne illness is caused by pathogenic organisms present in food.

As far as microbiological agents are concerned, there is, at present, no food safety policy associated with the setting of international criteria. Also, unlike chemicals, there is no concept of any levels of product contamination with specific pathogens that would provide an ALOP. The approach to microbiological food safety can be summarised as follows. The system begins with a quantitative risk analysis. Depending on the outcome, appropriate levels of protection are agreed and food safety objectives set. These objectives then need to be reflected in process, product and storage criteria for incorporation into the HACCP system.

There is some debate about whether a unified approach should be developed for both chemicals and microbiological agents, and essential differences in the risks that they pose to human health need to be understood and taken into account. Other important factors are given in the following:

- **Stability.** While concentrations of most chemicals remain relatively stable in foods during storage, microbial contaminants may die-off or even multiply, depending on the conditions.
- **Behaviour.** The storage behaviour of microorganisms in foods is affected by various intrinsic and extrinsic factors, and can vary considerably from food to food and from one organism to another.
- **Origin.** Chemical contamination of foods with residues of veterinary drugs, pesticides, etc. comes from extraneous sources, but many microorganisms occur naturally, especially in raw foods, and their presence cannot be avoided.
- **End-product criteria.** Although clearly useful for chemicals, such criteria are of less value for microorganisms. This is largely due to changes in microbial counts with time and the difficulty of detecting low numbers of specific pathogens, which, if present, are often distributed unevenly in the food. Therefore, a negative result is no guarantee that the target organism is entirely absent from the test batch.
- **Exposure assessment.** Because of the above-mentioned changes in microbial populations during storage, the value of any counts obtained for the purposes of exposure assessment will depend upon the timing of the tests and the subsequent storage history of the food.

- **Assessment of dose–response relationship.** The necessary information for microbial pathogens cannot be obtained from animal experiments and must be taken from feeding trials involving human volunteers or be based on count data from foods associated with specific and well-documented outbreaks.

It is clear that the risks to consumers from chemicals in foods are very different from those presented by microbial pathogens, and a unified approach to their regulation may not be feasible, as far as the setting of criteria for the end-product is concerned. The problem is compounded by the practical difficulties that arise when considering the dynamic nature of microbial populations in foods and the uncertainties surrounding the detection of pathogens. Therefore, the systems used in each case to ensure the required level of food safety are likely to remain separate for the foreseeable future.

2.5 Present and future uses of microbiological risk assessment

2.5.1 Trends in food safety control

Traditionally, food safety is assessed retrospectively through microbiological testing of randomly selected food samples. This is done by both the food producer and the appropriate regulatory body. The approach may confirm that the food meets certain statutory criteria at the point of sampling, but takes no account of the likely changes in microbial populations during subsequent handling and storage of the product up to the point of consumption. In practice, there is usually no information on whether such control criteria are effective in protecting consumers. Because of these shortcomings, food safety control is increasingly dependent on a more prospective approach, involving the application of GMP and HACCP principles. For this purpose, the use of predictive microbiology has proved to be as valuable as it was previously in developing processes for, for example, heat inactivation of microorganisms and their spores. Recent progress in predictive modelling has facilitated exposure assessment at each stage of the food chain and has permitted the introduction of risk analysis, which has provided a new milestone in the production of safe food. Thus, acceptably safe food can be produced almost entirely in a prospective and predictable manner, and it is possible to predict that any necessary criteria can be met at the time the food is consumed. The modern approach to safe food production, including the role of GMP, HACCP and risk assessment, is shown schematically in Fig. 2.5. The first step requires a quantitative risk assessment to identify the hazards.

These are then characterised, mostly in terms of dose–response relationships and the severity of the illness caused, followed by exposure assessment and risk characterisation. Finally, risk management requirements are established, using Codex Alimentarius standards, guidelines and recommendations. These involve all interested parties, such as food producers, regulatory authorities, consumer organisations and scientists (the so-called stakeholders). However, any resultant

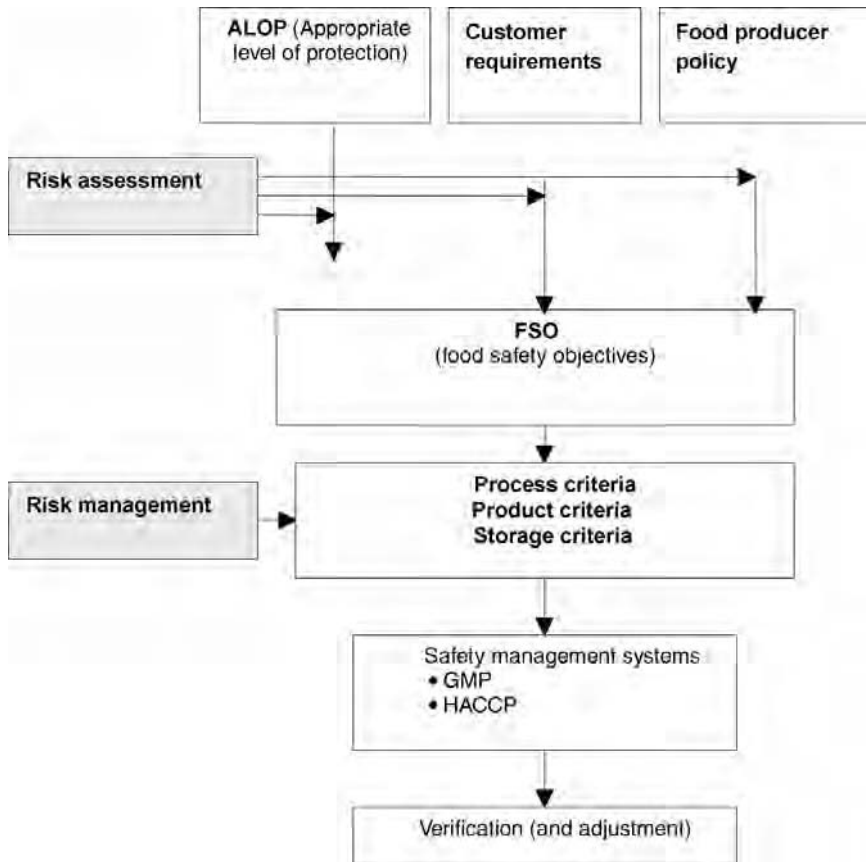


Fig. 2.5 Schematic presentation of the manner in which microbologically safe food is produced and the role of risk assessment and risk management. For further explanation see text.

microbiological standards are of limited value, for the reasons discussed previously, and only useful for microbologically stable food products. Therefore, participants at the IAFP congress in Minneapolis, USA, in August 2001, including members of the ICMSF, proposed a change from control based on food standards to a system involving an ALOP at the time of consumption of the food.

An ALOP results from the outcome of a risk assessment, taking account of the costs involved in any control action. Such an analysis is made by the stakeholders, with the knowledge that reducing the risk of a hazard occurring will increase the food production cost, but is hardly likely to reduce the risk to zero. The nature of the ALOP depends very much on the severity of the hazard and the type of food in question. For canned foods that are purchased by large numbers of consumers, the ALOP for toxigenic *Clostridium botulinum* implies that the occurrence of botulism is reduced to a negligible level. In the canning of low-

acid foods, it is generally agreed that the ALOP requires the use of a process giving a (theoretical) 10^{11} – 10^{12} -fold reduction in the level of *Clostridium botulinum*.

For freshly cut vegetables that are eaten raw, the ALOP may require a 50% reduction in foodborne disease over a 10 year period. A similar kind of target has been set in the USA, by the FDA for raw poultry meat (Buchanan *et al.*, 2001). Clearly the targets must be expressed in terms of food safety objectives. In relation to poultry meat, a 50% reduction in disease over 10 years can follow only from a corresponding decrease in pathogen contamination of poultry carcasses. The relevant calculation can now be made from a proper risk assessment. From the producer's viewpoint, the meeting of food safety objectives is just one consideration. Account must also be taken of any specific customer (retailer) requirements as well as the producer's own profitability.

In producing safe food, there are various aspects, which can be grouped in three main categories:

1. The type of process used, which may include heat treatment, irradiation, high-pressure technology, etc.
2. Product composition, including addition of, for example, salt, acids or other preservatives.
3. Storage conditions, involving storage temperature and time, gas packaging, etc.

Effective management of these aspects allows all food safety requirements to be met. In doing so, it is necessary to define criteria for process performance, product composition and storage conditions. The setting of the criteria is the task of the risk manager, and use of the HACCP concept is the managerial tool to ensure that the criteria will be met in practice. Finally, a verification step is needed to demonstrate that the ALOP, the customer requirements and the producer's own objectives are being met. If, for any reason, it is impossible to meet the ALOP, then production of the food in question must cease.

2.5.2 Some examples

Setting storage criteria for pasteurised milk

The presence of *Bacillus cereus* in pasteurised milk should be considered hazardous, because the organism is potentially pathogenic and can multiply in this product. The organism is also associated with foodborne illness resulting from the consumption of dairy products. In most European countries, a limit value of 10^4 organisms per ml or gram at the time of consumption has been set for dairy products and other foods. Some countries, including the Netherlands, accept the presence of 10^5 per ml in milk, and to meet this limit, the storage criteria for pasteurised milk are 7°C for a maximum of 7 days. Human exposure to *Bac. cereus* from milk consumption was studied by Notermans *et al.* (1997). Exposure was assessed by (i) enquiring about storage conditions (temperature and time) for pasteurised milk that were used by households in the Netherlands and (ii) carrying out storage trials at 6–12°C. The temperatures studied were

Table 2.5 Exposure to *Bacillus cereus* after consumption of pasteurised milk based on model experiments of Notermans *et al.* (1997)

Exposure dose (organisms/ml)	Probability (%)
> 10	99
>10 ²	21
>10 ³	14
>10 ⁴	11
>10 ⁵	7
>10 ⁶	4
>10 ⁷	<1

those observed in a survey of Dutch domestic refrigerators. The probability of exposure to different doses of *Bac. cereus* is given in Table 2.5.

The results demonstrated that 7% of the milk contained >10⁵ *Bac. cereus* per ml at the time of consumption. It was also shown that storing milk according to the producer's recommendations would prevent the limit value of 10⁵ per ml from being exceeded.

Risk management options

It is clear that managerial action is required to ensure that the official criterion is met. In order to take such action, it is necessary to assess the predominant factors that determine the final level of *Bac. cereus* when the milk is consumed. These are:

- The initial level of contamination with the organism (N_0), which is influenced by factors such as the grazing period for the cows and control of hygiene during milking.
- The storage time (t) for the pasteurised milk.
- The storage temperature (T) of the milk.

Zwietering *et al.* (1996) derived an equation for calculating the effects of each of the above variables on the numbers of *B. cereus* finally present (N):

$$N = N_0 e^{0.0137T^2 t}$$

From the equation, it can be observed that storage temperature has the largest effect on the level of *Bac. cereus* at the time the milk is consumed. This is followed by storage time, while initial count has only a minor effect. The effects are illustrated by the data presented in Table 2.6.

Selection of new control options

The simplest option for the milk producer would be to do nothing, since the prescribed storage conditions are quite adequate on the label. However, the situation is different if consumer complaints start to increase and the producer

Table 2.6 Storage times for pasteurised milk giving a final count of *Bacillus cereus* of 10^5 / ml: effects of initial number and storage temperatures (Notermans *et al.*, 1997).

Initial number per ml	Storage temperature (°C)			
	6	8	10	12
0.001	13.4 ^a	7.6	4.8	3.4
0.01	11.3	6.4	4.1	2.8
0.1	9.2	5.2	3.3	2.3
1	7.0	4.0	2.5	1.8
10	4.9	2.8	1.8	1.2

^a Storage time in days.

loses business. In this case, a lower storage temperature could be recommended on the label, although it is by no means certain that consumers would respond by reducing the temperature in their refrigerators. In addition, many countries have stipulated temperatures for storing chilled foods, e.g. 7°C in the Netherlands, and any decrease would involve negotiations with trading authorities, retailers and consumer bodies. The last option would be to reduce the maximum storage time, but this would raise other considerations. Retailers, for example, may well favour such a step, for the simple reason that consumers would need to purchase milk more frequently. While reducing the temperature would possibly be more costly to the retailer, a shorter storage time would necessitate more frequent deliveries and therefore be an additional cost to the supplier.

Because of progress in predictive modelling, the risk assessor is able to determine the effect on product safety of different storage conditions. It is, however, the risk manager who has to make the final decision on the action to be taken, and this involves consideration of all the relevant aspects of the problem.

From targets to HACCP criteria

In many countries, poultry meat products contribute significantly to foodborne disease, especially that caused by *Salmonella* and *Campylobacter* spp. Although various attempts have been made to improve the situation, little progress has been made until recently. One of the reasons may be the continuing deadlock in accepting responsibility. Consumers expect pathogen-free products, which cannot be achieved at the present time, while producers refer to the unhygienic practices of consumers, when food is prepared in the kitchen. In order to change this situation in the USA, the FDA has set a target, whereby foodborne disease from poultry meat will be reduced by 50% over a ten-year period (Buchanan *et al.*, 2001) and producers are held responsible for meeting the target.

For operational purposes the target, which is an ALOP, needs to be translated into appropriate process, product and storage criteria. To set the criteria, it is necessary to calculate the requisite reduction in contamination of poultry meat with the key pathogens (food safety objectives). The following steps are required:

34 Microbiological risk assessment in food processing

- Assessment of the prevalence of *Salmonella* and *Campylobacter* spp. in commercial broiler flocks.
- Quantitative assessment of product contamination with the pathogens at the end of processing.
- Determination of the effect of storage on pathogen contamination.
- Assessment of the effects of food preparation by consumers on the survival and spread of the pathogens.
- Collection of consumption data.

The information thus provided will allow an assessment to be made of human exposure to the pathogens at the time the food is consumed. Existing dose–response relationships can be used to determine the likely number of disease incidents or the probability of disease. These figures now need to be reduced by 50% and the new target for exposure can be determined again from the dose–response relationships.

There are several ways in which the new food safety objectives can be met. One approach is to set process performance criteria, which might include low environmental temperature, minimum processing time, spraying carcasses with lactic acid, washing in chlorinated water etc. Also, product storage conditions (low temperature, short time) may be important to minimise any risk of growth of pathogens. The processing procedures and the conditions of processing and storage provide the CCPs in the HACCP system. If information is available, critical limits can be based on published data, although this is not always possible for specific parts of the process or storage conditions. Until more sophisticated models have been developed, the necessary calculations must be based on simple *D*-values and modelling of growth parameters.

2.5.3 Current issues in microbiological risk assessment

As with all risk assessment procedures, MRA comprises hazard identification, hazard characterisation, exposure assessment and risk characterisation as the four basic elements. It is a relatively new discipline in relation to the production of microbiologically safe food. However, the principles embodied in the approach have been applied for many years, especially to heat processes developed for low-acid canned foods and treatment of milk in the 1930s and 1940s respectively. The resultant heating regimes have proved to be very successful in controlling any foodborne diseases that might be associated with these sources.

Although MRA was first introduced as a food safety measure in 1995, its use has been limited and the approach has yet to lead to internationally recognised microbiological criteria. It may take longer than anticipated for the concept to be universally accepted and applied, but initiatives taken by the WHO and FAO to organise meetings of experts (see Section 2.4) could help to stimulate interest. It should be recognised, however, that the application of MRA in the production of safe food will be hampered by the present lack of any comprehensive, microbiological food safety policy. The problem is compounded by the large

diversity of available food products that vary from fully processed up to almost unprocessed ready-to-eat products. Within these categories, there are differences in processing methods, product composition and storage conditions. In addition, microbial contamination may be introduced into the food chain, sometimes from the raw materials used in product manufacture. In other instances such contamination may come from organisms that are endemic in the processing environment or through human handling of the food, etc. Despite the use of various processes for reducing the microbial load on food, consumer safety cannot always be guaranteed because of the potential for recontamination.

As well as the above-mentioned product diversity, there are significant differences between products in the types of microorganisms that may be present. Among the variety of possible foodborne pathogens are rickettsiae, viruses, bacteria, moulds and parasites. Each of these groups contains organisms with particular growth characteristics, ecological behaviour and disease potential. With so much variation between products and the nature of the contaminants present, it is hardly surprising that separate risk assessments are not really feasible. This is especially so if end-product criteria based on MRA are required in each case. Such an approach has been attempted recently by the ICMSF, but without real success. For example, in relation to potential growth of *Listeria monocytogenes* in food and the varying sensitivity to this pathogen among different human groups, the ICMSF proposed 15 separate categories of food (ICMSF, 1994), each with its own food safety objective (FSO).

Among other weak points in current attempts to use MRA are difficulties in (i) exposure assessment, (ii) assessment of dose–response relationships and, consequently, (iii) the uncertain outcome of risk characterisation. Another aspect to be considered is human perception, which has no direct relationship to health problems, but carries significant implications for consumer confidence in the safety of the food supply. Finally, it should be noted that mistakes are sometimes made in attributing human illnesses to the consumption of contaminated food and a misleading impression may result.

Exposure assessment

Microbiological models are an important tool for this exercise. Suitable models are necessary because it is impracticable to test individual food products for this purpose (see Section 2.4). The value of end-product testing is mainly in relation to verification procedures, which are discussed below.

For the purposes of exposure assessment, the Monte Carlo type of model is particularly relevant and is based on the distributions of all appropriate variables in the food production process. These will include product composition and storage conditions, consumption patterns, etc. The approach involves taking random values for each of the distributions to assess the final exposure distribution. A weakness is that the distributions of variables must be independent of each other and often this is not the case. For example, storage time and temperature for pasteurised products are usually inter-dependent. Nevertheless, the Monte Carlo approach provides much more realistic data,

when compared with a worst-case scenario, as used in the past. Furthermore, it provides information that takes account of the uncertainty or variability in human exposure to microorganisms. Experimental data on human exposure to pathogenic organisms via beef hamburgers (Cassin *et al.*, 1998) and *Salmonella enteritidis* from pasteurised liquid egg (Whiting and Buchanan, 1997) show that exposure levels can vary widely, although no allowance was made for error.

Dose–response relationship

In risk assessment, much attention is given to dose–response relationships, which are considered essential in risk assessments for toxins, food additives, drug residues, etc. After MRA became a legal requirement in 1995, attention was also focused on microorganisms in this respect. Although it is clear that experimental use of animal models has provided important information on mechanisms of pathogenicity in organisms such as *L. monocytogenes* (Notermans *et al.*, 1998), the data obtained cannot be used to derive dose–response relationships for humans. Instead, such relationships are mainly based on data from human volunteer studies or the analysis of foodborne disease outbreaks involving microorganisms. These data show considerable variation, even between the serotypes of *Salmonella* (Kothary and Babu, 2001). Currently, however, reliable information on microbiological dose–response relationships is still very scarce. Among the difficulties is the fact that challenge studies on volunteers can only be carried out with the less dangerous pathogens and, of course, the volunteers will usually be healthy adults. In practice, foodborne infections are commonly seen in the more vulnerable groups within the general population (infants, the elderly, people undergoing treatment with immunosuppressive drugs, people with AIDS). These individuals may constitute about 20% of the whole population.

A further aspect, which must be taken into account, is the physiological condition of the disease agent. This will affect virulence and, in turn, the dose–response relationship (Abee and Wouters, 1999). The situation is complicated by the ability of some microorganisms to protect themselves against external stress factors that might arise in minimally processed food products (Abee and Wouters, 1999; Hecker and Völker, 1998). Protection may also be afforded against the acid conditions of the stomach, during passage of the contaminated food following ingestion (Abee and Wouters, 2002). On the other hand, virulence may be adversely affected by the nature of the food matrix, within which the organism is contained, so various factors must be considered.

Risk characterisation

This is the outcome of exposure assessment and establishment of the dose–response relationship, taking account of the severity of illness caused by a particular pathogen. However, it suffers from the fact that both exposure assessment and dose–response analysis are not yet clearly established in MRA. Only time will tell whether the present approaches in exposure assessment and dose–response analysis will result in widespread acceptance and application of

MRA. There is some debate about the possible use of epidemiological data on microbial foodborne illness as an alternative for the purposes of risk characterisation. Because relevant information is lacking in nutritional risk assessment, use of epidemiological data has become common and is applied successfully. In relation to microbial foodborne illness, data collected in countries such as the USA, the UK and the Netherlands could be used to determine, for example, the incidence rate for human salmonellosis caused by egg consumption, eating of poultry meat, etc. The uncertainty of the outcome of that kind of calculation is relatively well defined and very much less than that from data based on exposure assessment and dose–response modelling. Also, the use of epidemiological methods, such as case-control and cohort studies, allows the most important risk factors to be identified.

Where to go from here?

The introduction of MRA is essential in order to assess the risk and severity of a microbial foodborne disease. For the management of an unacceptable risk, FSOs would need to be formulated. These should not be simply microbiological criteria, such as a specified number of cells of a particular pathogen that can be present in a food at the time of consumption. A better approach is that used recently in the USA, where targets have been established as FSOs for raw poultry and red meat products (Buchanan *et al.*, 2001). The target for foodborne disease caused by poultry consumption is to reduce the present level by 50% over a period of 10 years (see Section 2.5.2). Setting a target for raw products of this kind is an attractive proposition, but its success depends largely on the availability of an appropriate means of reducing microbial contamination of the product and a reliable system for collecting data on foodborne disease.

Verification

Currently, an important issue in microbiological risk analysis is the process of verification, which is a means of determining whether the analysis, including MRA, has been carried out correctly and that an acceptable level of protection has been obtained. The process of verification is presented schematically in Fig. 2.6. Verification comprises several elements: (i) an evaluation to determine whether the risk analysis resulted in FSOs and, when introduced, whether these met the expectations of the stakeholders, i.e. all those involved in the process and, if not, (ii) adaptation of the FSOs, or (iii) re-evaluation of the MRA. The last step is also relevant when new scientific information becomes available that questions the value of the MRA. Adaptation of FSOs may also be necessary as a result of epidemiological data on the frequency of foodborne diseases, data from microbiological monitoring of the food product or any new information, such as that involving changes in risk factors. This last point illustrates the dynamic nature of the circumstances involved in the production of microbiologically safe food.

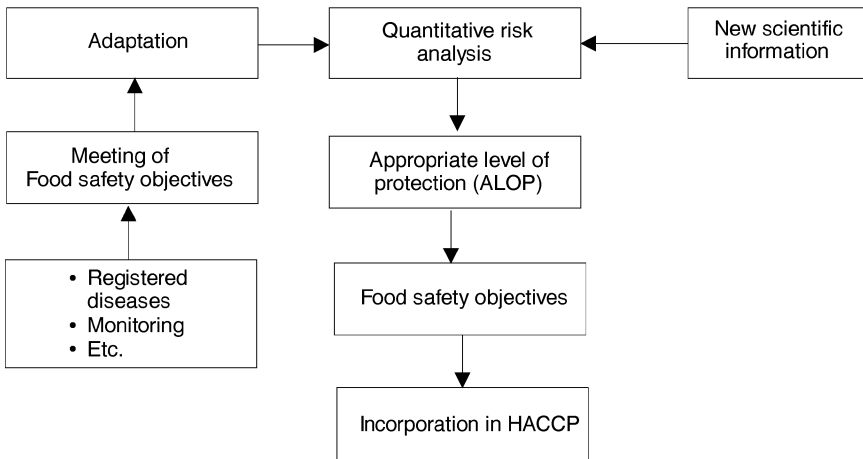


Fig. 2.6 The process of verification of microbial risk assessment.

2.6 List of abbreviations

ADI	Acceptable Daily Intake
ALARA	As Low As Reasonably Achievable
ALOP	Appropriate Level Of Protection
CAC	Codex Alimentarius Commission
CCFAC	Codex Commission for Food Additives and Contaminants
CCFH	Codex Commission for Food Hygiene
CCP	Critical Control Point
CCPR	Codex Commission for Pesticide Residues
CCRVD	Codex Commission for Residues of Veterinary Drugs in Food
FAO	Food and Agriculture Organisation of the United Nations
FDA	Food and Drug Administration
FSO	Food Safety Objective
GAP	Good Agricultural Practice
GMP	Good Manufacturing Practice
HACCP	Hazard Analysis Critical Control Points
HTST	High-Temperature, Short-Time
IAMFES	International Association of Milk, Food and Environmental Sanitarians
IAFP	International Association of Food Protection
ICMSF	International Commission on Microbiological Specification for Foods
JECFA	Joint FAO/WHO Expert Committee on Food Additives
JMPR	Joint FAO/WHO Meeting on Pesticide Residues
MRA	Microbiological Risk Assessment
MRL	Maximal Residue Level

NACMCF	US National Advisory Committee on Microbiological Criteria for Foods
PMTDI	Provisional Maximal Tolerable Daily Intake
PTWI	Provisional Tolerable Weekly Intake
QRA	Quantitative Risk Analysis
SPS Agreement	WTO Agreement on the Application of Sanitary and Phytosanitary Measures
WHO	World Health Organisation
WTO	World Trade Organisation

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Part I

The methodology of microbiological risk assessment

3

Microbiological risk assessment (MRA): an introduction

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3.1 Introduction

New or re-emerging microbiological food safety problems have established the need to ensure that microbiological hazards are managed against the background of a sound scientific process. Essentially, this process consists of gathering and analysing scientific information and data with the objective of identifying what pathogens and/or their toxins or metabolites, foods or situations may lead to foodborne illness, and then of determining the magnitude of the impact these may have on human health, together with an identification of the factors that influence it. This scientific process is known as 'microbiological risk assessment' (MRA). The present requirement is that MRA should be conducted according to a structured format, and the development of quantitative, probabilistic approaches is encouraged.

There are a number of areas where risk assessment may inform public or private decision making. Where public organisations are concerned, these encompass:

- Policy determination (determination of an 'appropriate level of protection', identification of risk mitigation strategies and establishment of priorities for action).
- Control activities (analysis and evaluation of the impact of production systems on food safety, identification of the best points at which to implement control, comparison of control options/mitigation measures).
- Design and implementation of monitoring and surveillance programmes and inspection systems.
- Apportionment of resources (how much public money is it desirable to spend for various purposes and on what?).

- Guidance for food safety and microbial research (acquisition of information and data that are lacking in the actual knowledge base).
- Education (advice to private organisations on how to manage food safety risks and to individuals on their food choices and related behaviour).

Similarly, in addition to complying with their statutory duty, private organisations involved in the production/manufacture of foods should ensure that they manage food safety risks in a way that is consistent with the expectations and requirements of society. They should, in particular, determine the relative importance of factors and parameters in the production/manufacture/handling systems they operate, their possible variations, and their impact on the safety of the food. They should equally design, or consider altering, their products, processes and/or control measures to meet the level of protection required. In doing so, food-producing companies should ensure that their specific policy choices and market constraints do not compromise the intangible requirement for food safety.

A formal, and preferably quantitative, microbiological risk assessment (MRA) is a useful tool in carrying out the above functions (Lammerding, 1996):

- It provides a structured and explicit approach to examining the nature and characteristics of the hazard(s) under consideration, the production to consumption pathways and how they impact on the fate of hazards and level of human exposure, the potential and severity of adverse consequences and the factors involved and the subsequent risk incurred.
- It improves an understanding of the key issues and assists the efforts to foster resources and interventions where they are most necessary and/or useful. In particular, it provides input for adoption of a goal-setting approach to legislation and standards into the food safety control and assurance programmes of the food industry.
- The MRA report serves as a source of information and a database for informed decision making. It also provides an aid to identify where gaps in knowledge exist and thus, where additional information is needed. It therefore helps to identify research needs, to establish research priorities and to design commissioned studies.
- It increases consistency and transparency of the analytical process. A formal MRA provides explicit data that are amenable to review. It describes shortfalls, such as the nature and extent of uncertainties attached to the data. It makes explicit, and focuses attention on, the structure of models used, and the assumptions made, and discusses how these impact on the risk estimates.
- It facilitates communication between the scientific and technical experts, the decision makers and other interested parties. It makes the risk and its determinants more transparent.
- It assists the appraisal of the health impact of risk management options by allowing model simulations of control measures before they are implemented. This also allows for more rigorous application of other tools utilised in decision making.

However, some inherent limitations of MRA have been discussed in many documents. Suffice it to say that MRA is, and will probably continue to be, an imprecise discipline. It utilises the information that is currently available: therefore the results of an MRA can only be as good as the information and models utilised. Uncertainties permeate the whole process, caused in particular by the incompleteness of data, the imperfect understanding of biological processes and the methodology adopted to design and operate models. Also, much criticism has been raised because value judgements and policy choices may be incorporated in the process. MRA often operates in a decision-making context that may impose pressures on the content of the assessment itself, unless appropriate safeguards are established. The usefulness of MRA depends on the decision context. Finally, one should be aware of the warning by Ralph Nader (1993) who perceived risk assessment as ‘a massive overcomplication and overabstraction’ that attempts to make precise something that by nature cannot be precise.

With regard to these limitations, the value of MRA should not be exaggerated. MRA will never provide simple solutions to complex problems: at its best, it can only be a credible, science-based input into the multidimensional, value-laden considerations that contribute to shape decisions regarding food safety. Risk assessment will never replace sound judgement and considered governance with regard to risk issues. It is the responsibility of scientists and risk assessors, combined with risk managers, to increase the reasonableness, consistency, transparency and credibility of MRA. This being ensured, it can be expected that, in many cases, MRA will contribute to improving decisions and be an essential aid to promoting understanding and confidence in resultant actions.

3.2 Key steps in MRA

In the food sector, microbiological risk assessments have been conducted for many years in one form or another by the scientific community, the food industry and regulatory bodies. Recently, however, the need to adopt more formal approaches and principles led to the development of framework(s) for microbiological risk assessment for foods.

In 1999, the Codex Alimentarius Commission adopted, on the proposal of the Codex Committee on Food Hygiene, a document entitled *Principles and Guidelines for the Conduct of Microbiological Risk Assessment* (Alinorm 99/13 A). This document defines microbiological risk assessment as

A scientifically based process consisting of the following steps:

(i) hazard identification,

the identification of biological agents capable of causing adverse health effects and which may be present in a particular food or group of foods,

- (ii) hazard characterisation, the qualitative and/or quantitative evaluation of the nature of the adverse health effects associated with the hazard. [A desirable feature of hazard characterisation is establishing a dose–response relationship, i.e. the determination of the relationship between the magnitude of exposure (dose) to a biological agent and the severity and/or frequency of associated adverse health effects (response)],*
- (iii) exposure assessment, the qualitative and/or quantitative evaluation of the likely intake of biological agents via food as well as exposures from other sources if relevant,*
- and (iv) risk characterisation, 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 characterisation and exposure assessment.*

This document provides an outline of the elements of a microbiological risk assessment, indicating the types of decision that need to be considered at each step. The Codex guidelines are interesting for several reasons. Although they bear similarities with the paradigms utilised in other fields of activities and thus ensure commonalities of approaches, they allow features unique to the attributes and concerns of microbiological food safety to be incorporated. They are flexible enough to handle a variety of applications, they may be used for planning and conducting qualitative or quantitative MRAs of varying complexity and they have been applied successfully to a variety of MRAs in different food safety contexts. As a consequence, they can be considered as an internationally recognised framework of primary interest to governments and other organisations, companies and other interested parties that need to prepare a microbiological risk assessment for foods.

In addition to Codex, several groups have developed guidelines of more general application, which have also been proposed for use in microbiological risk assessment for foods. These documents are generally centred on the same logic as the Codex guidelines and include all essential steps. However, they differ in the denomination and grouping of stages, and, at times, on the extent to which risk management and risk communication are integrated in the risk assessment framework. For instance, the framework developed by the ILSI Risk Science Institute (ILSI, 2000) places a specific emphasis on the need for a dialogue among the risk manager, the risk assessor and the stakeholders to utilise resources to produce scientifically sound risk assessments relevant to management decisions and public concerns. Therefore, the initial step in the ILSI framework is ‘problem formulation’, a systematic planning step that identifies the goals, breadth and focus of the microbiological risk assessment, the regulatory and policy context of the assessment and the major factors that

need to be addressed for the assessment. The risk assessment itself is defined by the ‘analytical phase’ which is the technical examination of data concerning potential pathogen exposure and associated human health effects. Elements of the process are ‘characterisation of exposure’, which includes pathogen characterisation, pathogen occurrence, exposure analysis and results in an exposure profile, and ‘characterisation of human health effects’ which include host characterisation, evaluation of human health effects and quantification of the dose–response relationship; the result is a host–pathogen profile. Risk characterisation is the final phase, combining the information of the exposure profile and the host–pathogen profile. In another context, the framework for import risk analysis developed by the Office International des Epizooties (OIE, 1998), recognises that hazard identification is the necessary first stage, but places it outside the risk assessment process. The risk assessment itself includes ‘release assessment’, a description of the biological pathway(s) necessary for a risk source to introduce biological agents into a particular environment, and a qualitative or quantitative estimate of the complete process occurring; ‘exposure assessment’; ‘consequence assessment’; and concludes with ‘risk estimation’.

Although differences in approach may create difficulties in communication and understanding, differences between frameworks are only a minor problem, provided that all the essential components described in the Codex document are included, and that the approach is adapted to its specific purpose, is internally consistent, and fulfils a number of essential principles. In particular,

- **An MRA should clearly state the purpose of the exercise including the form of the estimate that will be the output:** the purpose and objective of the MRA should be clearly identified, as well as the questions that the risk assessment should answer. This requires an appropriate dialogue between assessors and managers, without influencing the necessary independence and integrity of the risk assessment.
- **The MRA should be transparent:** methods, assumptions and judgements should be clearly stated and understandable to the intended audience, who should also be provided with the information necessary to evaluate the nature and adequacy of the data and methods utilised.
- **Data should be of sufficient quality and precision:** data and data collection systems should be of demonstrable quality, whereas the best available information and expertise should be applied in order to reduce uncertainty and increase reliability of the risk estimate.
- **The risk estimate should contain a description of uncertainty and where the uncertainty arose during the risk assessment process:** there should be a clear understanding and description of any limitations in the data, methods or models utilised in the risk assessment and of how these limitations influence the risk estimate.
- **Where appropriate, the MRA should consider the fate of the microbiological hazard(s) in food and the disease process following**

infection: the dynamics of microbial growth, survival or death should be explicitly considered (and also, where applicable, the dynamics of toxin formation and destruction). The interactions between humans and the pathogenic agent following consumption and infection as well as potential for further spread should be part of the assessment.

- **Risk estimates, where possible, should be reassessed over time against independent human illness data and when new data become available.**

Based on the Codex framework, qualitative or quantitative microbiological risk assessments may be undertaken (Lammerding and Fazil, 2000).

Qualitative risk assessments provide a descriptive treatment of information, based principally on collation and review of scientific literature and data. Most traditional microbiological risk assessments in the food sector have been, and still are, mainly qualitative. Qualitative risk assessments remain the only option when data, time or other resources are limited. Alternatively, they may be undertaken as a first evaluation of a food safety issue and/or to determine whether a more sophisticated, quantitative approach is necessary. Qualitative MRAs should follow the systematic approach delineated in the Codex framework and include sections dealing with hazard identification, hazard characterisation (including, where available, review of dose–response information), exposure assessment and risk characterisation.

Quantitative risk assessments are mathematical analyses of numerical data, based on mathematical (and probabilistic) models. The development of quantitative approaches to microbiological risk assessment is currently encouraged, based on the assumption that these would increase transparency, provide a better insight into the microbiological risk, while allowing for comparisons such as between processes or between the effectiveness of different control options. By developing mathematical models, risk assessors are forced to carefully consider and characterise the scientific basis for their estimates, including an explicit statement of all the assumptions made. The models utilised are, in themselves, important scientific tools: they provide a structured framework for analysing the information available, they aid in identifying data gaps and assist in optimising the collection of data where they are most needed, they provide a context for discussing the biological processes involved and for improving their understanding, and they help in identifying and focusing on critical issues. However, the expectations placed on quantitative MRA should not be exaggerated. The results should be interpreted carefully and are valid only as far as the data and assumptions are valid. Quantitative estimates are by no means exact values, but rather an indication of the order of probability of an adverse event occurring. Also, in developing models, mathematics and statistics at advanced and increasingly sophisticated level are used, making their review and use by non-specialists difficult. Significant efforts must be made to present the models and results of a quantitative MRA in a format accessible to the different groups that would make use of the outputs.

In the following sections, the Codex framework will be utilised as a basis to illustrate and briefly discuss the different elements that need to be considered at each stage.

3.3 Hazard identification

Hazard identification is conventionally the first step in risk assessment. With regard to food microbiology, the purpose of hazard identification is to identify the microorganism(s) of concern that may be present in food.

For most of the formal microbiological risk assessments undertaken so far in the food sector, the approach to hazard identification has been quite straightforward and involved usually the *a priori* definition of a pathogen/product or process combination, e.g. risk assessment of *Listeria monocytogenes* in ready-to-eat foods. Most microorganisms considered so far are established foodborne pathogens. The situation(s) to be assessed are identified by the risk managers that commission the risk assessment. In such circumstances, the association of a pathogen and a particular food is already well documented and the requirements for formal information are minimal. In fact, in qualitative risk assessments, hazard identification concentrates on gathering and collating existing information on the characteristics of the pathogen that affect its ability to be transmitted by the product and to cause disease in the host. In quantitative risk assessment, this information serves as an input to the development of the model utilised for further analysis.

This situation, however, is unique. It results from the fact that most formal risk assessments publicly available have been commissioned by public authorities with the aim of identifying, in relation to a given and well-established pathogen, the foods or groups of foods that require action, of determining appropriate preventive/control measures, and establishing numerical limits and standards. In other circumstances, hazard identification requires different approaches.

Hazard identification may be developed in relation to the assessment of the risk potentially associated with a given product. In that case, hazard identification is a categorisation activity, identifying which microbiological agents may be transmitted by the food and be potential hazards in a given set of situations. In that case, reliable hazard identification is dependent on the availability of microbiological and epidemiological data to determine which pathogens have been, or could be, associated with the product, and on the availability of human (or animal) health data on the occurrence and levels of pathogens in the product of concern. Recently, expert systems have been developed to assist in this approach (Van Gerween *et al.*, 2000).

Hazard identification may also be the first step in understanding a new, or emerging, food safety problem. In such circumstances, microbiological hazard identification is quite similar to hazard identification for toxic chemicals. Specific emphasis would be given to evaluating the weight of the scientific

evidence for adverse effects in humans or animals (i.e. in determining, or confirming, the strength of an association), in ascertaining the ways in which the adverse effects may be expressed and the major sources of exposure.

3.4 Hazard characterisation/dose–response assessment

In the Codex framework, whereas the first stage of a microbiological risk assessment consists primarily of identifying the microorganism(s) of concern in a food, hazard characterisation is centred on providing a qualitative and/or quantitative evaluation of the nature of the adverse effects. This would preferably include a dose–response assessment, so that the dose–response relationship identified at this stage can be combined subsequently with the potential for exposure, to provide an estimate of the probability of adverse effects which may occur.

In this context, it has to be borne in mind that the response of a human population to a pathogen is highly variable. The frequency, severity and duration of a microbiological disease is dependent on a variety of interacting factors related to the pathogen, the host and the environment including the food vehicle. These have been referred to as the ‘infectious disease triangle’ (Coleman and Marks, 1998) and the hazard characterisation stage of the risk assessment should provide information on their characteristics and on their interaction in determining adverse health effects. Therefore, microbiological hazard characterisation involves considering three elements: the review of the basic characteristics of the pathogen, the host and the matrix; the description and evaluation of the human health effects and the dose–response analysis. In qualitative risk assessments, the approach is mainly discursive and these three elements and the factors to be considered can be organised in the form of structured questions that would govern the collection and analysis of information and data. The approach may be the same in quantitative risk assessments, but in that case, the information and data collected are collated to serve principally as a basis for the elaboration of dose–response models.

3.4.1 Review of the characteristics of the pathogen, the host and the environment

When not already done during hazard identification, this stage involves determination and review of the characteristics of the pathogen that affect its ability to be transmitted to and cause disease in the host. Specific consideration should be given to the intrinsic properties of the pathogen that influence infectivity, virulence and pathogenicity, to the factors that may affect or alter these characteristics and to the variability in the microbiological population (e.g. strain variation). Additional consideration should be given to the tolerance to adverse conditions and resistance to control or treatment processes and to the potential for secondary spread.

The factors related to the host refer to the characteristics of the potentially exposed population that may influence its susceptibility to a given pathogen. Specific consideration should be given to the host's intrinsic or acquired traits that modify the likelihood of infection and the probability and/or severity of illness. Many host-related factors may be considered, such as age, immune status, genetic factors, concurrent or recent infections, use of medication, pregnancy, breakdown of physiological barriers, nutritional status, and social and/or behavioural traits. Not all of these factors would be relevant in a specific risk assessment. What is important is that hazard characterisation provides information of who is at risk, and on the stratification of the exposed population with regard to the relevant factors that influence susceptibility and severity.

With regard to foodborne pathogens, the factors related to the environment are principally those that influence the survival of the pathogen through the hostile environment of the stomach. These may include the conditions of ingestion, the composition and structure of the food and the processing conditions including the potential for microbial competition, etc.

3.4.2 Description and evaluation of adverse health effects

At this stage, the whole spectrum of possible effects should be considered, including asymptomatic infections and clinical manifestation whether acute, sub-acute or chronic (i.e. long-term sequelae). In all cases, the characterisation should include a definition of what is an 'infection' and what constitutes a clinical 'case'. An important element of the analysis of the clinical manifestations is an evaluation of the severity of their possible outcomes. Several indicators may be used (ILSI, 2000). For example, for mild gastrointestinal illnesses, consideration should be given to the duration of the disease, or to the proportion of the population affected. Where medical or hospital care is required, severity may be expressed in terms of costs (e.g. cost of treatment, value of workdays lost). Where pathogens are associated with a certain degree of mortality, an indicator would be the mortality rate. Recently, quality of life indicators have been proposed for use in the evaluation of the human health effects (Havelaar *et al.*, 2000). These include the number of years lost and the number of years lived with disability, integrated in one single indicator of the global health burden, the Disability Adjusted Life Years. A definition of the severity scale should be provided, specifying what is the indicator chosen and how it can be measured.

Information on the adverse health effects should also include consideration of the epidemiological pattern of the disease. The frequency, incidence and prevalence of the disease and/or its clinical forms should be addressed, together with their evolution with time and seasonal variations. The description should include a division of the clinical forms according to specific subpopulations. Specific consideration would also be given to the extent and amount of asymptomatic carriers and potential for secondary transmission. The description should include information on uncertainties and their sources. Wherever

possible, the characterisation should incorporate information on the physiopathology of the disease, i.e. on the biological mechanisms involved.

3.4.3 Dose–response analysis

Dose–response analysis consists of integrating a number of considerations to determine the relationship between the magnitude of exposure (the dose) and the manifestation, frequency and/or severity of associated adverse health effects (the response) in an exposed population. Elements to be considered may include the characteristics of the pathogen, the host and the matrix, the route and level of exposure, and the adverse effect considered. Where appropriate information is available, it also involves a discussion of the biological mechanisms involved.

Dose–response analysis is strongly influenced by the quantity and quality of data available. These may result from experimental studies (human volunteer feeding studies, animal models, *in vitro* studies) or from observational studies (epidemiological investigations, routinely collected data, specific studies). Each approach has advantages and disadvantages (Buchanan *et al.*, 2000). It is therefore critical to acknowledge the strengths and weaknesses of the methods of collection, and the quality of the data utilised, and to express any uncertainty that exists.

Several problems arise when determining a dose–response relationship for foodborne pathogens. In particular, there is a need to express clearly what constitutes the actual dose (number of pathogens enumerated per food unit, number ingested, number that survive through the stomach) and what is the response (infection, clinical case, specific outcome or indicator). A specific difficulty refers to the lack of data to characterise infection: the translation of infection into illness and of illness into different outcomes. In many cases, the available data may only allow the description of a relationship between a dose and clinical illness. Other difficulties arise from the numerous sources of variability that should be taken into account (e.g. in virulence and pathogenicity of the pathogens, in attack rates and in host susceptibility). Therefore, it is essential that the dose–response analysis clearly identifies which information has been utilised and how it has been obtained. The elements and extent of variability should be clearly acknowledged. The uncertainties and their sources should be thoroughly described.

In the traditional approach to microbiological risk assessment, the analysis of the dose–response relationship is based on the collation of the available clinical or epidemiological information. At present, there is a tendency to develop mathematical models. Mathematical models have been used for many years in the field of toxicology. With regard to microbiological risk assessment, it is expected that they would provide assistance in dose–response analysis when extrapolation to low doses is necessary, and that they would provide useful information when accounting for variability and uncertainty. An extensive discussion of dose–response modelling goes far beyond the scope of this introduction and may be found in Chapter 5. Suffice it to say that these models

and their use should be carefully considered. In particular, one has to be aware that the data utilised and the mathematical models selected become the major variables in the final risk estimate when extrapolating to low doses (European Commission, 2000). Fitting different models to the same dataset, or using different datasets with the same model, can give risk-specific doses (the dose associated to a given probability of infection or risk, e.g. 1 in 10^6) that differ by several orders of magnitude. In this context, there cannot be one single dose–response model, whereas the analyst can only make the best possible choice. This implies that subjective choices have to be made. Such choices and the dose–response relationship will have a profound influence on the final risk characterisation. Considering their impact on the decisions to be drawn from the risk assessment (e.g. degree of conservatism), these choices are often not divorced from policy considerations. They should be discussed and agreed with the risk managers that commission the risk assessment. For the sake of transparency, it is a requirement that the basis for dose–response analysis and for the selection of the mathematical model (as determining the slope of the dose–response curve) should be stated and justified, and their implications on the final risk estimate and its potential use clearly outlined.

3.5 Exposure assessment

Taking into account the Codex definition, the goal of exposure assessment is to evaluate the level of microorganisms or microbial toxins in a food at the time of consumption. However, the description of exposure may be more broadly understood, and include the characterisation of the nature and size of the population (or subpopulations) exposed, and of the route(s), magnitude, frequency and/or duration of that exposure. For microbial pathogens, it has to be realised that the description of exposure cannot include only the probability of presence or absence of the pathogen or its occurrence, based on concentration. It has also to consider the prevalence or distribution of microorganisms in space and over time. Microbial populations may evolve under particular processing/storage/product or vehicle/use/*in vivo* conditions. Because the nature and probability of adverse effects may vary with the levels of microorganisms, microbiological exposure assessment is faced with the need to develop a dynamic approach, so as to account for the numerical changes in the microbial population. This should include an evaluation of the role and impact of the intrinsic and extrinsic factors that may influence these changes. Microbiological exposure assessment should therefore involve the interactive characterisation of the source(s), the route(s) of exposure, and the pathogen prevalence/occurrence, to culminate in the evaluation of the magnitude, frequency and pattern of exposure to a pathogen.

All approaches to exposure assessment, whether qualitative or quantitative, are case-by-case exercises, and interpretative or evaluative scenarios are used. In the available MRAs commissioned by national public authorities, or for

international purposes, these scenarios are not intended to reflect one specific, local situation, but aim to be representative of mean, typical or most sensitive situations in a region (or even throughout the world). It has to be acknowledged that when a standard scenario is used, it is currently difficult to determine its applicability. In addition, scenarios should reflect the effects of the variety of factors that impact on pathogen levels and distribution and account for variability and uncertainty in the parameters involved. Such scenarios are built on available datasets. They may also be utilised as a basis for data collection. Therefore attention should be given to the nature and compatibility of data collected in different contexts, and on how they can effectively contribute to characterise a valid, or credible, 'reference' situation.

3.5.1 Characterisation of the source(s), route(s) of exposure and pathogen occurrence

Where the primary goal of a risk assessment is to evaluate the risk to a population from a given pathogen/product combination, the exposure assessment should utilise information and data as closely related as possible to the final exposure. In many circumstances, however, risk assessment is intended to provide information useful for policy making, and should therefore provide insight into the factors responsible for increasing the risk and, more importantly, ways to reduce it. This being the case, determination of the pathogen occurrence should incorporate information on the various factors that may influence the level or concentration of the pathogen before the product reaches the consumer, and their relative influence on the occurrence and prevalence or distribution of the pathogen. Exposure assessment then requires integration of different types of information.

The first relates to the characterisation of the source(s) of the pathogen and the route(s) of exposure. When the risk assessment is developed with reference to a specified product/pathogen combination, the characterisation of the source of exposure is straightforward. Nevertheless, pathogens that are mainly foodborne may also be transmitted by a variety of media, such as other foods, drinking water, household products or the general environment and relevant vehicle(s) should be identified. The associated units of exposure should be determined (e.g. the number and size of food servings). The production to consumption pathway(s) should be characterised, with their possible variability. The size and demographics of the population (or subpopulations) exposed should be determined. Consideration of the temporal nature (e.g. single or multiple exposure) or duration of exposure may be important as well as consideration of potential for secondary transmission. Exposure pathways and transmission potential may in turn be influenced by the behaviour of the potentially exposed population.

The second relates to the occurrence and levels of the microorganism or toxin in the food of concern and to their dynamics over time and at the different stages of the farm-to-fork chain. Information of interest includes that on the microbial

ecology of the food and on the presence of the pathogen in the raw materials and levels of contamination. The analysis then involves characterising the effects of the production, processing, handling and distribution steps on the level and distribution of the pathogen. In this regard, control processes (e.g. thermal inactivation) have significant effects on pathogen occurrence and should be considered. The variability, the reliability (level of process control) and the interdependence of multiple control processes should be analysed. The potential for (re)contamination (e.g. cross-contamination from other foods, recontamination after a killing treatment) as well as the methods or conditions of packaging, distribution and storage of the food should also be considered.

The third focuses on consumption/use patterns and on consumer practices that may affect microbial levels and intake. Elements that may be considered, according to the scope of the assessment, include socio-economic and ethnic background, consumer preferences and behaviour as they influence the choice and the amount of food intake, average serving size and distribution of sizes; amount of food consumed over a year, considering seasonality and regional differences, food preparation practices (e.g. cooking habits, cooking time and temperature, extent of home storage and conditions, including abuse), consumption by specific groups (such as infants, children, pregnant women, elderly or immuno-compromised populations) and distribution of microorganisms in the food (e.g. clustering, micro-colonies).

3.5.2 Use of models

The present tendency is to construct exposure assessment models that permit the description and analysis of the interaction of the above-mentioned factors. The structure, comprehensiveness and level of details of the model depend on the purpose and scope of the assessment, based on the risk management questions and end-points of the assessment. During the development of the model, the assessor is forced to structure the problem and to identify the key processes to be modelled and the information needed. The result can be summarised in a graphical outline of the model structure which should be presented to the stakeholders and to the risk managers with the underlying assumptions and uncertainties.

For qualitative (or semi-quantitative) assessments, simple models that describe the pathways of exposure can be developed. More complex representations may involve, for instance, event tree or fault tree analyses, which provide a framework to identify events that could occur and analyse their likelihood. These may incorporate a semi-quantitative expression of certain parameters and probabilities (European Commission, 2000).

In quantitative exposure assessments, the relationships between the determinants of the exposure are modelled mathematically. The model describes the pathways and processes leading to exposure and may be divided into discrete model units that can be linked to each other (Lammerding and Fazil, 2000). A significant feature of quantitative exposure assessment for microbial pathogens

is the use of predictive microbial approaches and models, within the larger exposure model. Predictive models use mathematical expressions to characterise the changes in the pathogen numbers under various intrinsic and extrinsic conditions. Significant advances have been made in this field in recent years. A comprehensive analysis of the use of predictive microbiology in exposure and risk assessment may be found in Chapters 6 and 10.

The same model structure may be the basis for a deterministic or probabilistic approach. In a deterministic approach, a quantitative assessment of the exposure is conducted based on a single point estimate of the model parameters. Deterministic models have several limitations, and, in particular, tend to ignore variability and uncertainty. In the probabilistic approach, variability and uncertainty are taken into account by using probability distributions instead of point estimate values. Probability distributions of the model parameters are assigned based on experimental data or may be derived from expert elicitation. A number of techniques may be used to calculate the distribution of the output of interest. Today, the tendency is to use stochastic simulation techniques, such as Monte Carlo simulation. This technique involves the random sampling of each probability distribution in the model to produce a large number of scenarios (iterations or trials). The result represents a distribution for the output of interest, based on the combined ranges and frequency of the input parameters. Several applications of Monte Carlo simulation have documented the merit of the method, and commercial software is available. In spite of its relative complexity, the probabilistic approach is now becoming the preferred approach to quantitative microbiological exposure assessment.

3.6 Risk characterisation

Risk characterisation summarises the information from hazard identification, hazard characterisation and exposure assessment in a deliberate process to bring key aspects of the microbiological risk assessment into an integrated picture. It provides an estimation (the 'risk estimate'), which should include the attendant uncertainties of the probability of the occurrence and severity of adverse effects in a given population.

It is important to realise that risk characterisation will bridge the risk assessment process with risk management and decision-making. Therefore, it is essential that the overall conclusion of the risk assessment is complete, informative and useful for decision-makers and managers. From this point of view, risk characterisation should encompass two components:

1. An estimation of the risk that is objective, realistic, credible and scientifically balanced.
2. A description explaining the degree of confidence in the risk assessment by clearly delineating the uncertainties and their sources, the assumptions, along with their impact on the overall assessment. This description should

include a discussion on the strengths and limitations of the assessment and of whether the risk assessment adequately addresses the questions formulated at the outset of the exercise.

The estimation of the risk can be qualitative or quantitative, depending on the data and methods utilised. It involves a description of the nature, severity and consequences of effects anticipated from exposure to a given pathogen, together with an estimation of the probability of a given population being subjected to whatever adverse effect being considered. The final result is usually expressed as an individual risk estimate (e.g. one in a million probability of illness) or as a population risk estimate (e.g. 10 illnesses per year in a certain region). In quantitative, probabilistic risk assessments, the output of risk characterisation is a distribution of the risk.

A specific aspect of quantitative microbiological risk assessments is that a sensitivity analysis of the result of probabilistic modelling should be performed. This refers to the evaluation of the variables used for data input with regard to their effect on the final risk estimate, to provide knowledge on how the effects of changes in the mathematical approach impacts on the results of the risk estimate (Vose, 2000). A sensitivity analysis may have two objectives. The first is to identify the elements or factors that have most impact on the magnitude of the risk. The second is to determine the robustness of the model toward the existing uncertainties and assumptions.

Dealing with the first aspect involves carrying out a sensitivity analysis for the parameters. This can be done in several ways, using well-defined techniques (Saltelli *et al.*, 2000), e.g. relative sensitivity analysis (where a small change in an input parameter is compared with the percentage change in the output) or rank order correlation techniques. Dealing with the second aspect is less defined, and may involve, for instance, investigating the effect of changing a distribution, or any other assumption, on the risk estimate. Similarly, scenario analysis can be used to determine which input parameter(s) contributes most significantly to a given outcome (e.g. an exceptionally high risk, an exposure below a certain value).

Variability and uncertainty, the two components that describe the degree of reliability of the risk estimate, should be clearly and distinctly described. Variability is a function of the system and inherent to any biological population or parameter. Uncertainty is related to the lack of knowledge and may include, e.g. in quantitative risk assessments, parameter uncertainty, model uncertainty and scenario uncertainty. Estimating variability and uncertainty separately will provide useful information for decisions that could follow from risk assessment (European Commission, 2000). For instance, if uncertainty is large, the reliability of future risk assessments may be improved by additional experimental measurements or by focused research. Where variability predominates (large heterogeneity in the system) managers could consider improving the reliability of future risk assessments, e.g. by reducing the number of possible scenarios, or reducing the heterogeneity of the system considered, e.g. by managing for a better control of the manufacturing process. In

quantitative microbiological risk assessments, it should be clearly stated whether the probability distribution of the risk represents variability, uncertainty, or both.

In relation to the above, a critical element of microbiological risk characterisation is an assessment of the assumptions that are made during the analysis, the sources of uncertainty and their impact on the risk estimate. In many assessments, relevant data may not be available for all aspects of the analysis, or may not be of adequate quality. Incomplete theory and gaps in knowledge may also exist. Therefore many choices and assumptions have to be made, each with varying degree of uncertainty. All choices and assumptions should be fully acknowledged. Uncertainties and their sources should be carefully identified and analysed. Choices, assumptions and uncertainties should be evaluated with regard to their impact on the risk estimate, and perhaps more importantly, on how they should be used.

It is important to consider an expression of the confidence in the risk assessment and the resulting estimate; this includes verification and validation. Verification refers to the technical approach taken and is mainly the responsibility of the assessors and may involve quality control procedures and specialist review. Validation refers to the scientific acceptability of the assessment and it may involve investigating the effects of plausible choices, assumptions or scenarios. A specific aspect of quantitative and probabilistic microbiological risk assessment is the comparison of the estimate with observed data from epidemiological studies (e.g. cross-sectional surveys, cohort studies, case-control studies, intervention studies). In this regard, there is a crucial need to conduct high-quality, targeted and more searching epidemiological studies to validate the models and to improve the estimations.

Finally, and with specific regard to the current development of quantitative microbiological risk assessment, it has to be emphasised that risk characterisation should encompass both mathematical estimates of the risk and qualitative information (narratives). Simplified numerical presentation of food safety risks is always incomplete and often misleading. Qualitative information is particularly useful and offers a number of benefits. It explains the nature of the adverse effects and the variability in population exposures. It identifies and explains assumptions, choices, and value judgements and their impact. It describes uncertainties and explains their impact. It provides information on the strength and consistency of the scientific evidence that support the assessment and provides information on the sets of data available, the sets of data chosen, the incompleteness of databases where appropriate, and how these impact on the characterisation of the risk. It provides information and guidance regarding additional or follow-up research. Additionally, the assessors may be able to identify the potential or availability of counter-assessments from different groups and explain the supporting analyses and their relative strengths and weaknesses. All such qualitative information will ensure that the non-scientists who will use the MRA get a clear message on the nature, likelihood and severity of the risk, together with an understanding of the plausibility, strengths and limitations of the assessment process itself.

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4

Hazard identification

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4.1 Introduction: the importance of correct hazard identification

The ability of a risk assessment to indicate requirements for food safety depends completely on correct hazard identification indicating the relevance of the hazard to the raw materials, the factory or the finished product. Hazard identification should provide an estimate of variability in behaviour or responses between types of the same pathogen (e.g. salmonella), so that the subsequent exposure assessment can take account of variations in behaviour caused by processing (e.g. prolonged chilled storage or freezing). These variations in behaviour may affect factors, such as toxin production, growth range, thermo-resistance and survival, and provide a more certain basis for estimating the effectiveness of controls, and hence risks to consumers. If hazard identification misses or excludes an important hazard, then the exposure assessment will not consider the impact of the supply chain and its controls on the hazard level in the final product. Both experience and analytical data are important means of identifying realistic hazards (Lammerding and Fazil, 2000). Generally there is good 'process' information on factory and final preparation steps, but more limited information on microbial levels during primary production and between major stages in the supply chain (e.g. manufacturing and retailing).

4.2 What is hazard identification?

The Codex Alimentarius (Anon., 1996) defines a hazard as:

A biological, chemical or physical agent in or property of food that may have adverse health effects.

Hazard identification is defined as:

The identification of known or potential health effects associated with a particular agent.

Hazards may pose current, emerging or potential risks to health, and they may vary in their likely scale and severity. Their effects may be limited to individuals or small groups, or may have epidemic or even pandemic potential. An alternative definition is:

A visualisation of the range of likely pathways (inputs and outputs) affecting the safety of the food product. This may include consideration of processing, inspection, storage, distribution and consumer practices.

Hazard identification can be looked at from two perspectives. From a product developer's perspective, the role of hazard identification is to identify potential hazards that need to be eliminated (for example by formulation, processing or guidance on usage) in order to provide a product that is safe for a target group of consumers to use. Hazard characterisation provides an analysis of the adverse effects associated with the hazards (for example through a dose–response assessment), while exposure assessment provides a 'what if' analysis of the possible level of exposure to hazards through intake of a food product by consumers. On the other hand, hazard analysis can also be retrospective, examining the epidemiological and other data after a food safety incident, to characterise adverse health effects among affected consumers, identifying the foods implicated in causing these adverse health effects, and isolating where possible the causative agent responsible.

4.3 What hazard identification should cover and produce as an output

Hazard identification should identify and characterise the microbiological hazards to be examined by the subsequent stages of the risk assessment. Identification of hazards should be based on both inputs and outcomes. It should cover inputs to the supply chain such as microorganisms or toxins from the raw materials and ingredients used in the product, and likely sources of contamination and growth during processing and storage. It should also cover outcomes such as the following:

- The effect of processing on levels of a hazard (a pathogen for example), defined by the characteristics and resistance of the hazard (for example to heat treatment) and the effectiveness of the process in, for example, delivering a required heat treatment.

- Control of the survival and growth of a hazard by the preservation properties of the final product during storage and distribution taking into account the effectiveness of storage and distribution conditions (such as chilled storage and transport).
- Its intended use and subsequent processing by the consumer (for example ready-to-eat or for cooking).
- The likely sensitivity of consumers to hazards.

This emphasis on both inputs and outcomes makes it more likely that all relevant hazards will be considered.

4.3.1 Scope

Hazard identification should show which hazards are realistic for a product, so that risk characterisation can take account of their probable occurrence and severity. Compiling an exhaustive list of all possible hazards, whether or not they are likely to affect consumers of a particular product in practice, can be as counter-productive as failing to list all relevant hazards for a product. Both may compromise subsequent stages in risk assessment, either by making the process over-complex and unmanageable or by missing key hazards. Hazard identification should therefore concentrate on those likely to be present in a particular food product and to cause foodborne illness. Physiological characteristics of hazards should be described in sufficient detail to allow predictions of likely responses to product composition (e.g. pH and water activity), processing operations (such as heating) and subsequent storage conditions (for example modified atmosphere packaging or chilled storage) at each step in the supply chain up to the point of consumption. The identification process may be extended to cover how each process stage influences microbial physiology or virulence and thus the likely level of risk to consumers. Where process controls may be weak, for example because of particularly contaminated raw materials or possible temperature abuse during distribution, it may be necessary to extend the list of realistic hazards.

4.4 What to do in hazard identification

To be considered realistic, hazards must be identified as the causative agents of waterborne or foodborne disease. This may require experimental work to demonstrate the causal relationship between a particular strain of an agent and a disease. Differing microbial strains (for example of *Escherichia coli*) may be pathogenic or non-pathogenic. Some strains may be associated with epidemic disease and serious illness while others may be associated with mild symptoms and small-scale, sporadic outbreaks. Hazard identification should therefore include an assessment of the impact of the hazard on human health and an analysis of when, where and how it achieves such an impact. Challenge study

data may be used to assess likely levels of a hazard which can then be compared with epidemiological studies. Where direct epidemiological data are missing, it may be possible to assess probable risks from studies of related products in similar environments.

Selected hazards should be compiled into a descriptive list of the bacteria or toxins (with details of species or types) associated with:

- Raw materials.
- Methods of production.
- The use of the food.

To be useful for hazard characterisation and exposure assessment, this list should indicate the specific routes of transmission for each hazard, including potential events (for example variations in the quality of raw materials or variations in storage conditions) that may affect levels in the food. Hazard identification must be done so that overlap with exposure assessment is minimised, but it must provide enough information to allow assessment of the final level of the hazard in the product at consumption. Information should allow the effect of changes in product formulation or processing, such as reduced cooling times or storage temperatures, to be assessed. It may be possible to analyse such changes through Monte Carlo simulations, for example, providing the correct kinetic data for the hazard are available.

4.5 Key information in hazard identification

Four basic types of information on hazards relevant to the product being studied should be assembled for hazard identification.

4.5.1 Microbial agent information

This information needs to characterise the pathogens of importance to the product and process. It should include the following:

- Estimates or measurements of the overall numbers and prevalence of the hazard in the raw materials and process equipment used. The microbial ecology of the product and raw materials may need to be described, so that factors affecting the characteristics and pathogenicity of the hazard can be accounted for.
- Information on resistance to the types of treatment being applied, especially growth, survival and heat resistance characteristics. These will allow estimation of growth or inactivation rates during processing and storage and establish the relevance of predictive modelling. Description of pathogens should provide the means for outlining pathogen response to intrinsic factors (e.g. pH, moisture content, nutrient content or antimicrobial constituents) and extrinsic factors (e.g. heating or storage temperature, relative humidity,

packaging atmosphere and the presence of other microorganisms) that affect behaviour within the product or process range.

- Production of disease may involve a variety of virulence attributes and host susceptibility factors. Not all strains will be equally virulent, but on the other hand not all people are equally susceptible to disease. Information should include a description of strain-specific pathogenicity attributes, such as the production of extracellular materials, e.g. toxins or proteases, phospholipases or bound cellular materials, e.g. antigens or polysaccharide capsules. The relevance of these factors for target consumers needs to be addressed. This may have to be obtained from literature searches and consultation with experts or generated by laboratory studies. Wherever it is found, confidence limits must be placed on its validity and applicability.

4.5.2 Consumer information

Information on consumers needs to include:

- Consumers affected or target consumers.
- Susceptibility to potential hazards.
- Patterns of food consumption.
- Scale of outbreaks.
- Incidence and severity of illness among those affected.

Microbiological data from clinical, epidemiological and food surveillance studies should be included. Probable consumers should be identified and their sensitivity to likely hazards noted, together with the severity of illness arising from exposure to a hazard. If necessary, reference should be made to the different sensitivities of young or old individuals, or those with pre-existing disease, chronic illnesses or immune-deficiency. Foods for these consumers should be identified as high risk. Healthy individuals may be at only occasional risk from relatively mild disease, and may therefore be placed outside the scope of an assessment. It is important to make a sensible assessment as to whether the risks faced by consumers are significant or negligible.

4.5.3 Food and process linked information

Process-related information should include the following:

- Prevalence and level of the hazard in raw materials and ingredients.
- Effects of processing and storage on the levels of the hazard at various stages up to consumption.
- Consumer use instructions and the risks of product mishandling.

This information links the physiological characteristics of the hazard to the properties of the food, its processing and consumer use. It acts as a check that the relevant characteristics of the pathogen have been covered. The origin (e.g. tropical or temperate) of raw materials may be important because of its impact

on types, prevalence and levels and the possible presence of other micro-organisms (e.g. lactic acid bacteria) that may interact with the pathogen and alter its characteristics. Sufficient detail must be provided for the exposure assessment to model the food production process and show the potential for growth, survival, elimination or alteration of virulence of the hazard up to consumption under different conditions of use (e.g. in home, restaurants and hotels).

4.5.4 Information quality

The risk assessment team should be aware of the quality of data available and any assumptions on which it is based. An analysis of information quality should outline the origins and sources of data and its relevance to the products and lines under study.

4.6 Tools in hazard identification

The examination of foods for the presence, types and numbers of pathogens (and/or their metabolites) is of major importance. A variety of routine or conventional methods are available, along with newer developments that are more accurate and rapid. Routine tests for identification or tracing are mainly based on growth characteristics of a pathogen on a selective medium, general features such as colony colour, form or smell, biochemical properties, detection of microbial antigens by antibodies or antibiotic susceptibility. More recent techniques are based on molecular methods allowing the classification and identification of any isolate based on phenotypic and chemotaxonomic analyses. Some of these techniques rely on the availability of large databases to ensure reliable results but, in some cases, these databases have been established for 'non-food' purposes and may provide misleading identities.

There are many web-based tools for assisting in identifying foodborne pathogens, for example:

- The 'bad bug book' issued by the US Food and Drug Administration (FDA) (<http://vm.cfsan.fda.gov/~mow/intro.html>)
- The CDC's mortality and morbidity reports and guidelines for clinicians (<http://www.cdc.gov/mmwr>)
- The US Government's Food Safety Information Center, USDA/FDA (<http://www.fsis.usda.gov>)
- Pathogen behaviour modelling program (<http://www.arserrc.gov/mfs/pathogen.htm>)

The introduction of molecular biological techniques for DNA-based typing can discriminate between isolates of a single species. This information can be used for epidemiological purposes and may provide insight into the fate or persistence of pathogens in food or processing. The detection and tracing of pathogens can be based on:

- Examination of the genotype, e.g. using phage typing, r-RNA sequence analysis or technologies by on the polymerase chain reaction (PCR).
- Analysis of the phenotype by serotyping, API or electrophoresis of cellular enzymes or metabolic products, for example.

The range of such techniques is covered, for example, in Betts (2002).

The performance of microbiological analytical and detection methods for pathogens is important for hazard identification. Thresholds of detection (often 1–10 cells/g) and the statistical significance of the sample size used (e.g. estimate average levels and variability) will determine the chances of detecting pathogens, and hence whether they are considered realistic (Betts, 2002). Attention should also be paid to process conditions, especially the reliability of process controls and the accuracy of records or measurements at the major risk determining steps (e.g. sterilisation, cooking, acidification, chilled or warm storage or poor hygiene). Critical control points (CCPs) in HACCP plans will always include process stages and therefore an assessment of equipment or supplier performance, on a day-to-day basis, may be obtained from quality assurance data. Confidence limits should be placed on limited or variable data (e.g. point estimates or use of a range) or it may be incorporated into scenarios (e.g. best, average or worst).

4.7 Microbial hazards

To manage food safety risks at least cost and with the lowest restrictions on marketing opportunities or the product range, it is important to identify which pathogens, foods or situations can realistically lead to foodborne illness (ICMSF, 1996). The microbial hazards typically associated with foods are listed in Table 4.1

Potential microbiological biological hazards in food include bacteria, toxins, viruses, protozoa and parasites. Of the microbiological hazards, the most important are bacteria and they cause a large proportion (approximately 90%) of all foodborne illnesses. To fix the scope of realistic hazards for any product or group of consumers, it may be useful to consider the sensitivity of the consumers of the food to specific hazards (microorganisms or toxins) and the robustness of the preservation system and any microbicidal treatment the food is likely to receive prior to consumption. The severity of differing types of hazard is described in Table 4.2.

The widest range of realistic hazards will be associated with food intended for consumption by at-risk consumers, e.g. the very young or old, immunocompromised or those unusually susceptible to microbiological hazards. Products may also require identification of a wider range of hazards if they contain contaminated ingredients or those from unusual or unreliable origins. Microbial survival/recontamination levels will be important if processing does not include steps (e.g. pasteurisation) to eliminate hazards before consumption

Table 4.1 Microbial hazards typically associated with foods

<i>Bacillus cereus</i>	<i>Mycobacterium bovis</i>
<i>Brucella abortus</i>	<i>Salmonella</i> spp.
<i>Campylobacter jejuni</i>	<i>Shigellae</i>
<i>Clostridium botulinum</i>	<i>Staphylococcus aureus</i>
<i>Clostridium perfringens</i>	<i>Vibrio parahaemolyticus</i>
<i>Coxiella burnetii</i>	<i>Vibrio vulnificus</i>
<i>Escherichia coli</i>	<i>Yersinia enterocolitica</i>
Enteropathogenic <i>E. coli</i>	Toxin-producing mould
<i>Listeria monocytogenes</i>	

(e.g. raw milk or ready-to-eat foods that typically do not require re-heating). These hazards may be compounded if there is potential for product abuse during distribution or consumer handling.

The highest risk products for consumers are ready-to-eat, or able to support the growth of pathogens, hence the identity of a pathogen and product use will suggest which steps in the supply chain are risk determining. It is essential to collect information on these. For example, if the hazard is an infectious

Table 4.2 The severity of differing types of microbiological hazards

Severe hazards	<i>Clostridium botulinum</i> types A, B, E and F, <i>Shigella dysenteriae</i> , <i>Salmonella typhi</i> ; <i>paratyphi</i> A, B, <i>E. coli</i> O157:H7, <i>Brucella abortis</i> , <i>Brucella suis</i> , <i>Vibrio cholerae</i> , <i>Vibrio vulnificus</i> , (<i>Taenia solium</i>) (<i>Trichinella spiralis</i>).
Moderate hazards – extensive spread from infection	<i>Listeria monocytogenes</i> , <i>Salmonella</i> spp., <i>Shigella</i> spp., enterovirulent <i>E. coli</i> (EEC), (<i>Streptococcus pyogenes</i>), rotavirus, Norwalk virus, <i>Entamoeba histolytica</i> , <i>Ascaris lumbricoides</i> , <i>Cryptosporidium parvum</i> .
Moderate hazards – limited spread	<i>Bacillus cereus</i> , potentially toxigenic bacilli, <i>Campylobacter jejuni</i> , <i>Clostridium perfringens</i> , <i>Staphylococcus aureus</i> , <i>Vibrio cholerae</i> (non-O1), <i>Vibrio parahaemolyticus</i> , <i>Yersinia enterocolitica</i> , <i>Giardia lamblia</i> , <i>Taenia saginata</i> .
Other microbiological hazards	These include naturally occurring toxicants such as mycotoxins (e.g. aflatoxin), scombotoxin (e.g. histamine), toxic mushrooms and varieties of shell-fish poisoning.
Toxins	Toxins of most concern are produced by <i>Clostridium botulinum</i> , <i>Clostridium perfringens</i> , <i>Bacillus cereus</i> and <i>Staphylococcus aureus</i> . All are the result of the growth of bacteria and production of toxins in foods that often have been mishandled. These bacteria are common in the environment but proper cooking, fermentation, cooling and storage of food can prevent their growth and, more importantly, the production of their toxins. However, cooking may not destroy several of these toxins once they are formed in food.

pathogen, then data on initial contamination, heating steps and recontamination will be essential. Where heating is a key part of the safety system, conditions must be quantified because, according to heat resistance, combinations of time and temperature will have a defined ability to reduce pathogen numbers. Growth range (e.g. temperature, pH, water activity – A_w) may also be important (Tienungoon *et al.*, 2000), if products are stored or distributed and illness is related to the level or dose of the pathogen or toxin, and especially if temperature control is an integral part of the safety system. Enteric pathogens (salmonella and pathogenic *E. coli*) are unlikely to grow at chill temperatures, but *Listeria monocytogenes* will continue to grow almost down to freezing point, although chill temperatures may inactivate campylobacter. If it is assumed that the survival of very low levels of infectious pathogens constitutes a hazard, then analytical data on incidence must be considered very critically, to ensure that safety is not assumed, based on limits of detection, or failure to recover injured cells.

If the pathogen is toxin-producing, then growth and toxin production, and the concentration and persistence of any pre-formed toxin both need to be considered. Heating may inactivate the cells, but pre-formed toxin may remain, as heating will not usually destroy it. On the other hand growth under conditions that do not allow toxin synthesis (e.g. at low pH) are not likely to lead to a hazard, unless changes in temperature or food composition (e.g. rehydration of a dried food followed by storage) allows toxin production.

4.8 Identifying the origin and distribution of microbial hazards

The assessment must identify hazard inputs at the beginning of the supply chain (e.g. raw materials) and during processing (e.g. cross-contamination). Factors influencing the input of pathogens (such as harvest or growth conditions) and the extent of detail required will be determined by the scope of the study. Primary raw material and pathogen origins may be included or a study may start at the factory gate. If origins are covered, then the prevalence and persistence of pathogens in areas where raw materials are grown or harvested and routes for contamination (e.g. irrigation water or harvesting machinery) should be considered. If the assessment starts at the factory gate, then contamination levels and their variability (e.g. regional (temperate *v.* tropical) or seasonal (summer to winter) differences) in delivered raw materials should be known. Pathogens in raw materials are often present at low levels and non-uniformly distributed; this determines the level of risk they pose. Distributions may be relatively uniform in liquid foods and more variable in solid or particulate foods. At the most extreme, heterogeneous distributions can lead to many uncontaminated portions and a few (highly) contaminated ones. The latter provide the greatest challenge to process conditions and a potential hazard to consumers: this should be covered whatever detail is provided in the exposure

assessment. Therefore, because of variability, historical data on average pathogen levels in raw materials and finished products can only provide rough guidance on risks to consumers.

Levels and variability of contamination or process conditions may be represented as single values, or as the lowest, average and highest levels or as frequency distributions. The incidence (% contaminated) and distribution of an agent (e.g. log normal, defined by mean log and standard deviation) may be used to refine the exposure assessment and assign probabilities to levels of contamination at particular stages. Estimated distributions of pathogens (e.g. log normal) may be used to bridge data gaps. Such distributions are often positively skewed, and this is consistent with the observation that microbiological populations in foods are log-normally distributed. Variability in the lethality of cooking treatments or the heat resistance of the target microorganism or the product's thermo-physical properties (e.g. portion thickness) may have a large influence on risk, influencing the chances of pathogen survival after in-factory or in-home heating (Brown *et al.*, 1998). The quantity likely to be consumed (portion size) will play a less important role than overall pathogen concentration in determining risk.

4.9 Changes in microbial hazards

Process conditions and the product environment may cause one or more of the effects below on microbial pathogens.

4.9.1 Growth

Within any food, any microorganisms present, including pathogens, may grow and this will always increase risk. They can also interact with each other and with intrinsic and extrinsic factors, leading to differences in metabolism, multiplication, survival or death. Growth and death may be predicted by models (Giffel *et al.*, 1999; Rasmussen *et al.*, 2001; Stewart *et al.*, 2001; Tienungoon *et al.*, 2000) covering the conditions in the food (e.g. pH, A_w) and various storage and process temperatures. Many models are limited to the behaviour of isolated species growing under laboratory conditions. In reality, an exposure assessment may need to go further and consider interactions between species and the food, limiting the predictive accuracy of models (Zwietering and van Gerwen, 2000). Microbial or environmental interactions may inhibit or promote growth of pathogens such as *Listeria monocytogenes*, *Salmonella* sp. or prevent toxigenesis by *Staphylococcus aureus*.

4.9.2 Death

Single factors (e.g. heat) or combinations of factors or 'hurdles' (e.g. acid and low A_w) are used to control pathogen death or survival (Ahvenainen *et al.*,

2002). How many steps are used to kill or inhibit pathogens will determine the complexity of the exposure assessment (EA) study. To make sense of the impact of conditions at the risk-determining steps, the EA team should know the kinetics of inactivation because heating and, for example, acidification have different rates of destruction for different pathogens (van Gerwen and Zwietering, 1998). As conditions are increased above the maximum for growth, injury and then death will occur. Generally higher numbers of cells will take longer to kill and their practically logarithmic rate of death makes it possible to predict numbers of surviving cells from knowledge of the process conditions (time and temperature) involved and the initial number of target cells. Heat sensitivity is often expressed as a *D*-value to indicate the time at a particular temperature required for a 10-fold reduction in numbers of a particular pathogen. Vegetative cells will have very much lower heat resistances than bacterial spores. To allow the prediction of the killing effect of different temperatures, the linking concept of 'z' is used to express the number of °C, that process conditions need to shift to alter the rate of killing 10-fold. Typically this is 7–12°C and the risk assessor should consider its impact when variability is noted at heating or cooling stages.

Different microorganisms grown under different conditions may respond differently to treatments; vegetative cells typically have very much lower heat resistances than bacterial spores. The hazard identification should provide sufficient detail for the correct values or characteristics to be used. Process and food-linked factors may also alter the rate of killing by heat, e.g. acid pH (decreased heat resistance) or A_w (increased heat resistance). If the prior history of the cells (e.g. starvation, heat or cold shock) is likely to induce a stress response and increase resistance, then this should be taken into account. Estimates of the changes in resistance caused by stress may be found from the literature or by challenge testing, where it is unknown it should be noted as an uncertainty.

4.9.3 Survival

Under process conditions outside their growth range (e.g. chilled, frozen or dry storage) microbial cells may remain alive (survive) and remain unable to grow until the damage is repaired or favourable conditions return. Such conditions may alter sensitivity to treatments (e.g. increased resistance to exposure to acid) or capability of causing harm. Exposure assessments should clearly identify process stages where conditions may prevent growth, but allow survival, especially if they are likely to increase resistance to downstream treatments. If the extent of the effects on resistance is not known, it can be noted as an uncertainty, but may be clarified by reanalysis and comparison with analytical or historical data.

4.9.4 Toxigenesis

Toxin-producing species do not produce toxin over their whole growth range and production of toxin will depend on the fate of the producing microorganism

Table 4.3 The relationship between the level of toxin and the fate of the toxin producing pathogen

Is the toxin-producing micro-organism present from previous steps?	Is toxin present from previous steps?	
	Yes	No
Yes	The level of toxin may: <ul style="list-style-type: none"> • increase, • stay the same, • decrease (denaturation). 	The level of toxin may: <ul style="list-style-type: none"> • increase, • stay the same.
No	The level of toxin may: <ul style="list-style-type: none"> • stay the same, • decrease (denaturation). 	The level of toxin stays the same.

at each step of the food chain. It is usually prevented, or inhibited, under adverse conditions (e.g. low temperatures or high numbers of a competing flora) and these must be identified (Stewart *et al.*, 2001) to understand the effects of supply chain conditions. If this is unknown, it should be noted as an uncertainty. Food handlers may also act as a source of contamination of unpacked products by *Staphylococcus aureus*. The impact of subsequent times/temperatures on growth and toxin production should be linked to stages where it is likely to occur. Table 4.3 gives some indications of the relationship between the level of toxin and the fate of the toxin producing pathogen.

4.10 Other biological hazards

Even though viral and parasitic agents may not grow in foods, different supply-chain factors can influence their impact on safety. Understanding of their importance is often limited by lack of data on the characteristics of the agents themselves. Points to consider include routes and sources of contamination (raw materials, environment, equipment or personnel), the level and distribution of the agent in the food and the effectiveness of any decontamination or inactivation steps. The influence of harvest and process steps on pathogenicity and survival, especially the presence of resistant, infective forms (such as cysts) should not be overlooked.

4.11 References

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5

Hazard characterization/dose–response assessment

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5.1 Introduction: key issues in hazard characterization

Hazard characterization is a description of the relationship between levels of a pathogen consumed (dose) and the probability of subsequent development and severity of illness or other adverse health outcome (response). This process is often referred to as the dose–response assessment; however, the term hazard characterization was coined to better describe the broader scope of the analysis, which typically includes a severity assessment and a consideration of sequelae. A dose–response relationship can be expressed as a mathematical relationship, using mathematical models in combination with observational data such as those from human trials, small animal studies, or outbreak investigations. In the final step of a food safety risk assessment, risk characterization, the dose–response assessment is integrated with the exposure assessment to estimate the likelihood and magnitude of a hazard such as the probability of illness from a foodborne pathogen.

Key issues explored in this chapter include the impacts of variability within a population, differences in strains of a pathogen, and interaction of food matrix effects on the interpretation of dose–response data. Also presented are the strengths and weaknesses of using various biological studies for dose–response modeling. Modeling difficulties commonly encountered such as the need to extrapolate from high to low dose when fitting observed data to models and coping with uncertainty and variability in the data and model estimates are addressed. Lastly research needs and future trends in dose–response modeling are discussed.

5.1.1 Hazard characterization v. dose–response

The guideline of the Codex Alimentarius Committee for the conduct of microbiological risk assessments is the conceptual framework most widely used to date (Codex Alimentarius Committee, 1999). It divides the risk assessment process into four components:

1. hazard identification
2. exposure assessment
3. hazard characterization
4. risk characterization.

Within that framework, there is ongoing discussion of what information should be provided in the hazard characterization and hazard identification components. In general, the microbiological risk assessments that have been undertaken have used the hazard identification to describe the basic epidemiology and etiology of a disease. Conversely, the hazard characterization has focused on detailed descriptions of the factors contributing to the disease process that could influence the dose–response relationship or the severity of the disease (e.g. virulence determinants, subpopulations with increased susceptibility, food matrix effects).

The World Health Organization (WHO) and the Food and Agriculture Organization (FAO) of the United Nations have sponsored expert committees to conduct risk assessments and develop guidelines for their conduct and use at the international level. An *ad hoc* Joint FAO/WHO Expert Meeting on Microbial Risk Assessment (JEMRA) developed guidelines for the conduct of hazard characterizations (WHO/FAO, 2001). The process begins with an initiation phase wherein the scope and purpose of the hazard characterization are described and the assessment is planned. Next, data are collected, evaluated, and a descriptive characterization is developed. With this information the data are analyzed and the dose–response model(s) prepared. Prior to presenting or publishing the results, JEMRA recommends that a peer review be conducted. The conduct of hazard characterization should be an iterative process, in which information learned at each step is used to refine the hazard characterization (WHO/FAO, 2001). The hazard characterization phase of a microbial food safety risk assessment should provide a thorough description of the adverse effects of the pathogen on the host. The technical report should include a complete description of host, pathogen and food matrix factors that impact the likelihood of the disease or other public health outcome and the data and model used to describe the dose–response relationship. Sufficient information should be provided to allow an analyst to reproduce the dose–response model, including sources of data, assumptions used, goodness of fit of the distribution, and uncertainty and variability (WHO/FAO, 2001).

While hazard characterization is typically used in combination with an exposure assessment to evaluate a risk, it may be conducted and reported as a stand-alone analysis initially and later used with exposure assessments developed for specific geographical regions, consumer groups, or product

categories. Although the hazard characterization may be a quantitative or qualitative evaluation, a dose–response model quantitatively describes the frequency and magnitude of the adverse event as a function of the exposure to the pathogen.

The specific organism of concern and its mode of causing a disease must be considered in designing and interpreting dose–response data for use in modeling. For infectious microorganisms (e.g., *Salmonella* Enteritidis) to cause disease viable cells must be ingested, attach in the epithelial cells in the gastro-intestinal (GI) tract, and then invade the epithelium to cause gastroenteritis or the body to cause septicemia. Toxicoinfectious microorganisms (e.g., *Escherichia coli* 0157:H7) are similar except they do not invade the body, but instead produce or release toxins after colonizing the surface of the GI tract. A third class of pathogens, toxigenic bacteria (e.g., *Clostridium botulinum*), produce the toxins in the food before it is ingested. These differences in mechanisms of pathogenicity will influence the dose–response model selected and its underlying assumptions.

5.1.2 The disease triangle

The likelihood that an individual becomes ill from ingesting a microorganism is dependent on the complex interaction among the host, pathogen, and food substrate. These three factors and their interactions are known as the infectious disease triangle or epidemiologic triad. While exposure (number of microorganisms or amount of their toxins ingested) is generally thought of as the administered dose, for dose–response studies the true or infectious dose is the portion of the administered dose that actually reaches the site of infection and causes the end-point of concern such as infection, illness, or death. Depending on the microorganism, health and age of the consumer, and type of food consumed, the infectious dose may range from one microbe to hundreds of millions (Jaykus, 1996). The nature and vast array of possible combinations of these factors makes the nature of dose–response relationships one in which there is a high degree of variability inherent in the estimate. Additionally, detailed knowledge of these factors and their interactions is typically lacking, leading to substantial uncertainty related to the estimate. This should not necessarily indicate that the dose–response relationship is poorly understood, but instead reflects the highly variable nature of the three biological systems being described, i.e., the exposed population, the pathogen, and the food.

Host factors

The human population is highly diverse in its vulnerability and response to microbial pathogens. The immune status, especially associated with those individuals who are immunocompromised due to disease or medical treatments such as immune-suppressive drugs, can influence occurrence and/or severity of foodborne diseases. A number of intrinsic factors such as age, sex, and genetics further influence the immune system, and thus the susceptibility of the

individual to disease. Additional factors such as the general health of the population, presence of underlying disease, or nutritional and physical stresses on members of the population influence individuals' responses. Different dose–response curves or even models may be needed to describe the relationship between exposure and illness for distinctly different subpopulations such as the general population v. high-risk subpopulations. Alternatively, highly susceptible or highly resistant subpopulations may be viewed as ‘tails’ of the general population being described by a dose–response curve.

Pathogen factors

Evaluation of the dose–response relationship requires knowledge of the virulence mechanisms and physical distribution of the microbial pathogen in the food environment. Virulence factors such as adherence, invasiveness, ability to evade host defenses, and release of potential toxic factors, are among the microbial characteristics that can influence the ability of a microorganism to cause disease. Other characteristics of the pathogen that can influence infection and its outcome are dynamic evolution of virulence from microorganism interaction with environment and host, microbial variability in response to environmental factors, and microbial tolerance to adverse conditions that may allow person-to-person spread.

The physiological state of a microorganism can also influence its ability to cause disease. For example, recent studies have suggested that virulence factors may or may not be expressed as a result of ‘quorum sensing’, i.e., chemical communication between microorganisms when there are sufficient numbers of cells present within an environment. Likewise, the behavior and characteristics of a microorganism can differ substantially when present as planktonic cells versus biofilms or microcolonies.

Considering the array of factors described above, it is not surprising that a dose–response curve developed for a specific pathogen strain cultured under one set of conditions may not be applicable for another strain or even the same strain cultured under different conditions.

Food matrix factors

In recent years it has become apparent that the food matrix in which the pathogen is transmitted can have a significant impact on the likelihood of disease. Food matrix factors such as fat levels, acidity, salt levels and other characteristics of the food should be considered in an evaluation of the ability of a pathogen to cause disease (Foegeding, 1997). The consumption of highly buffered foods or antacids may decrease the number of microorganisms needed to cause illness because of the foods' modulating effect on gastric pH. For example, studies with *V. cholerae* O1 indicate that cooked rice, which provides buffering capacity, may have substantive impact on the measured dose–response relationship (Levine *et al.*, 1981). Similarly, achlorhydria, the decrease or cessation of acid production in the stomach, would be expected to impact the effective dose (Buchanan *et al.*, 2000). Additional dietary factors that impact the

physiological response of the gastro-intestinal tract, particularly the stomach, may alter the dose needed to produce infection. For example, gastric bactericidal lipids, which protect against *Listeria* infection, accumulated in rats fed a high milk fat diet (Sprong *et al.*, 1999). Gastrin, the hormone that is the most potent stimulant of gastric acid secretion, is released after eating a protein-rich meal (West, 1985). Because most enteric pathogens are sensitive to acids, the increased production of gastric acid following a protein-rich meal such as oysters would provide greater protection against infection, thus increasing the infectious dose.

The physical distribution of the pathogen in the food environment can also impact the passage of pathogenic bacteria through the intestinal tract (WHO/FAO, 2001). Pathogen clumping, aggregation, and intimate association (e.g., coating, absorption) with food particles may increase their survivability and allow intact passage through the stomach to the intestinal epithelium. This may, in part, account for the decrease in effective dose observed with certain enteric pathogens suspended in foods with high lipid contents. To date, food safety risk assessments have not been developed to a level of sophistication that permit a direct accounting of food matrix effects.

5.1.3 Theories of infection

Two hypotheses related to the initiation of infection, minimum infectious dose (threshold model) versus single-cell (non-threshold model), have been used to describe the dose–response relationship. Threshold models assume that there is some level of the pathogen that particular individuals can tolerate without becoming infected. Conversely, non-threshold models assume that a single microbial cell is capable of causing illness.

When dose (e.g., log number of microorganism ingested) is plotted against response (percentage of population infected), the shape of the curve is often sigmoidal, which has been interpreted as indicating that there is a minimum infectious dose below which a pathogen will not cause disease (Buchanan *et al.*, 1998). However, efforts to measure this level in humans have not been successful for infectious and toxico-infectious microorganisms, and have been alternatively interpreted as indicating each bacterial cell has the potential, albeit small, to multiply in the host and cause disease.

Fitting dose–response data using a non-threshold model and then displaying it by plotting log (dose) versus percent response gives a sigmoidal curve. However, in this instance if the graph is replotted using the log (percent response) versus the log (dose), the non-threshold nature of the model becomes apparent, as the graph becomes linear at low doses (Buchanan *et al.*, 2000). Figure 5.1 illustrates this using the exponential distribution function.

The hypothesis that a single ingested cell could cause infection is increasingly accepted as a default assumption for dose–response modeling of infectious foodborne pathogens. The reasons for this are two-fold. First, non-threshold models appear consistent with reports of a number of large outbreaks

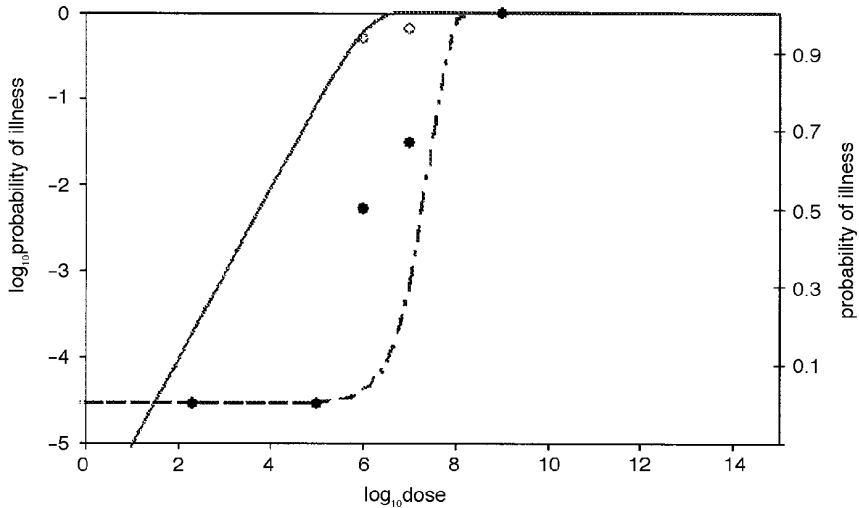


Fig. 5.1 Example of a dose–response curve using an exponential distribution plotted as either a log(dose) versus response (shown as a dashed line) or as a log(dose) versus log(response) (shown as a solid line).

where the number of infectious bacteria was very low. Second, since the lower limit of infectivity would be virtually impossible to prove, models that are linear or log-linear at low dose provide a conservative but biologically defensible default assumption. Toxigenic microorganisms represent a different case since the response is based on the levels of a pre-formed toxin and not the number of organisms ingested directly. Threshold-based models appear to be a better choice for toxigenic microorganisms, such as *Staphylococcus aureus* and *C. botulinum*, that produce acute toxins (Buchanan *et al.*, 1997).

For both threshold and non-threshold-based models, the probability of infection or morbidity increases as the dose increases. However, a 50% increase in dose does not necessarily yield a 50% increase in the probability of illness (Cassin *et al.*, 1998a). The possible occurrence of multiple infection sites in the host may account for observed increases in infection with higher doses. Having a greater number of cells may increase the probability of an infection by increasing the probability that one or more cells survive the stomach and come in contact with an appropriate binding site within the intestine. Having multiple binding sites would increase the probability of infection if a percentage of infection loci are asymptomatic, or that a sufficient number of pathogens be present before the body's defenses are overwhelmed and the disease becomes symptomatic. One of the factors that is well established is that increasing the dose decreases the 'incubation time' between when the cells are ingested and when overt symptoms appear. For gastrointestinal diseases, infection is generally defined as the presence of organisms in the GI tract, but it may not necessarily lead to illness. That is, given infection the probability of illness might increase, decrease, or be independent of dose (Teunis *et al.*, 1999).

5.2 Types of dose–response data

The development of dose–response models depends on the availability of data that quantitatively describe the relationship between the levels of the microbe ingested and the frequency and severity of illness. Data necessary to develop a dose–response model can be obtained from clinical trials, epidemiological investigations, and small animal studies, as well as *in vitro* studies. Dose–response models have also been developed using a combination of epidemiological and food survey data. For example, annual estimates of incidence of listeriosis were combined with data on levels of *Listeria monocytogenes* in smoked fish to develop a purposefully conservative dose–response relationship using the exponential model (Buchanan *et al.*, 1997). The various types of data used in dose–response modeling are described below and the strengths and limitations of each are summarized in Table 5.1.

5.2.1 Clinical trials

The primary source of data for dose–response modeling has been clinical trials, which are also referred to as human volunteer feeding studies. In these studies, a known dose of a pathogen is administered. The results of these studies provide a relationship between the number of organisms that cause illness and the severity of the illness in volunteers administered a specific dose or level of a specific pathogen. Data obtained from these studies show that the infectious dose and the dose–response relationship are dependent not only on the strains used, but also on the age and physiological condition of the volunteers. For example, the range of infectious doses of *Salmonella* spp. and *E. coli* strains can vary from 1 microorganism to 1×10^9 organisms among the different serovars (Kothary and Babu, 2001). However, only a limited number of volunteer feeding studies have been conducted. For foodborne microorganisms that cause potentially fatal diseases, such as enterohemorrhagic *E. coli* (EHEC) or *L. monocytogenes*, there are no existing feeding studies and it is highly unlikely that any studies will be conducted for ethical reasons. This necessitates the need for alternate approaches, such as using epidemiological data and animal studies, to estimate dose–response relations.

The majority of the available studies were conducted in conjunction with vaccine trials wherein the pathogen was suspended in a saline solution, administered concurrently with antacids. Very rarely was the pathogen administered in a food matrix, which would provide better estimates of the infective dose. Epidemiological data have shown that for several pathogens, the infective dose obtained from feeding studies is much higher than that observed with foodborne illness; which is likely due to the protective effect of the food vehicle (Kothary and Babu, 2001). A major drawback associated with volunteer studies is the routine use of healthy young men and women. It is known that age and physiological condition, as well as the immune response of an individual, affect the outcome of infection. This makes it difficult to apply results from

Table 5.1 Summary of types of data used in dose-response modeling

Data source	Benefit or advantage	Limitation or other considerations
Clinical studies	Humans are test subject, no need to extrapolate data to other species Known dose	Volunteers are not representative of whole population Small number of participants/trial High doses used Organism often administered in buffered solution, not food matrix
Epidemiological studies	Human test subjects, no extrapolation to other species needed More representative of whole populations	Ingested dose is seldom determined Attack rate typically not determined Number of individuals that consumed implicated food but did not become ill often lacking
Animal studies	Simpler and cheaper than human studies Allow screening for effect of virulence factors on dose-response Relatively large number of test subjects can be used	Interspecies extrapolation required
<i>In vitro</i> studies	Rapid testing of parameters	Need to correlate response to <i>in vivo</i> responses
Biomarkers	Evaluation of end-points other than illness or death	Currently, no quantification or relation to specific exposure levels in humans
Expert opinion	Available in absence of observational data	Information may be biased

these studies to the very young, aged or to immune-compromised subpopulations (Kothary and Babu, 2001).

5.2.2 Epidemiological data

Epidemiological studies provide information on various factors influencing the occurrence, distribution, prevention, and control of disease in a defined human population. Analysis of epidemiological data can be used to establish the relationship between human exposure to a hazard and the biological response.

Outbreak investigations of foodborne diseases associated with ready-to-eat foods that support growth of microbes have provided unique settings to increase our knowledge of dose–response relationships in human infections with foodborne pathogens. With knowledge of attack rates (i.e. the number of people exposed v. number of people ill) associated with the consumption of different amounts of the implicated food and the concentration of the pathogen in the food, we can estimate the dose–response relationship, albeit with qualifications. An example of how epidemiological data can be used to determine the infective dose is the analysis of a multistate outbreak of *Salmonella enteritidis* associated with ice cream consumption (Vought and Tatini, 1998). In this investigation, the infective dose was calculated as no more than 28 cells based on consumption of a single sundae cone, which caused severe illness in an 8-year-old boy and only moderate to mild illness in the adult parents.

Another innovative approach is the use of attack rates from multiple outbreaks to evaluate published dose–response models (FAO/WHO, 2000). Since 1997, Japan has advised large food service establishments to freeze and retain subsamples of raw foods and cooked dishes for possible examination in the event of an outbreak or reported illness. This food-saving system allows measurement of pathogen levels in incriminated food, a variable often lacking in most outbreak reports. By having multiple outbreak investigations available, it was possible to fit the data using various dose–response models.

5.2.3 Animal studies

In the absence of human data, small animal studies can be used to assess the virulence potential of different strains and serotypes, susceptibility of the sensitive subpopulation (i.e., immune-compromised), and to study the role of specific virulence determinants. Small animals such as mice, rabbits and monkeys are administered known levels of the pathogen and the response of interest is measured. These studies are particularly useful to evaluate the interactions of pathogenic strain and food matrix effects on the host. For example, the effect of fasting and administration of sodium bicarbonate alone and in combinations on the ability of different strains of *Salmonella* Enteritidis to invade the spleen in rats has been evaluated (Havelaar *et al.*, 2001). Extensive evaluations such as this could not be conducted in human clinical trials.

Susceptible animal models have been developed to provide enough data to develop correlative dose–response models with human data especially with respect to immunocompromised individuals, which cannot be conducted in susceptible humans. However, the virulence potential observed in animals may not reflect the response in humans, particularly for strains that are host adapted. The challenge for successfully using animal data in dose–response modeling is to extrapolate data acquired in animal models to humans. Adjustments may be needed to account for body weight differences, body mass, surface area of the lower gastrointestinal tract and host specificity in expression of pathogenicity and virulence. In order to extrapolate the data,

there is the assumption that the response of the small animal to a particular pathogen is similar to that of humans, and the mechanism of pathogenesis of the microorganism is the same for both animals and humans. Another drawback to animal studies is that generally healthy animals of similar weights and age are used. Also laboratory animals are highly inbred and lack genetic diversity (Buchanan *et al.*, 2000).

5.2.4 *In vitro* studies

In the absence of human or animal studies, data obtained from cell, tissue, or organ culture studies could be used in developing dose–response models. Tissue culture involves the maintenance or growth of tissues or cells out of the body (*in vitro*), in a manner that allows differentiation and preservation of their architecture and/or function. *In vitro* methods using tissue culture cell lines have been used to study virulence functions, such as invasion of epithelial cells and survival in macrophages. A correlation between animal *in vivo* and *in vitro* studies has been demonstrated for adherence and invasion properties of *Salmonella* and shiga toxin-producing *E. coli* (La Ragione *et al.*, 2001; Ferreira *et al.*, 1997).

5.2.5 Biomarkers

Biomarkers are measurable indicators of host exposure to a pathogen. They include determination of levels of the pathogen or a metabolite in the host, and other indicators such as biochemical or physiological changes that indicate disease. Once identified, biomarkers may be particularly important as surrogates of disease or to indicate end-points other than illness for substances or agents for which little epidemiological data are available. There is a need to quantify biomarkers and relate them to specific exposure levels. In particular, biomarkers based on alterations in molecular and biochemical parameters may be useful in microbial risk assessment for establishing the presence of an exposure, ranking relative risks among exposed individuals, and estimating risks at low levels of exposure. Dose–response data in humans obtained from biomarkers can help reduce the assumptions and uncertainties that arise from interspecies and high-dose to low-dose extrapolations, thereby making these risk assessments more reliable, meaningful, realistic, and cost effective.

5.3 Modeling dose–response relationships

A dose–response model is a simplified description of the complex relationship between a dose and the adverse event caused by a specific pathogen. Data from studies obtained under specific conditions are used to predict adverse outcomes from different, non-tested doses by fitting these data to predictive, mathematical models. Fitting models often requires extrapolation beyond the range of the

observed values. Important concepts in modeling dose–response relationships include variability and uncertainty, the criteria to select data used in the model, and determination of appropriate distributions used in the model.

5.3.1 Variability and uncertainty

Because a model is only a representation of the interaction of many variables and often based on incomplete information, there is considerable variability and uncertainty associated with the output of pathogen dose–response models. Variability refers to the true heterogeneity of the biological system and as such cannot be reduced by additional knowledge. On the other hand, uncertainty refers to our imperfect knowledge and can be reduced with research. For example, each strain of a pathogen has different potential for virulence in humans (variable) and it is often unclear which strains of this pathogen are the most virulent (uncertain). In the example of pathogen strains, additional research will not change the fact that there is diversity in the biology of the pathogen strain (variability) but can help us understand the differences in the virulence of these strains (uncertainty).

Separating uncertainty and variability in the model, referred to as second-order modeling, is preferable. By not separating variability and uncertainty, the risk assessor assumes that the impact of either variability or uncertainty is negligible and this assumption can quantitatively affect the predicted risk (Nauta, 2000). One method of incorporating uncertainty along with experimental variation is to combine estimates from several different models rather than rely on a single dose–response model (Kang *et al.*, 2000). This approach does not reduce uncertainty but will reduce the biases of individual models in the predictions. Additional information about variability and uncertainty in modeling can be found in Byrd and Cothorn (2000) and Vose (2000).

5.3.2 Empirical v. mechanistic models

Most efforts at dose–response modeling have used empirical models, which are limited by the range of the experimental data. However, mechanistic models would allow more effective extrapolation of predicted responses. For example, they could be used to extrapolate data from healthy males to pregnant females. Buchanan and collaborators (Buchanan *et al.*, 2000) developed a simple mechanistic model as an example of how this approach might be used for foodborne pathogens. The example model was based on three compartments which addressed the impact of stomach acidity, ability of cells to attach to and colonize in the intestine, and the likelihood that an infection progresses to morbidity. Before mechanistic models can more fully developed and applied to food safety issues, additional research is needed on the impact of host, pathogen and food factors on infection mechanisms. Once developed, mechanistic models would allow *in silico* analysis of interactions to be explored that are not possible

in humans or small animals and can assist in understanding different disease outcomes for different exposed or infected individuals (Kirschner, 2001).

5.3.3 Selection and development of models

Model selection and development will depend on the purpose of the risk assessment, the availability of data, and the resources available to the risk assessor (WHO/FAO, 2001). The selected model should be consistent with the behavior of the study data and the nature of the known or assumed relationship between exposure and infection, illness, or disease. These factors as well as the modeling assumptions used determine how accurately the model reflects reality, both biologically and in relation to the observed data (Bernard and Scott, 1995).

Important considerations in selecting a model include: the need to extrapolate from studies that use high doses to expected responses for low doses; the need to extrapolate data collected from healthy adults to subpopulations with increased susceptibility; and the endpoint of interest such as infection, morbidity, or mortality. Extrapolation beyond the observed data points is often done to predict the probability of illness from low doses and to account for differences between the test subjects and the populations of interest. For example, extrapolating from small animals to humans or from healthy young adults to an elderly or high-risk subpopulation. For these reasons, it is critical that the risk assessor document the basis of model selection and the possible impact that that decision has on the risk assessment results.

Selecting surrogate pathogens for dose–response modeling should include a consideration of the similarities in taxonomy, epidemiology of human disease, and genetic control of pathogenesis (Coleman and Marks, 1998). Coleman and Marks (1999) used murine challenge studies as a surrogate to account for the differences in human host susceptibility to non-typhoid salmonellosis. A family of dose–response curves representing subpopulations with different susceptibilities to infection was developed using data from mice sensitized via administration of antibiotics (which removed the protective effect of normal microflora) prior to challenge with *Salmonella* Enteritidis.

While model selection may include a statistical evaluation of the fit, it should not be the only consideration. For the model to be credible, consideration must also be made of the biological characteristics and other events that influence the modeled response (Teunis and Havelaar, 2000).

5.3.4 Examples of distribution functions used in dose–response models

One challenge that risk assessment modelers face is deciding the shape of the dose–response function, especially in the lower dose region of the curve where observational data are generally sparse, absent, or practically unattainable. Other challenges are to describe the probability of illness, infection, morbidity or other endpoints over a wide range of dose levels for different subpopulations.

Table 5.2 Summary of selected distribution functions used in dose-response models

Distribution	Assumptions	References
Beta-Poisson	Assumes infectivity is dose dependent. Accounts for pathogen virulence or host susceptibility differences, or both. Predicts mean percentage of population for a particular dose. Non-threshold function.	Haas, 1983; Buchanan <i>et al.</i> , 2000
Beta-binomial	A modified beta-Poisson. Accounts for variability of the probability of illness predicted for a particular dose.	Cassin <i>et al.</i> , 1998b
Exponential	Assumes the probability of a cell causing infection is independent of dose. Non-threshold function.	Haas, 1983; Buchanan <i>et al.</i> , 2000
Weibull-gamma	Assumes that the probability that any individual cell can cause infection is distributed as a gamma function. Provides flexibility as it can take on several different shapes depending on the parameter values selected.	Farber <i>et al.</i> , 1996; Whiting and Buchanan, 1997
Single-Hit	Risk cannot exceed the probability of exposure (maximum risk curve limits upper confidence level).	Teunis and Havelaar, 2000

Commercial software packages are available that allow use of numerous distribution functions.

Table 5.2 summarizes some of the different distribution functions used in dose–response modeling. Vose (2000) provides mathematical equations for these and other probability distributions. The three most commonly used distribution functions for dose–response modeling are the exponential, beta-Poisson, and Weibull-gamma (Whiting and Buchanan, 2001). The exponential function assumes that the host susceptibility and pathogen virulence are constant for a specific population. The beta-Poisson and Weibull-gamma include host-pathogen interactions that are beta or gamma distributed, respectively.

5.3.5 Examples of models used in recent quantitative microbial risk assessments

Several different approaches have been used to develop models for microbial risk assessment and no single model seems best for all pathogens or ranges of data. International expert consultations sponsored by FAO/WHO evaluated dose–response curves for salmonellosis and listeriosis that had been developed using different sources of data, biological end points, and modeling approaches (FAO/WHO, 2000). For *Salmonella*, five dose–response relationships, three based on clinical trial data and two based on outbreak data were evaluated. For *Listeria* the dose–response relationships evaluated included different endpoints (infection, morbidity, and mortality), different subpopulations (neonates, elderly, general population) and different data sources (disease statistics, animal models, and outbreak data). These risk assessment experts concluded that no single approach to defining the dose–response relationship was superior. With either of these diseases, the various dose–response curves examined either under or over predicted illness compared to observations from outbreak data. However, each group did select a dose–response model that they felt was most useful for the risk assessment that they had been asked to conduct, and provided a detailed rationale for the selections.

Table 5.3 provides a summary of dose–response models from selected national or international microbial risk assessments. Different risk assessments have focused on different biological endpoints of the data used in the models such as infection or colonization, morbidity, mortality, and sequelae. It is important to emphasize that dose–response data or the dose–response relationships derived from the data can only be compared directly if they are describing the same biological endpoint.

Because of the differences in dose–response studies and difficulties in selecting models that fit the data, it is even more difficult to compare infectious doses for different organisms. Holcomb *et al.* (1999), evaluated six dose–response models using data from four human feeding studies to determine whether a single model could be fit to diverse data. The Weibull-gamma, a flexible three-parameter mathematical model, provided the best overall fit for the four pathogens. However, increased flexibility must be counterbalanced against uncertainty, increasing the number of model parameters increases both flexibility and inherent uncertainty.

5.4 Problems in hazard characterization

Absence of human data, incomplete epidemiology information, difficulty in extrapolating animal data to humans, and lack of mechanistic models are major factors that limit the use and development of dose–response models and contribute to the uncertainty in the model estimates. Another common problem is the lack of well-defined criteria to evaluate data quality and to select data to include in the model. Criteria are also needed to identify outliers that should

Table 5.3 Summary of dose–response models used in national and international microbial risk assessments

Pathogen/commodity (reference)	End-point examined	Type of data used	Model distribution function used
<i>E. coli</i> O157:H7/ ground beef (USDA, 2001)	Morbidity and mortality	Exposure data and human feeding trials using surrogate pathogens	Beta-Poisson
<i>Salmonella</i> Enteritidis/shell eggs and egg products (USDA, 1998)	Illness	Surrogate human feeding trial (<i>Shigella</i> <i>dysenteriae</i>)	Beta-Poisson
<i>V. parahaemolyticus</i> / oysters (US FDA, 2001)	Illness	Human feeding studies	Fit multiple models (beta-Poisson, probit, Gompertz)
<i>L. monocytogenes</i> / ready-to-eat foods (USD HHS/USDA, 2001)	Morbidity	Animal (mouse) lethality and human fatality statistics	Fit multiple models (logistic, exponential, Gompertz-log, probit, multihit)
<i>Salmonella</i> spp./ broilers and eggs (FAO/WHO, 2000)	Illness	Human feeding and outbreak data	Compared three models using beta- Poisson but different data; outbreak data using exponential and beta-Poisson models
<i>L. monocytogenes</i> / ready-to-eat foods (FAO/WHO, 2000)	Infection	Expert elicitation; animal (mouse) study	Compared fit of multiple models: Weibull-gamma; exponential, and beta-Poisson
<i>L. monocytogenes</i> / ready-to-eat foods (FAO/WHO, 2000)	Morbidity	Annual disease statistics and food survey data; or outbreak data (butter, Mexican-style cheese)	Exponential
<i>L. monocytogenes</i> / ready-to-eat foods (FAO/WHO, 2000)	Mortality	Animal (mouse) lethality and human fatality statistics	Exponential
<i>L. monocytogenes</i> / ready-to-eat foods (FAO/WHO, 2000)	Febrile gastroenteritis	Outbreak data (chocolate milk, corn salad)	Exponential

validly be omitted from the dataset. Furthermore, a dose–response model developed for the general population may not be applicable for a susceptible subpopulation (i.e., elderly).

5.4.1 Conducting severity assessments

A hazard characterization consists of two phases: determination of the dose–response relationship and assessment of severity. As documented above, there have been significant advances during the past several years in determining dose–response relationships, both conceptually and technically. Severity assessments have not received the same degree of attention. Currently, this phase of the hazard characterization is considered qualitatively and the results of the dose–response relationship are interpreted in light of the spectrum of consequences associated with the disease during the risk characterization phase of the risk assessment. Conceptually, it has been proposed that this could be performed by developing dose–response relationships for several biological end points (e.g. morbidity, mortality, sequelae), weighting the various biological end points in relation to their impact, and integrating the estimates to provide a total disease burden (Buchanan *et al.*, 1998). In this manner, the impact of different foodborne diseases could be compared; a measurement that could be useful for decision making related to allocation of limited resources. However, risk assessors should be careful about undertaking such a process. It requires the risk assessors to make societal value judgments in order to set the weighting values (e.g. how many hospitalizations are equal to one death), and as such may be beyond the risk assessors’ mandate. In the absence of such a mandate, the reporting of multiple biological end points is likely to be the extent to which a severity assessment should be conducted.

5.4.2 Lack of human quantitative data

Clinical trials, a primary source of dose–response data, are generally conducted with healthy adult volunteers. However, as mentioned previously, one must be cognizant of the limitations associated with volunteer studies. These data do not reflect the entire population and may overestimate the dose needed to adversely affect humans and therefore underestimate the risk to more highly susceptible subpopulations. Also, because of financial and ethical considerations only a limited number of volunteers are included in each trial so the degree of uncertainty associated with hazard characterizations can be substantial. Furthermore, clinical trials using potentially fatal microorganisms such as *L. monocytogenes*, *V. parahaemolyticus*, and enterohemorrhagic *E. coli* are not possible due to ethical reasons, so generation of accurate dose–response curves requires alternative approaches. While the use of foodborne outbreak investigation data is a promising alternative means for acquiring human data, it also has significant limitations. By the time the agent has been identified, the incriminated food may no longer be available. Also, it is difficult to determine the levels of the microorganism in the food at the time of consumption because

the pathogen could grow (levels increase) or die off (levels decrease) during storage of the food. All these factors contribute to a lack of abundant human quantitative data for dose–response modeling.

5.4.3 Lack of methods to extrapolate high doses to low doses

Criteria are needed to assist risk assessment modelers in selecting dose–response models to use in different situations. Better methods are needed to evaluate model fit. Guidelines must be developed to address measurement error (accuracy of analytical methods to enumerate microorganisms and determination of exposed individuals) and guidelines developed for selecting data used in dose–response modeling (FAO/WHO, 2000). The ability to extrapolate from high to low doses is also likely to be influenced by continuing research on how quorum sensing and other extracellular microbial communication strategies affect the expression of virulence determinants.

5.4.4 Extrapolation from animal to human

Animal models have been used as surrogates to provide a basis for extrapolating dose–response estimates for humans. Measures of the severity of illness used in animal studies often do not correspond with definitions of human illness on which reporting statistics are based (Bernard and Scott, 1995). In chemical risk assessments, in extrapolating small animal data to humans, the modeler must account for the difference in life span, body weights, and differences in metabolic rates (Byrd and Cothorn, 2000). However, for infectious agents, the similarities between the surrogate animal and humans in the disease process including specificity of receptors, immune response, and physiological functions are more important considerations. There have been few attempts to directly compare the disease process in humans and surrogate animals to eliminate potential confounding factors (e.g. strains used, means of delivering dose, immune and physiological status, genetic diversity).

5.4.5 Sequelae

Foodborne illness is typically thought of as involving clinical manifestations associated with the gastrointestinal tract (e.g. diarrhea, vomiting). However, it is becoming increasingly evident that a number of chronic severe sequelae such as ankylosing spondylitis, arthropathies, renal disease, cardiac and neurologic disorders, and nutritional and other malabsorptive disorders (incapacitating diarrhea), may arise in some of the individuals infected by foodborne pathogens (Lindsay, 1997). Sequelae can be life-threatening, such as cases of hemolytic uremic syndrome that occur, generally in children under the age of 10 years, as a consequence of enterohemorrhagic *E. coli* infections.

The association between a particular microorganism or its products and these long-term sequelae ranges from convincing to circumstantial (Council for

Agricultural Science and Technology, 1994; Bunning *et al.*, 1997). The reason for this uncertainty is that, except in rare circumstances, current surveillance systems are not adequate to link chronic complications to a foodborne infection. Furthermore, chronic sequelae can arise as a result of otherwise asymptomatic infections. The chronic sequelae may be unrelated to the acute illness and may occur even if the immune system successfully eliminates the primary infection. In fact, in many cases it is the activation of the immune system due to the infection with a foodborne microorganism that initiates the chronic condition as a result of an autoimmune response (Council for Agricultural Science and Technology, 1994; Bunning *et al.*, 1997). This is further complicated by the fact that such autoimmune responses are typically associated only with individuals with a genetic predisposition. For example, cases of reactive arthritis in a population exposed to *Salmonella* appears to be linked primarily to individuals having the HLA-B27 immune marker.

Consideration of sequelae is often critical to performing adequate severity analyses, but how this is best done is one of the challenges currently facing risk assessors. Sequelae often appear not to be directly related to the same type of dose–response relationships associated with acute responses or fatalities. In some instances, it appears that the incidence of sequelae is most easily described as a percentage of active infection; however, the general lack of data relating sequelae to specific instances of foodborne disease has hampered consideration of this approach.

5.4.6 Validating models

Generally all available data are used in the development of a dose–response model, so typically it is difficult to find data to use in validating a new model. When additional data are available, the reasonableness of model predictions and the appropriateness of the modeling assumptions can be evaluated by comparing model output to relevant data that were not used to develop the relationships and distributions of parameters in the model *per se*. For example, data from two outbreaks of *E. coli* 0157:H7 were used to validate the dose–response relationship at low doses predicted by a beta-Poisson model fit to animal data (Haas *et al.*, 2000). Another approach is to use data generated in one country to develop the dose–response model and then use it with the exposure and health statistics data from a second country (WHO/FAO, 2001), evaluating the degree of agreement between the number of predicated and observed cases.

5.5 Future trends

Assessing and then managing risks has always been an integral part of food safety throughout history. With improved modeling tools, we can now conduct risk assessments with a higher degree of sophistication. In recent years there has been an increasing international focus on risks associated with microbial pathogens and specifically on reducing those risks through a comprehensive,

farm-to-table approach to food safety. Critical needs for national and international efforts include initiation of new research and expansion of current surveillance efforts, advancement of modeling techniques, development and standardization of study designs, and improvements of our ability to share data, ideas, and modeling tools.

Important areas to advance our ability to conduct hazard characterizations are as follows:

- Development of a central repository for outbreak and other data used in dose–response modeling.
- Improvement in modeling techniques to allow exploration of the interactions of host, pathogen, and food matrix in models along with the development of mechanistic models.
- Advancement of model tools to enable use of multiple dose–response models as a method of accounting for uncertainty.
- Development of criteria for selecting dose–response data, models and tools of comparison.

Although dose–response models developed at the national level can be generic so that they can be used at the international level, it would be preferable to validate models using regional data. Information on disease incidence for each region of interest is needed for these internationally focused risk assessments.

5.5.1 Research needs

Some of the research needs for improving our ability to conduct hazard characterizations include the following:

- Biological information for the development of mechanistic models.
- Enhanced outbreak investigations to provide data on the level of pathogen in the implicated food, amount of implicated food actually consumed, characterization of health and immune status of symptomatic and asymptomatic cases, and calculation of attack rates.
- Quantitative data on the effect of food matrix on likelihood of infection.
- Potential for development of sequelae following illness and techniques for modeling these sequelae.
- Evaluation of the impact of secondary (person-to-person) transmission of disease.
- Identification of the key virulence factors for each pathogen so that strain differences can be fully accounted for in the assessment and determination of the frequency and distribution of specific virulent pathogen strains in food.

5.5.2 Risk assessment in a risk analysis framework

Conducting risk assessment within a risk analysis framework improves subsequent regulatory decisions. It is important for risk assessors and risk

managers to interact on a regular basis throughout the risk assessment process and continually refine the questions the risk assessment should answer, the scope of the project, and the key assumptions used in the model. As practical experience is gained with this approach, both the conduct and use of complex risk assessment in management and trade decisions will increase and improve. Risk assessments can also be valuable as a tool to identify critical research needs before a full quantitative risk assessment is attempted. Such activity is often referred to as data gap analysis.

5.5.3 Intensive outbreak investigations

Epidemiological data would be useful for developing risk assessment models if standard outbreak investigations were expanded to provide detailed information on the amount of food consumed and the degree of contamination of that food. Outbreak investigations typically focus on acquiring the minimum amount of information needed to identify the source of an outbreak in order to prevent further disease cases. However, in the longer term the knowledge gained from more thorough investigation may prevent more cases by providing the type of information needed to identify risks that can be managed. This information would allow the development of the relationship between the amount of contaminated food(s) consumed and the severity of subsequent illness, as well as the relationships between the dose of contaminated food items ingested and the severity of the resulting illness controlling for host factors.

As a means of making additional resources available, the US Chicago Department of Public Health (CDPH) developed in cooperation with the US Food and Drug Administration a protocol to carry out such intensive investigations of foodborne disease outbreaks, which also includes molecular, environmental, and virulence characterization of the microbial isolates. This protocol is available on the internet (www.foodriskclearinghouse.umd.edu) and has been used to investigate a *Salmonella* outbreak. Investigations of this type will allow quantitative analysis of disease-associated foods and better estimates of the total population exposed, both critical values needed to calculate attack rates and thus use this type of epidemiological data to develop dose–response relationships for foodborne pathogens.

5.6 Sources of further information and advice

The field of microbial risk assessment including dose–response modeling is advancing rapidly, as new data and modeling tools become available. A number of national government agencies and international organizations and professional societies are active in the area of public health and microbial risk assessment. Some resources that provide up-to-date information on the state of the art include:

- the Society for Risk Analysis (www.sra.org)
- the World Health Organization (www.who.int/fsf/mbriskassess/applicara/index.htm)
- the Food and Agriculture Organization (FAO) of the United Nations (<http://www.fao.org/es/ESN/pagerisk/riskpage.htm>)
- the Centers for Disease Control and Prevention (www.cdc.gov).

Information and links to current information on microbial risk assessment are also provided by the Food Safety Risk Analysis Clearinghouse at www.foodriskclearinghouse.umd.edu and the US government food safety web site at www.foodsafety.gov. Subscribing to electronic mailing lists is another way to keep informed of current thinking in the area of dose–response modeling (Byrd and Cothorn, 2000). RiskAnal is a popular active list. To subscribe, simply send an email to lyris@lyris.pnl.gov with ‘subscribe riskanal your name’ in the message.

5.7 References

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6

Exposure assessment

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6.1 Introduction

The aim of this chapter is to provide an explanation and practical guide to exposure assessment (Schothorst, 1997), so that readers can tackle evaluation of the level of microorganisms or microbial toxins in a food at the end of the supply chain, when it is consumed. The exposure assessment procedure explained and used as a reference is qualitative and suitable for routine assessment of the likely impact of process and formulation changes on the microbiological risks associated with a food product. How the output is presented must be dictated by the needs of the users.

Microbiological exposure assessments are overall models of the level of pathogens or toxins in foodstuffs moving through the supply chain. Their function is to provide an estimate of levels in a product at the point of consumption. Risk assessors are responsible for using them with other risk assessment information to evaluate how raw material quality and all the factors in the supply chain including consumer use, can fix or alter the exposure of consumers to foodborne hazards. Because each exposure assessment identifies the elements of the food chain that are relevant to preventing or managing food safety problems, users must be aware of their strengths, limitations and scope.

In practice an assessment will be directed at a specific food (e.g. cooked meat) made by an identified supply chain. It may focus on the fate of a specific hazard (e.g. salmonella), or be repeated (using the same supply chain and consumer data) until the full range of realistic hazards has been covered (e.g. salmonella, *Staphylococcus aureus* and *Listeria monocytogenes*). Each assessment needs to describe potential routes of contamination and control measures, combined with knowledge of the characteristics of the pathogen, and

is used to estimate the level or the probability of toxin presence in a portion at consumption. Assessments can use simple descriptions, point estimates or ranges of values to describe variables (e.g. time, temperature or pathogen level) and should make variability, uncertainty and assumptions explicit and show how far the selected control measures actually control food hazards. Hence, realistic exposure assessments need to collect and make use of information about all the risk-determining steps from raw material to product consumption (Lammerding and Fazil, 2000). Typical information includes raw material quality, the performance of manufacturing equipment and consumer usage; plus in-house or literature data on the characteristics of realistic pathogens (e.g. growth range, heat sensitivity, prevalence) in the product. Technical personnel and microbiologists involved directly with the supply chain will usually provide this information. Sometimes it also comes from consumers and may be backed up by consultation with outside experts or industry colleagues.

6.2 The role of exposure assessments in microbiological risk assessment

Risk assessment has emerged over the last 10 years as an accepted, science-based approach to making choices between options for managing the microbiological safety of food (Lammerding, 1997; Klapwijk *et al.*, 2000). It is a systematic process based on four inputs, hazard identification, exposure assessment, hazard characterisation and risk characterisation (Codex Alimentarius Committee, 1999; Voysey, 2000). Exposure assessments use information and expert opinion to identify and measure or rank what happens to microbial hazards in food, and hence the dose likely to be presented to consumers in a portion. They can provide an estimate of the impact of the individual stages in a supply chain or changes in a supply chain on microbiological safety (McNab, 1998). Changes may lead to food companies redefining microbiological risks or hazards and actions needed to protect their customers (Moy, 1999). Specifically, exposure assessments can provide predictive or 'what if' information to help with managing the impact of new raw material sources, milder product formulations or new groups of customers (e.g. children), and may lead to revised control measures or the re-focusing of quality assurance resources (Giffel *et al.*, 1999). Alternatively they can be used to examine historical data and trace the likely origins and extent of food poisoning outbreaks or produce an early warning of problems. Exposure assessments can be used in both ways because they are a data-based and systematic approach to identifying hazards and understanding what affects the riskiness of food products for specified groups of consumers (Balbus *et al.*, 2000). Risk assessments do not judge whether a product or a process is 'safe' or 'unsafe'. Their function is to use exposure assessment data to produce an estimate of risk that can be understood and used by risk managers in industry or regulatory agencies to improve or maintain safety standards (Voysey and

Brown, 2000). In this context a risk manager is anyone in an organization who has the responsibility for deciding how to manufacture or to sell a food product.

Risk assessments may be carried out by different groups of experts and with difference scopes and levels of complexity. Governments may do full risk assessments for global risks or new hazards, e.g. Bovine spongiform encephalopathy (BSE) (European Commission, 2000) or enteropathogenic *Escherichia coli*. At lower levels of complexity, industrial or research institute experts may be involved in 'routine' decision making on altered process conditions or products, where there may be new or altered risks of food-poisoning. At the most everyday level, quality assurance (QA) managers, company microbiologists or regulatory agencies may do informal or operational risk assessments as part of hazard analysis critical control point (HACCP) studies (Hoorstra *et al.*, 2001; Meredith *et al.*, 2001), to set criteria (Norrung, 2000) or to follow-up consumer complaints or food-poisoning incidents. Two general approaches to risk assessment have been described by FAO/WHO (1995) and Codex Alimentarius Commission (1999). Examples of quantitative risk assessments with detailed exposure assessments are being published (Table 6.1).

Exposure assessments measure or estimate changes in pathogen or toxin levels along the supply chain to predict the likely level of infectious pathogens

Table 6.1 Examples of quantitative risk assessments

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- USFDA (2000) Draft Risk Assessment on the Public Health Impact of *Vibrio parahaemolyticus* in Raw Molluscan Shellfish.
 - HHS and USDA (2000) Draft Assessment of the Relative Risk to Public Health from Foodborne *Listeria monocytogenes* Among Selected Categories of Ready-to-Eat Foods.
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 - FAO/WHO (2000) Joint FAO/WHO Activities on Risk Assessment of Microbiological Hazards in Foods: Risk Assessment: *Salmonella* spp. in broilers and eggs – Preliminary Report – Exposure assessment of *Salmonella enteritidis* in eggs MRA 00/04 (Ebel, E.D., Kasuga, F., Schlosser, W. and Yamamoto, S.)
 - FAO/WHO (2000) Joint FAO/WHO Activities on Risk Assessment of Microbiological Hazards in Foods: Risk Assessment: *Listeria monocytogenes* in ready-to-eat foods Preliminary Report – Hazard identification and hazard characterization of *Listeria monocytogenes* in ready-to-eat foods. MRA 00/01 (Buchanan, R and Lindqvist, R)
-

or microbial toxins in a portion of food. This prediction is based on microbiological data and supply chain data.

Microbiological data consists of the relevant characteristics of the pathogen (e.g. heat sensitivity) affecting their activity (metabolism, growth, death or survival) during food processing. Experimental data from challenge testing and growth/death models may be used to estimate responses to process conditions. Identifying the correct pathogen characteristics is important because the same preventative or control measures will not have the same effect on all pathogens (e.g. different heat sensitivities between infectious pathogens and spores). Supply chain data include analysis of the physical and chemical properties of the food, product and process design, measurement and inspection of processing conditions, and data on consumer use. Data requirements will be determined by describing the supply chain and potential risks at each step. A generic supply chain model is shown in Fig. 6.1.

Putting together process, product and microbiological information provides a factual basis for making decisions about risks and hence where 'safety' resources and control measures should be directed to give the best cost/benefit ratio in preventing food poisoning, and in turn protecting the reputation of a brand or business. Both science and judgement play important roles in using these estimates to reach decisions about which hazards and controls are realistic. Recommendations may sometimes be controversial, if conclusions are inconsistent with the concerns of stakeholders, as necessary actions may sometimes increase costs. Controls may arise from increased levels of quality management or inspection, tighter specifications, changes to process conditions at risk determining steps, restriction of product shelf life or exclusion of some sources of supply (Notermans and Hoornstra, 2000; Rasmussen *et al.*, 2001). Appropriate actions will depend on the severity of the hazard (e.g. spoilage, mild or life-threatening illness: Jouve *et al.*, 1999) and the level of risk that managers are prepared to accept on behalf of their customers and employers.

Effective risk management practices can be implemented only when a realistic and reliable exposure assessment has been produced and communicated to the risk assessment team. If control of new hazards or the hazards not previously associated with a particular food causes changes to control measures, any new requirements need to be clearly communicated to suppliers, buyers, product development, quality assurance and manufacturing personnel and possibly outside the company to regulators.

6.2.1 Exposure assessment and HACCP

Formal and informal exposure assessments (EA) are already done during many activities in the food industry related to microbiological safety, e.g. product development and process optimization. The hazard analysis part of HACCP studies requires similar information, because it is the risk management tool often used to ensure that production is under day-to-day control for identified hazards (Serra *et al.*, 1999). If a formal approach to data collection and analysis, similar

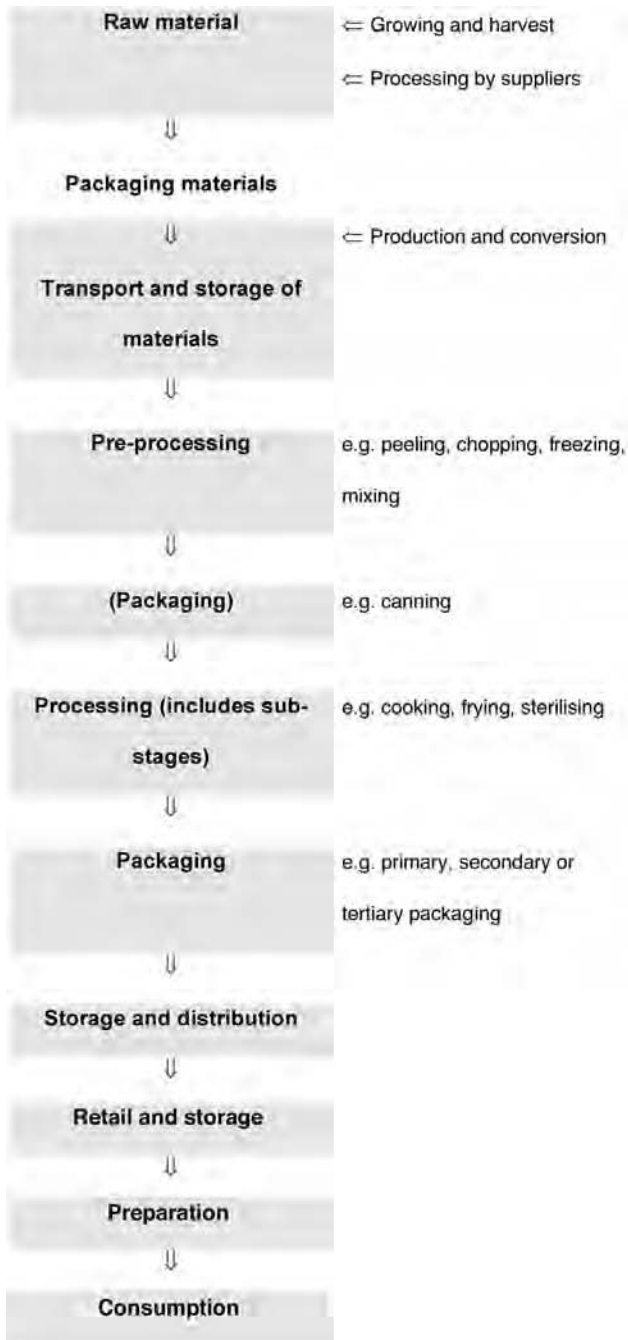


Fig. 6.1 A generic 'production to consumption' model of a supply chain, each stage may be risk determining and may provide inputs of hazards or opportunities to reduce hazard levels or limit increases. Probable risk-determining steps shaded.

to an EA, is used as an input to a HACCP study, this will form a reliable and consistent basis for evaluating current processes or the impact of any changes. Thus documentation and explanation are key elements of the contribution of exposure assessments to the overall risk analysis.

6.3 What's in an exposure assessment?

To aid understanding and acceptance of the risk assessment conclusions, exposure assessments need to be based on a clear process of information collection and analysis. This starts with formulation of the food safety problem (e.g. salmonella food poisoning associated with a pre-fried meat dish for microwave heating). It is followed by a statement of purpose and definition of the scope of the assessment (e.g. to determine the effect of raw material quality, process conditions and the variability of microwave heating on levels of salmonella in a portion for ready for consumption). The scope will often be defined by the needs of the risk manager (e.g. to find out if a change of supplier or raw material quality will affect the level of risk). The output needs to meet his/her needs (e.g. ranking of the risks in the existing and proposed supply chains) and its limitations must be clear. These can include:

- Variability (e.g. in process conditions).
- Uncertainty (e.g. lack of knowledge (Kang *et al.*, 2000)).
- Lack of resources.

Examination of these factors may show if an assessment can be improved by collecting more data (if easily available). If this cannot quickly and easily be done, expert opinion, generic data from suppliers or assumptions (e.g. an infectious dose is one cell) can be used, but its basis and limitations should be explained. Any assumptions and conclusions should be easily understandable to users and should normally be fail-safe or worst-case. For example, if prevention of re-contamination after heating is a risk-determining step, then the assumption should be that it occurs, unless there are data to show it is prevented, with back-up information on the systems and facilities showing that it is consistently achieved.

6.3.1 Stages in an exposure assessment

Preparing an exposure assessment follows a well-defined series of stages shown in Table 6.2. All risk assessments aim to provide an estimate of the probability and severity of illness from consuming potentially contaminated food. Qualitative, or even informal, risk assessments should be more than a summary of information and should follow the same systematic approach as a quantitative risk assessment (Vose, 1998; Coleman and Marks, 1999; Notermans and Teunis, 1996). Data structured in the supply chain model, based on the steps described in Table 6.2 should provide answers to the questions shown in Table 6.3. The

Table 6.2 Stages in an exposure assessment

1. **Formulation of the food safety problem:** showing the hazard, food product, supply chain and market being covered.
2. **Hazard identification:** including characterisation of the pathogen relevant to the conditions in the supply chain and the product.
3. **Statement of purpose:** agreed output and detail required by the risk assessor or risk manager and within the capabilities of the team.
4. **Scope:** extent of the supply chain covered and any additional factors to be considered, such as abuse.
5. **Data collection:** to construct a model of the supply chain:

Supply chain data	Microbiology data
<ul style="list-style-type: none"> • Overall product and process design • List of raw materials, specification and analytical data • Description of final product including characteristics and use instructions • Process specifications + QA and process records • Description and assessment of the sequence of process stages, based on scope and including microbiological effects from records or measurements, concentrating on the risk-determining steps • Description of sequential changes in the physical and chemical characteristics of the food and the interaction of process steps with the product (e.g. heating or cooling) • Equipment hygiene and routes of contamination • Primary packaging, ability to exclude pathogens • Conditions in storage, distribution and handling • Product use, e.g. portion size, levels and pattern of consumption by various groups • On-site validation of risk-determining steps and description and assessment of variability and uncertainty in the data 	<ul style="list-style-type: none"> • Characteristics of the identified hazard under supply chain conditions from harvest/supply to consumption • Pathogen inputs and levels from raw materials, factory, equipment and product • Measurements of microbial numbers in raw materials and products (finished product and at consumption) • Measurements of microbial numbers in-process material • Availability and application of relevant kinetic models
<ol style="list-style-type: none"> 6. Production of a supply chain model, including a flow diagram linking product, process and microbiology information to outline the effects of process stages and treatments on the identified pathogen. This may include the use of predictive models. 7. Identification of major risk-determining steps and the cumulative effect of processing on pathogen levels. 8. Description of variability, uncertainty and assumptions for raw materials, pathogen characteristics, specified process stages, etc. 9. Presentation of information to meet the statement of purpose and the needs of the risk assessment team, e.g. point estimates, scenarios or quantitative risk assessment (QRA). 	

Table 6.3 Key questions on the risk-determining steps that should be answered by the supply chain model

Topic	Key questions
Hazardous microorganisms in raw materials	<p>What is the frequency and level of contamination of the raw materials making-up the product?</p> <p>What is the range of contamination in the raw materials?</p> <p>What is the origin of the data – e.g. analytical samples or predictions?</p> <p>What is the variability or uncertainty of this estimate?</p>
Effects of processing/decontamination	<p>What are the effects of harvest, handling and storage before processing, on the level of the hazard entering the process with each raw material?</p> <p>What is the intended effect of all processing and any decontamination stages on the level of the pathogen in the product after manufacture?</p> <p>What is the variability or uncertainty of this estimate?</p>
Occurrence of toxins from toxin-producing pathogens	<p>What is the likelihood of toxin presence, if the microorganism can produce toxin in raw materials or product?</p> <p>What is the variability or uncertainty of this estimate?</p>
Re-contamination after processing or decontamination	<p>What is the frequency of re-contamination of the final product with the hazard in the factory after processing or decontamination?</p> <p>What is the likely level of re-contamination after processing or decontamination?</p> <p>What is the variability or uncertainty of this estimate?</p>
Primary packaging	<p>Is the product put in its primary packaging before or after decontamination? If the answer is yes, how effective is packaging at preventing recontamination before consumption?</p> <p>What is the frequency of recontamination after packaging?</p> <p>What is the amount of recontamination after packaging?</p> <p>What is the variability or uncertainty of this estimate?</p>
The effects of storage and distribution	<p>What are the conditions during storage and distribution and how does this affect the level of the hazard in the product after manufacture?</p> <p>What is the effect of storage (according to the instructions) on the level of hazard at the point of sale?</p> <p>What is the variability or uncertainty of this estimate?</p> <p><i>Additional questions for toxin-producing microorganisms</i></p> <p>What is the effect of storage conditions on toxigenesis (If the level of the microorganism changes and it produces toxin)?</p> <p>What is the likelihood of toxin production in the product?</p> <p>What is the variability or uncertainty of this estimate?</p>

Table 6.3 (continued)

Topic	Key questions
Consumer use	<p>Is the product intended as single- or multi-use with storage after opening?</p> <p>If the product is multi-use in a domestic or food service application, then what is the effect of recontamination and open shelf life on the level of microorganisms or toxin?</p> <p>What is the variability or uncertainty of this estimate?</p> <p><i>Additional questions for toxin-producing microorganisms</i></p> <p>What is the likelihood of growth and toxin production during open shelf-life?</p> <p>What is the variability or uncertainty of this estimate?</p>
The effects of storage, usage and preparation on the level of hazards	<p>What is the effect of customer or food service, preparation and usage on the level of the pathogen?</p> <p>What is the variability or uncertainty of this estimate?</p> <p><i>Additional questions for toxin-producing microorganisms</i></p> <p>What is the effect of usage and preparation on toxin level and production?</p> <p>What is the probability of toxin presence at the point of consumption?</p> <p>What is the variability or uncertainty of this estimate?</p>
Food intake	<p>What is the likely quantity of the food consumed by a customer on a specified occasion or over a period of time?</p> <p>What is the variability or uncertainty of this estimate?</p>
Exposure estimate	<p>What is the likely level of the hazard in a portion at the point of consumption?</p> <p>What is the variability or uncertainty of this estimate?</p>

degree of detail in those answers will determine whether the output is qualitative or quantitative.

Microbiological risk assessments include an element of prediction, because it is not often possible to measure the real level of a pathogen in a food at the time of consumption. It is most important to know the levels of pathogens at the risk-determining steps, because the overall exposure assessment has to provide an estimate of the amount of pathogen or toxin likely to be ingested in a portion. Analytical data, or predictive, kinetic (sub) models, can be used to estimate sequential changes in the behaviour, or levels, of pathogens (Ross *et al.*, 2000); and so understand what happens to them in the supply chain or in the hands of consumers (Walls and Scott, 1997; Foegeding, 1997; Kleer and Hildebrandt, 2001; Whiting and Buchanan, 1997). Predictive models for growth or death need to use point or range estimates and be based on the fastest growing or most resistant strains likely to be present in the food.

6.4 Who should do an exposure assessment and when?

Information for an exposure assessment study should be collected and examined by a team including experts, production and QA personnel. By the beginning of a study this team should have collected and analysed the minimum information on product, process and microbiology needed to build a supply chain model. To interpret the impact of processing and product formulation on microbial numbers, the team needs microbiological expertise to consider the effects of the hazard (e.g. wide risk of infection or limited risk from toxigenesis) and the sensitivity of consumers (e.g. rates or disease among consumers or the minimum harmful dose). Such expertise will help the risk managers define their response to the risk estimate. This information should be structured within the overall model of the supply chain, showing what happens at each stage and especially at the risk-determining steps. Therefore they need to have the skills and information:

- To estimate the presence or concentration of the hazard in the raw ingredients.
- To summarise the overall effect of the sequence of stages in the supply chain (e.g. processing, distribution, handling and preparation) on the level (and severity) of the hazard at the point of consumption. Taking into account the effects of consumption patterns, consumer abuse or under-processing, if necessary.
- To provide an estimate of pathogen levels in a portion of product at the point of consumption, with a clear explanation of uncertainty and variability.
- To outline the geographical distribution and quantity of the product sharing a common hazard and risk.

An assessment may be triggered by the need to understand what happens in the supply chain and especially at the risk-determining steps, or to establish whether changes in processing or materials may increase or decrease risk. The technique may be used to determine likely sources, if problems have been found (e.g. food-poisoning or premature spoilage). Timing, scope and detail should be determined by the requirements for risk management (Oscar, 1998) and, wherever possible, relevant information from previous assessments or records should be used to minimise the resources needed.

6.5 Building up supply chain data for an exposure assessment

Microbiological exposure assessments need to collect and analyse data on each stage where pathogens or hazards can be introduced, increased, reduced or eliminated, to assess their cumulative impact up to the moment a product is consumed. To be effective, the assessment process has to be shaped by risk managers so that the output addresses their needs and concerns (Schlundt, 2000), but they should not affect its scientific integrity. This principle is equally true for hazard analysis; where the HACCP study team should impartially select the data

used to meet the needs of the HACCP study implementation team. Data on microbial levels and process conditions over a representative period of time or number of batches can be used to improve the reliability of a risk estimate.

Exposure assessment must consider the effects of food handling, patterns of consumption and intake quantities on pathogen levels at consumption and the sensitivity of consumers to the pathogen. There are differences in agent–host and food–host interactions and in minimum hazardous dose between infectious agents (e.g. salmonella) and toxins (e.g. *Staphylococcus toxin*) and different groups of consumers, such as young, old, etc. When an agent is infectious, harm is caused when it is ingested and grows in the body to cause infection. In principle, one cell may be sufficient to cause an infection, but in reality higher doses are usually needed. For example the hazardous dose of *E. coli* O157 may be 1–10 cells/g, while *Listeria monocytogenes* is a severe hazard at higher levels (<10 000/g of food) to a small number of sensitive consumers the young, old, pregnant or immunocompromised (YOPIs), whereas healthy consumers may consume even higher levels without ill-effects. Where the agent is a toxin, it has to be pre-formed in the food at a sufficiently high concentration to cause illness. Some of the bacilli (e.g. *Bacillus cereus*) may cause food poisoning by producing a toxin during spore germination and growth in the gut), in this case sufficient numbers need to be ingested to cause a harmful level of toxin to be produced (McElroy *et al.*, 1999). An exposure assessment should stop at producing an estimate of the level of the hazard in a portion at the point of consumption; analysis of the effects of pathogen level in the portion on the consumer is the function of hazard characterisation.

Exposure assessments should also specify the portion size or ingredient contribution to the portion, often specified in the use instructions for products. If possible this should be related to the portion size previously implicated in illness. The unit of exposure is typically a *per meal* portion. The impact of these differences on the dose consumed may not be as large as those attributable to other factors (such as decontamination treatments or stages allowing growth) in the exposure assessment. For example changes in pathogen levels, prior to consumption and the minimum hazardous dose, can differ on a log-scale, whereas differences in portion size are linear (from a few grams to a few hundred grams). Therefore if the hazard is an infectious pathogen, then the effect of portion size may be negligible, but if the hazard is the toxin produced by the microorganism and response to the toxin is linear, then portion size may be important.

Food consumption patterns, food preparation and consumption practices (e.g. cooking habits and/or cooking times and temperatures, home storage conditions, including abuse; typical serving sizes and habits plus any seasonal, regional or cultural differences relevant to the product) are part of the exposure assessment. Information on consumer behaviour is needed where it is likely to influence the dose of pathogen ingested. Where possible, exposure assessments should include demographic and social information to identify consumers who may be more susceptible to infection or illness (e.g. because of age distribution or increased sensitivity – infants, children, pregnant women, elderly or immunocompromised

populations). Such groups may also have different eating habits and levels of exposure (Gerba *et al.*, 1996). When risk assessments are conducted for international trade purposes, differences in exposure data between countries and regions and for different populations must be considered.

Mixing or blending raw materials or ingredients can result in contamination of larger volumes of material and widen the distribution of a pathogen (e.g. into other products or to different consumers). If there is no growth, pathogen levels may be diluted below a hazardous level or there may be a decrease in the number of harmful portions, if contaminated and uncontaminated foods are mixed. Unlike chemical risk assessments that deal with relatively static hazard levels, microbiological risk assessments are usually concerned with dynamic hazards (e.g. changing numbers of microbial pathogens in a food from production to consumption). For this reason all of the wide mix of factors that can influence pathogen levels need to be covered by the exposure assessment and will need updating, as new information becomes available or changes are made in the supply chain.

For each stage in the supply chain, information on temperatures, times and other key parameters should be collected, recorded and structured sequentially to give an overall model of the supply chain (Table 6.3). A flow diagram may be a useful starting point to indicate the scope of the assessment and to define the steps involved in the supply chain. The degree of sophistication will depend on the detail needed to describe the fate of the hazards. Simple models (e.g. Fig. 6.1) can describe pathways of exposure and different routes of control and contamination, but more complex representations may be needed to describe other important parameters (e.g. growth or survival of pathogens in residual material, in the manufacturing environment or re-contamination) at risk-determining steps. If exposure assessments are used to investigate food-poisoning outbreaks, information should always be linked to the production circumstances involved and, if sample integrity can be assured, the results of any microbiological examination of the foods involved should be included.

6.6 Sources of information

Data can be obtained from many sources including:

- A review of quality assurance and process data.
- On-site inspection and sampling.
- Process and product design information.
- Equipment and ingredient specifications.
- Records of raw material quality.
- Specific analyses of in-process materials or finished products.

From this information, pathogen inputs and the effects of processing conditions can be put into the supply chain model. Additional data may be derived from the analysis of samples taken along the line, or by using predictive models in

conjunction with process data (Betts and Earnshaw, 1998). Pathogens usually have a relatively low prevalence in raw materials and because of the limitations of current methods of detection, their distribution is not well understood. Many factors can affect pathogen inputs; usually there are not sufficient quantitative data to describe what happens during harvest or before the factory gate, and modelling of changes in pathogen numbers is limited to processing and distribution stages where data are available (Ross *et al.*, 2000). Where models are used to predict levels, the possibility that previous processing may alter pathogen resistance or growth rates should be considered. Surveys of performance data (e.g. in the process or distribution chain), storage or challenge tests, or laboratory studies (e.g. laboratory assessment of *D* values for raw material contaminants or survivors of the heat treatment) may provide additional data on likely changes.

Time and resources may limit the process, formulation or complaint data information available to an 'exposure assessment' team. And scientific journals may not provide useful data on microbial behaviour under the relevant conditions. Exposure assessments should at least be based on a coherent set of descriptive or point values (e.g. high or low or a temperature or pH value) for a line manufacturing a product. At a more sophisticated level, data should indicate material or process variability, (e.g. minimum and maximum values) and distributions defining variability should be built up if sufficient data are available. Typical variables include the level of contamination in a raw material or finished product and temperatures at the various stages in production. Where sufficient data are not available to indicate the range of values, worst-case point values can be used to create best, average and worst scenarios. If constraints are so severe that reliable data cannot be obtained, then the study should be stopped to prevent presentation of an invalid assessment.

6.6.1 Variability, uncertainty and data quality

Data collection should, as far as possible, highlight variability (e.g. raw material quality or process conditions) and minimise uncertainty (Huss *et al.*, 2000). Characterising variability is most important if a decontamination step has only marginal capability to ensure pathogen absence or prevent growth at its 'upper' and 'average' values, because lower end values, or a higher challenge, may lead to pathogen presence. Sometimes to improve accuracy or take account of variability, data sets from similar lines, or different times, may be combined to provide suitable information (e.g. if a problem that occurred some time ago is being examined). Where this is done, the procedures and techniques used to provide a composite view should be explained. If variability leads to a high risk being estimated, then better control of the process, lower pathogen numbers in raw materials or more predictable consumer use may reduce the risk. If a product is assumed to be risky as a result of uncertainty, then focus on improving knowledge may apparently reduce risk. However, if control actions are urgently needed, and reliable information is not available, then a cautious

decision might be justified on the basis that more information could allow less severe, or restrictive, risk management measures in the future (Schlundt, 1999). If an exposure assessment shows that there are consistently high risks (e.g. survival of pathogens in products cooked according to their specification) or that process variability leads to periodic contamination of products, then the effectiveness of control measures should also be reviewed based on exposure assessment data.

The origins and importance of uncertainty should always be noted with the best description possible (Maarten and Nauta, 2000; Nauta, 2000). It may stem from lack of knowledge or doubts about the underlying science relating to a hazard (e.g. the effect of pre-processing conditions on the heat resistance of a pathogen at a process stage), an inability to characterise the effects of processing (e.g. the microbiological effects of heating a dry ingredient or routes of product recontamination) or the preservative effects of product formulations (e.g. the ability of combinations of pH and salt to prevent pathogen growth). Uncertainty and the dependence on assumptions can be reduced by better knowledge, but on the other hand more knowledge may sometimes produce only a better description of variability.

Variability and uncertainty can be accounted for by putting different point estimates into scenarios or using high and low boundaries based on observed variability. To fail safe, worst-case estimates should be used and any assumptions identified, but if this is done for all process stages and material qualities, then unrealistic (pessimistic) assessments will be obtained. Monte Carlo simulations (Cassin *et al.*, 1998b; McElroy *et al.*, 1999; Braud *et al.*, 2000; Smout *et al.*, 2000; Giannakourou *et al.*, 2001) are used to provide a more balanced view, based on the probabilities of encountering combinations of adverse values or conditions. In any case, explanation of the origin, accuracy and variability of data within the assessment process will play an important role in establishing trust in its outputs. Credibility will be improved if stakeholders are involved in and understand how all the information available has been obtained and used to make the supply chain model. However they should not be involved in the exposure assessment process itself, particularly the admission or exclusion of data, the management of uncertainty (lack of information) or accounting for variability (day-to-day changes in parameter values, e.g. chiller temperatures), as this may lead to bias.

A risk assessor should not use an exposure assessment based on poor-quality or limited information. A usable output has to be based on reliable data that may be descriptive (e.g. high, medium or low) or show a range (e.g. high, average or low) or contain point-estimates (i.e. deterministic, the average level of a pathogen in a product, the highest level of contamination of a raw material or an average portion size). The most useful outputs are based on a range of data representing variability and showing it as defined distributions or probabilities (i.e. stochastic). The main difference is in the amount of data required (e.g. 65°C, 65 ± 5°C or mean 65°C and SD 0.6°C) and the reliability of the risk estimates. Point-estimates can be derived from single best or worst case values or averages.

If there are more data available, distributions can be used to describe the range of values at risk-determining steps (e.g. frequency or probability) and produce a range of exposure levels (Duffy and Schaffner, 2001). Ranges of values can also be used if facts are sketchy or there are high levels of variability likely to result in different pathogen levels in the product.

Assessments may identify knowledge gaps: having been found, the team should determine their influence on the validity or accuracy of the risk estimate (e.g. lack of knowledge of process conditions or pathogen survival). If the team has to use non-representative or amalgamated data to reach a conclusion, this should be clearly shown and any influence from high or low values made explicit. The overall validity of data collection, sampling and testing procedures should also be carefully examined, because these may directly affect an assessment. In some cases, poor methodology (such as counting pathogens from process stages causing injury without using resuscitation techniques: Mafart, 2000)) may lead to inaccurate data and this should be noted in the assessment document, with a rationale if it is excluded. Using expert opinion is one way to reduce uncertainty in an exposure assessment. Such opinion is not evidence in itself, but inference based on suitable evidence. Similar 'rules' should be used for acquiring and using data (e.g. from records or laboratory experiments) and expert judgement.

6.7 Types of data used in an exposure assessment

6.7.1 Scope

The risk manager's problem and the information available will determine the scope of the exposure assessment (i.e. from farm or factory gate to fork). To do this the initial phase has to develop a clear and understandable statement of the scope and context of the problem (a risk profile), so that data collection and output meet the needs of the risk manager. If the goal is to estimate the risks from a food-pathogen combination, then the exposure assessment needs data and information about the supply chain and consumer use right up to consumption (Brown *et al.*, 1998). Data on multi-stage processes must take account of the conditions and variations at each stage, any changes caused, estimating the inputs and outputs at each stage and the cumulative changes that will determine the level of pathogens or toxin in the finished product. If the end-point of the assessment is consumption, variations in hazard levels after consumer handling should also be estimated, because these are likely to be affected by temperatures and times during storage and preparation.

Exposure assessments are most robust if they focus on one pathogen in one food. For example, published risk assessments include salmonella in eggs or *E. coli* in ground beef (Cassin *et al.*, 1998a and see Table 6.1). Such assessments have a narrow focus; so that the information they produce may have limited value in gaining insight into factors increasing risk or ways of reducing it in other plants. Exposure assessments providing the most useful information enable

a risk manager dealing with one plant or product clearly to identify the influence of the risk-determining stages in the supply chain (Schlundt, 1999). If this requirement cannot be met, then the technique should not be used and input from experts should be relied on.

6.7.2 Core supply chain information

The overall supply chain model should identify the hazard inputs and control measures that determine hazards in the product. It should be built-up stage by stage, and the scope should determine where and how data are collected. A decision has to be made before data collection starts about whether the aim is a single point representation of each stage, or a representation of the range of conditions at each stage; and therefore the different levels likely to be encountered in the final product when combinations of contamination levels and treatments are put together (e.g. $10^6/g$ in a raw material with a process giving a 6 log reduction against $10/g$ in a raw material and a 3 log reduction). This aim will determine the extent of data collection (e.g. the period over which data should be collected, the number of measurements and their scope in the supply chain, from the field or the factory gate to release of the product or consumption). Collected data should also indicate the quantity of food likely to be produced under the conditions studied and its distribution among consumers. The more severe the hazard, the more attention should be paid to collecting reliable data about process conditions, the effectiveness of control measures and their variability. Sources of information can be diverse, but the team should focus on collecting and analysing direct observations, audit information, QA or process records and experimental data representing the supply chain. For the risk-determining steps, additional information on QA sampling plans, analytical test methods and any procedures used for validating control measures should also included, as these may allow the quality of the data to be evaluated. Data from quality monitoring (e.g. analytical or microbiology), processing or consumer complaints is usually held by food companies, and may also be held by regulatory agencies.

Data on the initial quality of ingredients and raw materials (e.g. level of contamination and its variability) and changes in pathogen level from the field (or raw material reception), through processing, storage and distribution until the product is prepared for consumption need to be estimated. Consumer use (e.g. ready to eat, ambient-stable or cook thoroughly) should be used as a basis for interpreting the significance of pathogen inputs and control measures during manufacture, and guide data collection about the supply chain (Carlin *et al.*, 2000). For example, pathogen presence at low levels in a raw material intended for cooking (pasteurisation) before consumption is not a severe hazard (Cassin *et al.*, 1998a). Collecting data on contamination routes for infectious pathogens will not be critical, if specified heating conditions immediately prior to consumption will make the product safe. However, data on cooking and its variability are essential. On the other hand, information on the possible presence of similar pathogens in a ready-to-eat product is essential, data on

decontamination and re-contamination is needed to produce a useful risk estimate. Where the process steps are designed to cause specific changes in numbers of pathogens (e.g. heating) or restrict their access to the product (e.g. primary packaging), then additional data may be sought to validate effects. This data may come from company QA or process information (e.g. pasteuriser performance or sample examination), from experimental data (e.g. heating studies on a defined microbiological challenge in the product) or literature sources (e.g. pathogen heat sensitivity under defined conditions).

6.7.3 Microbiological information

The characteristics of the identified hazard will determine its prevalence in raw materials and responses to process and storage conditions. Data on key physiological properties of the chosen pathogen(s) should be obtained (e.g. growth range, stress tolerance or heat resistance). What is needed will depend on the processing and preservation systems used. Quality assurance records or specific investigations of in-process material or equipment hygiene should be used to show pathogen numbers and identify realistic inputs from raw materials, factory, equipment and personnel.

If the hazard has been identified and process conditions and product factors are known, kinetic models can be used to predict growth or death during processing and storage (McDonald and Da-Wen-Sun, 1999; van Gerwen and Zwietering, 1998; Stewart *et al.*, 2001; Tienungoon *et al.*, 2000). Kinetic models require quantitative data on times, temperatures, etc. to predict the fate of pathogens. Within limitations, they can predict how microbial numbers change in response to time, temperature and other variables (e.g. pH and salt level) at the risk-determining steps up to the time of consumption. Worst-case estimates based on the fastest growing strains likely to be present can be used as the default by published models. A sigmoid growth curve (the Gompertz function) is assumed in many of these growth models: it shows growth rate monotonically increasing up to a maximum and then falling to zero, as the bacterial population reaches a steady state at its maximum level. Using the maximum rate of growth is fail-safe, because this rate is often approached rapidly and does not decline significantly until conditions change, or the maximum population is reached. However, this type of model may not be appropriate if gradual changes stop growth and induce a survival phase. Under these conditions actual measurements of numbers will provide a more realistic basis for the exposure assessment.

Product temperatures and changes in temperature will often depend on the type of product, and its interactions with equipment and with heating (Braud *et al.*, 2000) or cooling media. When temperatures are selected for modelling, account should be taken of the fact that product temperatures do not equilibrate instantly, but gradually, at each processing stage. This can lead to significant differences between process conditions and the heating or cooling treatment that products and pathogens receive. A practical approach to estimating process effects is to start with single temperature inactivation (e.g. D and z where D = the time at any

specified lethal temperature required to inactivate a population of spores or vegetative cells by one logarithm cycle or 90% – mathematically D is equal to the reciprocal of the slope of the superior curve; and $z =$ the number of Celsius degrees for the thermal destruction curve to transverse one logarithmic cycle – mathematically z is equal to the reciprocal of the slope of the thermal death curve.) or growth models and then progress to, or build, more complex models to cover additional factors such as survival and re-contamination or heat transfer, if they are important. Hence predictive microbiological models are useful sub-models within the overall supply chain model (see Zwietering and van Gerwen, 2000).

6.7.4 Additional information

In addition to in-house information on the process and materials in question, the team should collect relevant published literature and consult experts who may have access to additional sources of information. These can include suppliers, food processing personnel, microbiologists, food scientists, epidemiologists, health experts, nutritionists, research institutes and public health authorities. Consumer organisations can be another source of information about consumer practices, and many food trade associations also have data about food/commodity consumption rates. It may also be useful to compare the collected data with historical or outside experience. Animal health data may be relevant for meat and poultry products (Bryan and Doyle, 1995) likely to be contaminated with zoonotic pathogens. Information on routes for infection and contributory events may be extracted from well-conducted outbreak investigations; however, usually quantitative exposure information is not collected, or is very limited. Nevertheless, information from reconstruction of the chain of events that led to an outbreak can be useful in identifying realistic or potential scenarios of exposure (European Commission, 2000).

6.8 The output of an exposure assessment

Risk assessors use exposure assessments to produce risk estimates of the probability and consequences of exposure to a food poisoning hazard; depending on the quality of information available. Assessments will have different levels of reliability and should always explain levels of uncertainty and variability in the supply chain covered and any assumptions made. The output of an exposure assessment should communicate pathogen or toxin levels in the food at the time of consumption and may also show how they are likely to vary because of handling, raw material quality, processing and preparation. Whatever level of detail is used, the output has to be understandable to its users; if it is not, then the benefits of any approach will be lost. Table 6.4 illustrates examples of exposure assessments.

Assessments can be characterised as informal, qualitative (e.g. describing risks as serious, life threatening) or quantitative (e.g. estimating risks as one in a million potentially toxic or a defect rate of 1 in 10 million packs). Qualitative

Table 6.4 Examples of exposure assessments for infectious and toxin-producing pathogens in various foodstuffs

Microbiological hazard	Toxin-producing, pathogen	Infectious pathogens	Toxicogenic pathogen
Product type	<i>Staphylococcus aureus</i> Cooked ham	<i>Salmonella</i> Fully cooked frozen product	<i>Staphylococcus aureus</i> Canned low-acid food hazard from wet pack handling
	<i>Listeria monocytogenes</i> Cooked ham	<i>Salmonella</i> Frozen raw poultry	

Occurrence of hazardous microorganisms in the raw materials

What is the frequency of contamination of the raw materials making-up the product?

Very low frequency: 0–1%
0–10 cells/g

Frequent

0–10⁴ cells/g

Negligible: 0–0.1%

0–100 cells/g

Frequent

0–30% contaminated, 0–10 000 cells/g

Negligible: 0–0.1%

0–10 cells/g

Effect of processing/decontamination

What is the effect of storage before processing on the level of the hazard?

Survival

Some growth

Survival

Survival

Survival

What is the intended effect of all processing and any decontamination stages on the level of the microorganism?

Complete inactivation – at least a 6 log reduction

Complete inactivation – at least a 6 log reduction

Complete inactivation – at least a 6 log reduction

Survival

Partial inactivation

Occurrence of toxin (if the hazardous micro-organism is toxin-producing)

What is the likelihood of toxin presence if the microorganism can produce toxin and is present in the raw materials, product or process environment?

Negligible: 0–0.1%

Re-contamination after processing or decontamination

What is the frequency of re-contamination of the product in the factory after processing or decontamination, so that the hazard is present in the final product?

Very low frequency: 0–1%

Negligible: 0–0.1%

High frequency: 10–50%

Negligible: 0–0.1%

What is the likely level of re-contamination after processing or decontamination?

0–10 000 cells/g

0–10 cells/g

0–10 000 cells/g

0–10 000 cells/g

What is the variability of recontamination?

Very low, good quality data on materials over a period of months or tens of intakes

Low, fair quality data on similar materials from QA data

Very low, good quality data on materials over a period of months or tens of intakes

Medium, medium quality general information on supplier assurance concerning levels

Very high, no data, opinion

Packaging

Is the product put in its primary packaging before the decontamination step?

Yes

If the answer is no, what is the frequency of recontamination of decontaminated product before packaging?

Negligible: 0–0.1%

Negligible: 0–0.1%

N/A, but high risk of cross contamination during domestic use

What is the level of recontamination after packaging?

0–10 000 cells/g

0–10 cells/g

N/A

0–10 000 cells/g

Table 6.4 (continued)

Microbiological hazard	Toxin-producing, pathogen	Infectious pathogens	Toxigenic pathogen
Product type	<i>Staphylococcus aureus</i> Cooked ham	<i>Salmonella</i> Fully cooked frozen product	<i>Staphylococcus aureus</i> Canned low-acid food hazard from wet pack handling
	<i>Listeria monocytogenes</i> Cooked ham	<i>Salmonella</i> Frozen raw poultry	
Effect of product/pack storage			
How does the level of the hazard change during storage (storage according to the usage instructions)?	Survival	Survival	Growth, large increase in numbers
	Some growth: < 3 log increase in numbers		
Effect of product/pack storage on toxigenesis			
What is the likelihood of toxigenesis in the product?	Very low frequency		Negligible
What is the effect of storage conditions on toxigenesis (If the level of the micro-organism changes and it is toxin-producing)	No change during chilled storage, survival		No change to rapid toxin production
Consumer use			
Is the product intended as single use (S) or multi-use (M), where it will be stored after opening?	M, fridge or ambient	S	Usually S

If the answer is M: This means that the product is multi-use either in a domestic or food service application and the usage and preparation section should be completed.

The effect of open shelf-life on the microbial hazard

What is the effect of open shelf-life storage on the level of the pathogen?
 No change (at chill)
 Low

What is the variability of re-contamination during open shelf-life?
 Some growth
 Low

No change (at chill)
 High

No change (at chill)
 N/A

Growth
 N/A

The effect of open shelf-life on toxigenesis

What is the likelihood of growth and toxin production during open shelf-life?
 Slight increase, low frequency of toxin production
 Unchanged

What is the effect of the intended storage conditions on toxigenesis?
 Unchanged

Unchanged, low frequency
 Large increase

The effect of usage and preparation on hazards

What is the effect of customer or food service preparation and usage on the level of hazard?
 No change, survival or growth and toxin
 toxigenesis

Some growth: < 3 log increase in numbers
 Complete inactivation, if used according to instructions

Complete inactivation, if used according to instructions

No change or increase

The effect of usage and preparation on toxigenesis

Is toxin likely to be present when the product is consumed?
 Very low frequency

What is the effect of usage and preparation on toxin level and production?
 Slight increase

Very low frequency
 Unchanged

Food intake by a consumer

What is the likely quantity of the food consumed by a customer on a specified occasion or over a period of time?
 Low intake
 50–100g

Low intake
 50–100g

Low intake
 50–100g

High intake
 100–200g

Risk estimate

Presentation of the risk estimate in the way most informative to the user or risk manager

assessments are the lowest level of detail providing a systematic description of a problem and its contributory factors. Quantitative assessments include mathematical analyses of relevant data (van Gerwen *et al.*, 2000; Hoornstra and Notermans, 2001) and provide numerical estimates of risk. They should only be done if there are sufficient resources for data collection, the attendant calculations and a substantial amount of scientifically respectable data. When there is less data, effective guidance for risk managers may still be provided by a description and ranking (e.g. serious, realistic, unrealistic) of the hazards and a detailed description of the risk determining steps. When data, time and/or other resources are limited, the best option will usually be to conduct a qualitative risk assessment, as described in the examples (Table 6.4). In fact, such studies are often undertaken for preliminary evaluation of a food safety issue to determine if a more detailed analysis is warranted (Tompkin, 1999). Such preliminary studies must at least identify the hazards and parts of the food chain to consumption that require further detailed examination during a quantitative exposure assessment.

If reliable quantitative data are available, exposure assessors may use quantitative terms to describe risk. If quantitative data are not available, a qualitative approach is likely to be more meaningful. Data from an exposure assessment may be used under three headings:

- 1 Identification of the hazard covered (e.g. salmonella) with an overall supply chain model showing the origin(s), routes and effects of processing, handling and preparation on the hazard as defined by the scope. The probability of contamination or presence may be rated between negligible, high or certain, or may be expressed numerically. Based on changes in the hazard level, risk-determining steps in the supply chain can be shown.
- 2 An estimate (e.g. 1 in 10^6 portions will contain 100 cells) or a description (e.g. high) of the probability that a portion will contain a harmful dose for the designated consumers (Buchanan *et al.*, 2000). To do this, the critical level required for disease and the dose in a portion need to be known (or assumed). In many cases exact values will not be available and it may be appropriate simply to state that one cell in a portion causes illness. If information on critical exposure levels is not available, risk assessors may use the exposure assessment to describe processing and food composition factors that are likely to influence the level of exposure.
- 3 The quantity of food likely to be covered by the exposure assessment and hence the extent of the risk arising because of the level and distribution of the hazard. Factors that influence distribution of the disease agent and its wider spread are important for controlling the impact of disease. An exposure assessment should indicate the distribution of significant doses from different uses of a contaminated raw material.

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7

Risk characterisation

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... great uncertainties are introduced at every step in the risk assessment procedure, and risk characterisations should be seen as indicators only and all the uncertainties carefully spelled out. Risk characterisations, as they are presently derived, should never be assumed to present accurate representations of the real situation. (Benford and Tennant, 1997)

7.1 Introduction: key issues in risk characterisation

Risk characterisation is defined as 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 population based on hazard identification, hazard characterisation and exposure assessment (FAO/WHO, 1995; Codex 1999). It represents the integration of the hazard identification, hazard characterisation and exposure assessment to give a risk estimate. The information to bring together for a risk estimate may be quantitative and/or qualitative in nature, however it should be of the best quality, be the most relevant and the most up to date that is available. This information will never be completely 'made-to-measure', thus 'expert opinion' and uncertainty will always have a role in the risk characterisation step, and consequently in microbiological risk assessment (MRA) as a whole.

A broad range of skills is required to carry out the risk characterisation step, since information and data of a wide range of types (quantitative and qualitative) and sources will need to be handled. Some mathematical knowledge (for example in modelling data), knowledge of the process under consideration, and

microbiological knowledge and expertise is invariably needed. Voysey (2000) divides risk characterisation into six stages:

1. combining previous MRA steps
2. summarising the risk
3. variability in risk
4. sensitivity analysis
5. uncertainty
6. validation against experience

These will be addressed in turn.

7.1.1 Purpose

This heading can be used to cover the stages of combining previous MRA steps and summarising the risk described by Voysey (2000). The above definition of risk characterisation reflects the purpose of this step, which is to bring together the information derived from the previous MRA steps. These are hazard identification, exposure assessment (probability of occurrence) and hazard characterisation (severity of known or potential adverse health effects). This can then be used to provide an estimate (qualitative or quantitative) of risk to a given population or sub-population.

The handling of combined factors associated with the food, the process, the pathogen and the person is complex. Consequently, considerable skill is needed by the team carrying out the risk characterisation step to ensure that the output from this step matches the anticipated output as declared in the Statement of Purpose. It must also be in a format that the risk manager can use to make a decision based on the findings of the MRA.

7.1.2 Variability

In summarising the risk, some detail will not be included. Consequently, an 'average' or 'overall' risk will not be as applicable to some groups of the population, or some circumstances, as others will. Variability in factors relating to the manufacturing process for the food, the characteristics of the food itself, the pathogen or people, can result in variability in the final risk. A 'sensitivity analysis' is an important guide in planning assessment of variability.

If variability in a factor has been included in its uncertainty, it will carry through to uncertainty in the final risk. If variability in a factor has been identified and carried through the process, the final risk will be dependent on source factors. For example, this might result in different final risks for different groups of people, or an expression for final risk which depends on storage life. In such a case, it is important to report clearly the dependence, and the variation in risk between different circumstances or groups.

7.1.3 Identification of risk factors

It is possible that the estimated final risk is not substantially affected by credible variations in the various factors, parameters, assumptions, models, and so on. It is more likely that some have a larger effect than others. Identification of process and food factors that have a substantial effect on the final risk (sensitivity analysis), is an important benefit of risk assessment. It allows effective direction of risk reduction measures and targeted consideration of the effect of variability. Assessment of the effect of parameter values, assumptions and models on the final risk assessment is often the only way of transferring uncertainties in them through to the final values. Often this can effectively be performed by varying these assumptions and observing the effect on the final risk assessment.

7.1.4 Uncertainty

The uncertainty expresses the range of values that may credibly be true. It may be that the best estimate would lead to one decision, but that uncertainties are so large that a value leading to another decision is quite credible. It is essential to accompany any indication of risk with an indication of the associated uncertainty. In principle, it is possible to estimate the final uncertainty by tracking the uncertainties of all the inputs to the risk assessments, modifying and combining the uncertainties as the inputs are modified and combined. Often this is impractical and the effects of input uncertainties on the output must be estimated by sensitivity analysis.

7.1.5 Validation

It is essential to ensure that the results of the risk assessment accord with common sense and with experience.

7.2 Risk characterisation requirements

Risk characterisation aims to describe the risk to the relevant population from consumption of the relevant food. There are real and substantial differences between members of the population and between food items with consequent real differences in risk. For microbiological risk assessment in food processing, the description of such differences is often more important than estimates of average or typical risk. Judgements on the acceptability of any given risk level are properly the prerogative of government, which few food processors would wish to usurp. For a food processor a conclusion that the processed food presents no greater risk than the equivalent fresh food, or that a process modification does not increase the risk, is more useful than a numerical estimate of illnesses. That is, a food processor is more concerned with risk relative to variability (within the scope) than with absolute risk estimates. An appropriate handling and description of variability is central to successful risk characterisation. Unless

the risk characterisation includes a well considered and described handling of variability, the risk estimate will be partial and may often be misleading.

7.2.1 Clear statement of purpose

Hazard identification, hazard characterisation, and exposure assessment collect and process external information for use principally within the risk assessment. Risk characterisation integrates their results to give risk estimates (Codex, 1999) which are the principal outputs from the risk assessment. It is important that there is a clear understanding of what those outputs should be. Although a clear statement of purpose is necessary to undertake an appropriate hazard identification, hazard characterisation, and exposure assessment, failures in these stages due to inadequate definitions of objectives and required outputs may not become apparent until the risk characterisation stage. Accordingly, we associate the requirement for a clear and complete statement of purpose with the risk characterisation rather than earlier stages. The statement of purpose should include, *inter alia*, objectives, scope and required outputs (Codex, 1999; Voysey, 2000).

Setting objectives(s)

Mitchell (2000) states 'At the very beginning . . . you need to work out why you are doing this particular Risk Assessment. Otherwise you can become easily confused and the MRA will not do what you want'. Voysey (2000) notes that the objective would 'generally take the form of an objective to carry out an MRA . . . within the agreed scope and to an agreed timetable and output'. In hindsight this seems inadequate. The statement of purpose should include a clear statement of the need that the risk assessment is intended to address, that is motivations as well as specific objectives. Without such clarity in purpose, it is difficult to define appropriate scope, timetables and outputs.

A clear statement of the motivation for the risk assessment is especially important to a food processor because his available time, information and other resources are substantially less than for governmental risk assessments, and are unlikely to allow risk estimates as complete and precise as might reasonably be wished. A clear objective allows the risk characterisation to make informed compromises. It should be in sufficient detail to allow the degree of achievement of objectives to be estimated, and the relative value of different results to be assessed. The act of recording encourages clarity of thought, and the record avoids later drift in perceived objectives.

Defining the scope

A careful definition of the scope in the statement of purpose can greatly alleviate the difficulty of all steps of any risk assessment, but especially of the risk characterisation step and particularly when risk assessment is applied to food processing. Variation and uncertainty are closely linked, if there were no variation there would be no uncertainty, and variation is a reflection of scope.

Governmental risk assessments generally have a broad scope. The population considered is national or international, the foodstuff is a broad category and the food chain contains many variants. The broad scope demands substantial resource in the hazard characterisation and the exposure assessment. The broad variation demands much of the risk characterisation. The risk to any particular person from any particular food item depends on the characteristics of the person and the food item. Incorporating that dependence in a risk estimate is challenging, the more so as the breadth of the variation increases. Failure to incorporate such dependence leads to uncertainty in applying typical or average estimates to specific circumstances.

The scope of microbiological risk assessments in food processing is generally much more restricted. The population considered may still be national or international. However, in food processing the objective of the risk assessment is often to look at differences. The population can often be considered constant for the alternatives being compared so that the effect on the conclusions of variation and uncertainty from that source is minimised. For a food processing risk assessment the foodstuff and food chain are usually very well defined. This eases the exposure assessment; often directly relevant data can be gathered from existing records. It also reduces the range of variation to be encompassed in the risk characterisation. Clearly the scope must include the range of alternatives to be compared and realistic deviation in other variables. However the variation implicit in a risk assessment of a particular product subject to a particular process and distributed by a particular chain is very much less than a typical governmental risk assessment.

The reduction in scope does limit the range of application of the conclusions. However, microbiological risk assessments in food processing are generally conducted within strictly limited time-scales for specific objectives. The scope should be as narrow as possible, consistent with the objectives.

Form of output

The statement of purpose should include a clear and explicit statement of the output to be produced. Codex (1999) say that:

The output form and possible output alternatives of the risk assessment should be defined. Output might, for example, take the form of an estimate of the prevalence of illness, or an estimate of annual rate (incidence of human illness per 100,000) or an estimate of the rate of human illness and severity per eating occurrence.

Voysey (2000) and Mitchell (2000) give similar examples of alternatives. These examples illustrate different bases for risk estimates but the alternatives given are by no means a complete list. Other bases for risk estimates are especially relevant when applying microbiological risk assessment in the food processing industry, when differences and ratios may be more appropriate; for example, the proportionate reduction (or increase) in risk consequent on a process change.

More fundamentally, while these example forms of output specify the basis of the risk estimate, they do not address the expression of variability. There are many ways in which variability can be estimated and expressed, and it is important that the methods chosen are appropriate to the purpose of the risk assessment. Hypothetically, a process change may result in a lower risk on average, but, due to increased variability, a substantial increase in the risk presented by the extreme 10% (say) of the product. The 'average' risk associated with processed foods is very low so that risk management decisions are likely to be based on variation from the average. If the manner in which variation will be assessed and described is not considered and specified at the outset, it is unlikely to be successfully achieved by the risk characterisation at the end of the risk assessment.

The specification of form of output should also explicitly address the expression of uncertainty. It is essential that uncertainty and variability are clearly distinguished. The implications of the two following risk estimate statements:

1. process change results in 95% of production presenting a reduced risk; and
2. process change results in 95% confidence of a reduced risk

are very different, and neither statement is adequate. A satisfactory risk estimate statement will include indications of both variability and uncertainty and is likely to be much more complex than either of these examples.

Preliminary investigation

A microbiological risk assessment performed by, or for governmental and regulatory agencies may be well justified even if the information and data available do not allow clear conclusions to be drawn. The absence of information is itself of interest and may serve to direct precautionary measures, as well as further investigations. In contrast, microbiological risk assessments in food processing are generally performed with specific objectives. The narrower scope limits the spin-off value if the assessment does not achieve its objectives. The clear statement of objectives, form of output, and scope described above are of little value if the objectives are not met because of limited resources, information or data. When describing the statement of purpose step Codex (1999) said that 'the microbiological risk assessment may require a preliminary investigation phase'. Voysey (2000) recommended an outline MRA as a preliminary 'Step 0'. Such a preliminary investigation may indicate which objectives are feasible and what resources may be needed to achieve them. Of course, one possible outcome of the preliminary investigation is that the MRA is not feasible and should not be attempted. However, a well executed and interpreted preliminary MRA will identify information and resources and permit a clear and complete statement of purpose, including the form of the risk assessment and the handling of variability and uncertainty. This will allow the risk characterisation to be carried out with a clear and achievable objective in view.

7.2.2 Appropriate inputs

The risk characterisation depends directly on the results of the exposure assessment and hazard characterisation steps, which in turn depend on the statement of purpose and the hazard identification. If the exposure assessment and hazard characterisation do not produce the required information then the risk characterisation cannot succeed. A well designed, executed and interpreted preliminary investigation should have ensured the availability of appropriate resources, including information. A clear and complete statement of purpose should have ensured that the exposure assessment and hazard characterisation were appropriately directed.

However, risk characterisation is the stage at which the exposure assessment and hazard characterisation come together, and it is at this stage that incompatibility will become apparent. Incompatibility can arise through different approaches to variability. The variability can be broadly divided into that within the exposed population and that within the food chain. Both hazard characterisation and exposure assessment are likely to address variability by sub-setting the scope. Hazard characterisation is likely to divide the exposed population into sub-groups of differing sensitivity to the hazard, and may divide the food scope into areas of different associated virulence. Exposure assessment is likely to divide the exposed population into sub-groups of differing behaviour and the food scope into areas of differing contamination.

Unless the hazard characterisation and exposure assessment use compatible data, sub-setting the risk characterisation will not be able to combine them without substantial loss of precision in the description of variability. If hazard characterisation divides the exposed population according to medical criteria and exposure assessment divides them by socio-economic grouping, the risk characterisation will not be able to describe the variation in risk by either criterion. Expressing this formally, the exposure assessment estimates exposure as a function of variable factors; hazard characterisation estimates harm as a function of variable factors. Unless the domains of the two functions are compatible the risk characterisation will not be able to estimate risk as a function of variable factors. Microbiological risk assessment in food processing situations is less likely to suffer from such incompatibilities if the statement of purpose adequately describes the objective and scope, directing the exposure assessment and hazard characterisation to common and appropriate subsetting.

7.2.3 Skills and tools

A successful and valid risk characterisation requires a broad range of skills. Because this step synthesises the results of the hazard characterisation and the exposure assessment it requires a deep understanding of the techniques used in those steps, and their limitations, approaching that required to perform those steps. Here we consider the skills in the order:

- mathematical, statistical and computing skills
- microbiological and medical skills
- food processing skills

This list is not in order of importance; all the skills are essential. If anything, and especially for risk assessment in food processing, their importance to the validity of the conclusions is the reverse, with food processing knowledge and experience the most important.

Mathematical, statistical and computing skills

Microbiological risk assessments commonly represent and summarise rates and levels of contamination, the behaviour of the food and the pathogen during processing and distribution, and the behaviour using a range of dose–response empirical and mechanistic mathematical and statistical models and techniques implemented as computer programs. The availability and usability of such programs has removed many technical barriers, however it has encouraged a ‘black-box’ approach to sophisticated techniques where the results may be considered without due regard to the assumptions and limitations of the techniques and the data. An appreciation of these issues at the risk characterisation step is essential to a proper handling of uncertainty and requires a good understanding of a broad range of mathematical and statistical techniques.

Microbiological and medical skills

Not surprisingly, it is critically important that expertise and knowledge is available on the characteristics of microorganisms. Information will be required on the growth, survival and death of a wide range of pathogens and in some cases spoilage organisms. An understanding will be required on how the different microorganisms respond to a variety of preservation mechanisms and technologies, and in particular the interaction of preservation methods. The properties and attributes of microorganisms will be closely linked to the foodstuffs in which they are found. With the advent of novel molecular techniques for identifying and differentiating microorganisms it is also important that members of the team undertaking the MRA embrace this new knowledge.

In the area of dose–response, a clear and informed view will be necessary on the definition of various ‘illness end-points’ if one is going realistically to attribute illness with data on prevalence and distribution patterns. The implication of microorganisms in illness (whether it be outbreaks or sporadic cases) needs to be undertaken with great care, and medical expertise in epidemiological investigative science will be vital. It is likely that such expertise will become increasingly important as microbiological risk assessment addresses severe illness syndromes (e.g. haemolytic uraemic syndrome associated with *E. coli* O157:H7, and sensitive sub-populations, i.e. pregnant women and immuno-compromised).

Food processing skills

Expert knowledge is also required on the implications of all stages in food processing which may impinge on the outcome of the risk assessment. This will include sources of raw materials (growing and harvesting methods or production techniques), primary processing, manufacturing through to distribution and retail sale to the consumer. It is evident that many stages in the food production chain can impact on the levels of microorganisms which may be present in the final product. Skills may be necessary in disciplines such as mechanical and chemical engineering, food science and technology, agriculture and consumer and sensory sciences. The use of such expertise will maximise the opportunity for identifying intervention strategies which will lead to the greatest reduction in risk.

7.3 Risk characterisation methods

This section often uses mathematical terminology. This usage is, however, only for brevity and does not imply that the inputs or estimates must be expressed mathematically. Almost always the inputs and outputs of the risk assessment are at least partly qualitative. Even then the risk characterisation must still explicitly consider the variability, sensitivity, uncertainty and validation of the risk estimates which will depend in turn on the exposure assessment and hazard characterisation. A summary of these three stages is shown in Fig. 7.1 where inputs are grouped into those associated with the process (including the foodstuff), the pathogen, and the person at risk.

Exposure assessment estimates the exposure of members of the target population to the pathogen. Hazard characterisation estimates the harm to members of the target population conditional on a given exposure to the pathogen. Risk characterisation combines these estimates to produce estimates of the harm to members of the target population, the required risk estimates. The methods used by the risk characterisation to combine the exposure assessment and hazard characterisation estimates depend on the nature of those estimates and of the required risk estimates, as specified in the Statement of Purpose. Figure 7.1 represents all three estimates as functions of the inputs, F_E , F_H and F_R . Risk characterisation may be seen as the joint integration, or convolution, of the exposure assessment and hazard characterisation estimates.

The hazard characterisation estimate of harm is conditional on an assumed level of exposure. As the frequency of harm depends on exposure, the hazard characterisation output is intrinsically multi-valued, often expressed as a dose-response curve. This multi-valued estimate does not, in itself, represent variability (see section 7.3.3). The multiple values do not represent different individuals in a population but different assumed doses. Indeed each value, the frequency of harm associated with a given dose, is generally an average across a population and conceals the variability of response within that population.

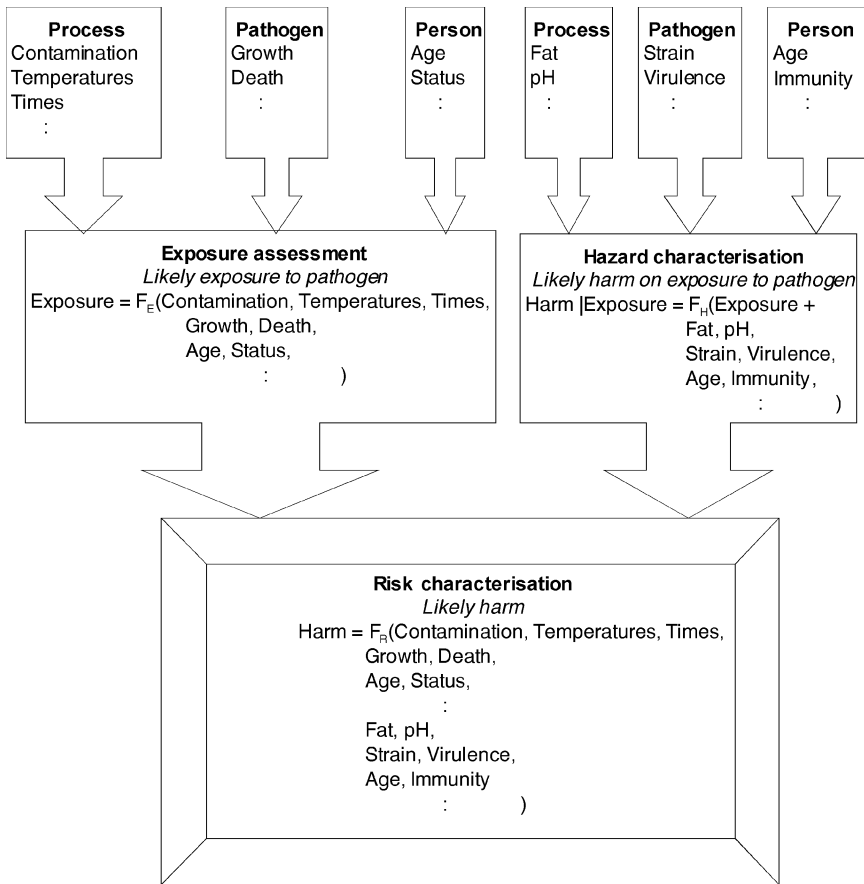


Fig. 7.1 The relationship between exposure assessment, hazard characterisation and risk characterisation.

7.3.1 Sensitivity analysis

Inasmuch as the purpose of a risk assessment is to deduce risk estimates from the input factors, the dependence of the estimates on the input factors is central to the whole process. However, formal sensitivity analysis is usually required both to meet the objectives of the risk assessment and appropriately to handle uncertainty.

Sensitivity analysis involves determination of the change in risk resulting from changes in the inputs. This is important both in handling uncertainty (section 7.3.5) and in determining and describing the risk determining factors (section 7.3.4).

Viewed mathematically, sensitivity analysis is differentiation of the risk with respect to the inputs which may be expressed as equation 7.1.

$$dF_R = \sum \frac{\partial F_R}{\partial x} dx \quad 7.1$$

where F_R is the risk estimate and the x 's are all the values on which the risk depends.

This makes clear that the influence of an input on the risk estimate can be considered in two parts. First is the partial differential, $\partial F_R / \partial x$, defining the effect on the risk estimate of a unit change in the input. To evaluate the actual effect of a change on the risk estimate this must be multiplied by the magnitude of the change, the total differential of x , dx .

The term *sensitivity* is often used to mean the total effect of an input on the risk estimate and *sensitivity analysis* is used to mean the process of determining and describing those factors with most effect on risk. We prefer to reserve the term sensitivity, or more specifically *sensitivity coefficient*, for the partial differential and the term sensitivity analysis for the process of determining the sensitivity coefficients.

It is rare for the form of the risk estimate to permit the explicit, mathematical determination of the effect of all the inputs, in the manner implied by equation 7.1. Almost always the effect of some inputs must be determined semi-quantitatively at best. It is essential to consider all important inputs and to avoid the temptation of restricting the sensitivity analysis to those inputs amenable to mathematical treatment. Even when the sensitivity analysis is qualitative, it is useful to divide it into the two parts implied by equation 7.1. Firstly, what is the effect of a small change in the input, with all other inputs unchanged? Secondly, what is the likely magnitude of a change in that input?

Analogy of the sensitivity analysis to a mathematical differentiation also clarifies two issues which may be missed in a qualitative application. Firstly, the partial derivative with respect to an input may be a function of that input and other inputs. It is important to consider how the sensitivity may vary with the value of all relevant inputs. Secondly, a purely mathematical application of equation 7.1 would evaluate the change in risk, ΔF_R , by integrating the expression over the frequency distribution of the inputs, x . It is important to consider the frequency of different input values and especially the correlations between them. Conversely, the mathematical analogy can encourage the neglect of inputs which are not expressed as simple numbers; this must be avoided. Many inputs will be categorical, e.g. sex, or choices and an example of choices would be models; all these inputs must be considered.

Sensitivity analysis, as defined here, is not an objective in itself. It is an approach which is useful in drawing conclusions and assessing uncertainty. Sensitivity analysis is likely to be used in several stages of the risk characterisation, rather than forming a distinct stage itself. When determining and describing the risk determining factors the x 's considered will generally be the process, pathogen and person input factors shown in Fig. 7.1. When studying uncertainty the x 's considered will generally be estimates of parameters, although often those parameters will be descriptions of the variability in input factors.

7.3.2 Distinguishing variability and uncertainty

There is much confusion in the use of the terms variability and uncertainty. Codex (1999) says that ‘Differentiation of uncertainty and variability is important ...’ but does not define either term. Other authors (Vose, 2000; Voysey, 2000; Smith, 2002) distinguish between uncertainty and variability but there is not complete agreement and the authors of this chapter do not find any of these definitions completely satisfactory.

There is general agreement that uncertainty and variability both describe values which are to some extent random or stochastic. There is also agreement that variability reflects ‘real’ differences while uncertainty reflects lack of knowledge on the part of the risk assessor which is, at least in principle, reducible by further investigation. To provide clarity, while retaining the sense of other authors we suggest that the distinction between uncertainty and variability lies in the entity with which each is associated. Variability is a characteristic of a population, uncertainty is a characteristic of an estimated value (which value may be non-numeric). We present the following definitions:

Variability represents the heterogeneity in a well-characterised *population*, usually not reducible through further measurement or study.
(from Burmaster and Bloomfield, 1996, our emphasis)

Uncertainty of an *estimate* characterises the dispersion of the values that could reasonably be attributed to the estimated value. (based on the definition of uncertainty of measurement in (BSI, 1995))

The population with variability may be other than people, for example the population of process temperatures applied to a product. Variability will often be expressed as a frequency distribution but this may be non-numeric.

Parameters of a variability frequency distribution may be estimated with associated uncertainty. For example, the risk to which a population is exposed may be described by a median and percentiles, when those parameters will have associated uncertainties. Although the variability within the population may influence the uncertainty, it is more difficult to characterise a more variable population; the variability does not form an intrinsic part of the uncertainty. At least in principle, further investigation can indefinitely reduce the uncertainty of the estimated parameters. On the other hand, if an estimate relates to an individual from the variable population the variability becomes part of the uncertainty of the individual estimate. Even in principle the uncertainty of the individual estimate cannot be reduced below the population variability without information specific to the individual.

7.3.3 Variability

This makes it very important that the Statement of Purpose adequately specifies the nature of the required risk estimates and the report makes clear the nature of the reported risk estimates. It is unlikely that all members of the population have

the same chance of harm, their risk will depend on factors such as age, immunity and dietary habits. A single valued risk estimate may conceal large variability between the risk to individuals. It is important that the risk characterisation captures and conveys such variability and that risk estimates relating to populations are not applied to individuals without due caution.

Qualitative estimates will express variability in qualitative terms. Numerical risk estimates may express variability as frequency distributions, defining the proportion of the population with any given level of risk. However even numerical risk estimates may be derived from non-numerical information and it is important that all substantial variability is included with the risk estimate, avoiding the tendency to concentrate on quantifiable aspects to the neglect of qualitative information. Inasmuch as risk characterisation adds no new information, merely combining that from the exposure assessment and hazard characterisation, it is important that those steps do not suppress variability information by premature averaging.

For example, it is common to represent the results of the hazard characterisation as a dose-response curve defining the frequency of a stated response at any given dose. That frequency represents an average across other factors relating to the process, the pathogen and the person. Thus, the representation of the hazard characterisation as a two-dimensional curve is a simplification. A complete hazard characterisation would be multidimensional, relating frequency of response to all of its input values.

In principle, at least, details of such multidimensional dependence should be passed to the risk characterisation so that it can be combined with similar information from the exposure assessment to estimate variability in risk. In practice, many dependencies cannot be described in any more than the most general qualitative terms by either the exposure assessment or the hazard characterisation so that the unknown dependency becomes a component of uncertainty.

7.3.4 Risk determining factors

Often identification of the factors with most influence on risk is more important than the risk estimate itself. If a risk assessment is to inform risk management decisions the risk characterisation must identify those factors that most influence the risk. Where those factors are associated with the person this may influence, for example, the groups to whom information is directed, or advice on dietary behaviour. Where the factors are associated with the process this may direct risk management efforts.

Identification and description of risk determining factors will generally be by some form of sensitivity analysis as described in section 7.3.1. As stated earlier, it is important that the changes and levels in input factors considered are realistic and that realistic combinations are considered. Often information on distributions of factors, and especially correlations between them, is much poorer than information on typical or average values. Such uncertainty is often

mitigated by stating the sensitivity conclusions in conditional terms such as: 'If input changes by x and nothing else changes then risk changes by y '. However such conditional statements should be used with appropriate caution as they will often be read as implying that the hypothesised change is feasible. This may reduce the uncertainty in the conclusions of the sensitivity analysis compared to the absolute risk estimates. However the changes in risk may be very sensitive to the assumed mechanisms, that is the models, mathematical or otherwise, which are implicit in the risk assessment process. Such model uncertainty can be difficult to estimate but must be carefully considered.

7.3.5 Uncertainty

Every conclusion produced by the risk assessment should be subject to an uncertainty estimation. Where the estimate is multi-valued the uncertainty should also be multi-valued. For example, the within population variability in risk may be represented as a frequency distribution specifying the proportion of the population exposed to any given level of risk. It is not meaningful to associate a single uncertainty value with the frequency distribution. If the frequency distribution is represented by a parameterised equation then each parameter has an associated uncertainty. If the frequency distribution is represented by a graph then each point on that graph, that is the estimated proportion of the population exposed to each given level of risk, has an associated uncertainty.

When a frequency distribution is represented by a line on a graph it is tempting to represent uncertainty by an additional pair of lines representing a confidence interval. However such a representation is easily misinterpreted. For example, the illustrative graph shown in Fig. 7.2(a) may be interpreted as showing confidence intervals on the frequency associated with each level of risk (Fig. 7.2(b)). This is probably the correct interpretation. However it may be interpreted as showing confidence intervals on the quantiles, the level of risk to which a given proportion of the population is exposed (Fig. 7.2(c)). It may even be interpreted as showing confidence intervals on the level of risk to which an individual in the population is exposed. Graphical representations of uncertainty must be clearly labelled to avoid misinterpretation.

The uncertainty in risk estimates can be evaluated by the kind of sensitivity analysis indicated in section 7.3.1. However, identification and description of risk determining factors are also important conclusions and the uncertainty in those conclusions should be assessed. The effect of risk determining factors is itself a result of sensitivity analysis, a differential in the sense of equation 7.1. In principle, the uncertainty of those effects should be determined by sensitivity analysis of the sensitivity, a double differentiation. In practice, the original sensitivity analysis is perforce semi-quantitative at best. Estimation of the uncertainty relating to identification and description of risk determining factors can rarely be better than qualitative, nevertheless, it can and should be explicitly considered.

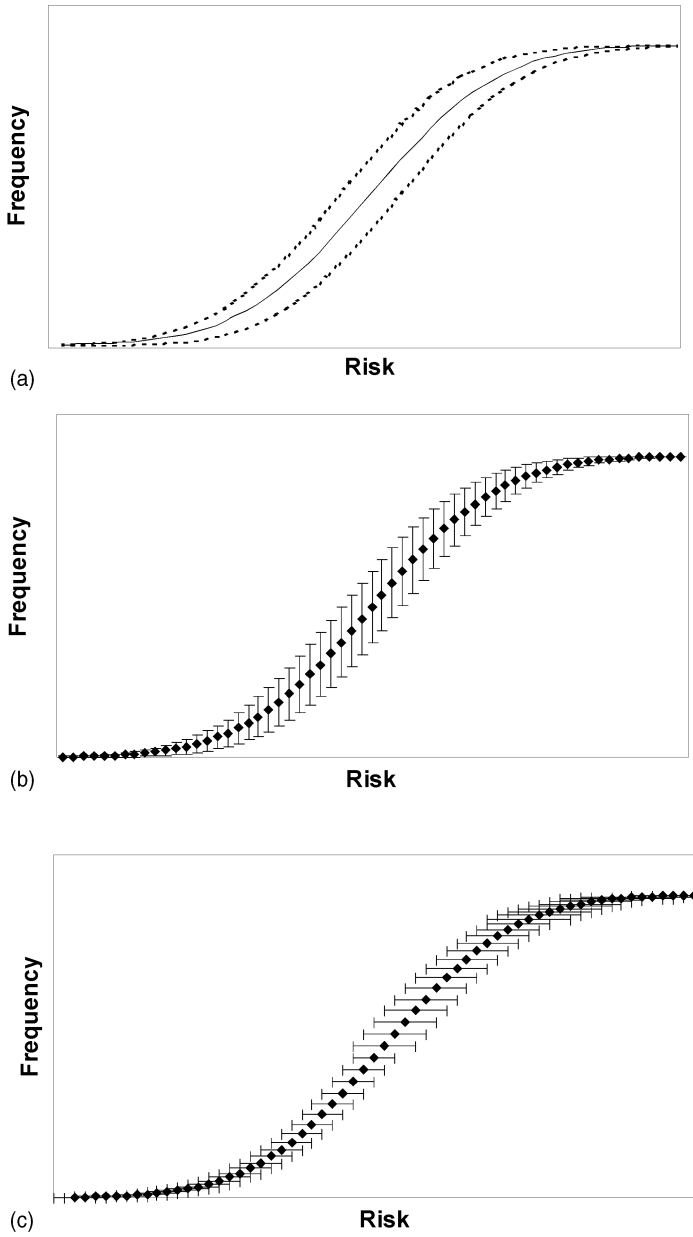


Fig. 7.2 Different interpretations of graphical confidence intervals: (a) ambiguous; (b) alternative 1; (c) alternative 2.

7.3.6 Validation

Voysey (2000) states that ‘it is essential to ensure that the results of the risk assessment accord with common sense and with experience’. Ideally the conclusions of the risk assessment should be validated against information which has not been used to produce the conclusions. The conclusions of the risk assessment result from a model, which may be mathematical but generally is at least partly conceptual or qualitative. It is well known that testing of a model against the information used to produce the model gives only weak confidence in the model’s validity. It is generally good practice to keep a validation ‘test set’ distinct from the ‘calibration set’ used to produce the model. In practice this is unlikely to be possible for MRA. The paucity of relevant information requires the use of all data which is available in producing the MRA conclusions, leaving none for validation purposes.

Independent third-party peer review of the MRA offers an alternative approach to validation. The difficulty of such review should not be underestimated. The authors of an MRA often become so involved that it is difficult for them to see where assumptions or preconceptions may limit the valid scope of their conclusions; the reviewer must be truly independent. The review must consider all the information, assumptions and models which lead to the conclusions. This requires a level and breadth of skill and knowledge similar to those of the MRA authors. Clearly, the review requires that the MRA is very well documented.

7.4 Quantitative and qualitative outputs

Although often couched in mathematical language the principles above apply equally strongly when the information being handled and the conclusions produced are non-numeric. In practice, MRAs and their risk characterisations are rarely either totally numeric (quantitative) or totally non-numeric (qualitative). Some aspects of the exposure assessment or risk characterisation will be blessed by good numeric data and validated mathematical models, others will suffer from lack of knowledge and understanding. Sometimes available quantitative data or tools may be consciously neglected as unjustified for the stated purposes of the MRA.

7.4.1 Qualitative outputs

The ultimate MRA output (as the discipline was originally conceived for governmental or regulatory agencies use at least), is a quantitative one. By definition, this necessitates all the information and data needed to draw up the risk characterisation to be numerical in nature. The reality of this will be discussed in more detail later in this chapter.

What has become very clear as the number of MRA’s being carried out has steadily increased, is that all the necessary data and information is very rarely if

ever solely in a quantitative format. This means that resources, including time, need to be expended to fill gaps in the quantitative data available, if it is possible to do so. As discussed earlier, quantitative information is not easy to come by in some critical areas. An important, if not the most important, example of this, is the area of dose-response. It is extremely difficult if not impossible to determine specific numbers of microorganisms that would need to be consumed by the population under consideration in a specific study, because of ethical issues. It is not likely that enough ‘volunteers’ of a target population could be found to consume pathogenic microorganisms in food, sufficient to make them extremely ill or even kill them!

This leaves the risk assessor with the option of carrying out an MRA with as much quantitative information and data as is available, and filling the gaps in with ‘expert opinion’ and/or qualitative material. This **semi-quantitative** MRA output will be discussed later. The other option open to the assessor is to use solely **qualitative** information and data to produce an output to the MRA.

The Codex Alimentarius Commission (Codex, 1999) defines qualitative risk assessment as:

A risk assessment based on data which, whilst forming an inadequate basis for numerical risk assessments, nonetheless, when conditioned by prior expert knowledge and identification of attendant uncertainties permits risk ranking or separation into descriptive categories of risk.

In simple terms, a qualitative risk assessment is ‘a risk assessment that cannot be expressed in a precise numerical format but can still be useful, particularly based on expert knowledge and expressed in terms of categories such as high, medium or low, or as risk comparisons’ (Mitchell, 2000). Whether this type of MRA can be used by government bodies or regulators depends on their purpose for carrying out the MRA. If it is to set food safety objectives, then probably not.

Studies at Campden and Chorleywood Food Research Association have found that a qualitative MRA output may certainly be adequate for industrial or manufacturers’ MRAs. For example, a company may be considering modifying an existing line to produce a ‘less risky’ product. Or, a company which can show that it can achieve a 20-day shelf life from an existing product, may wish to make a cheaper version of the product with only a 10-day shelf life. These **comparative** MRAs can be usefully performed with little if any quantitative data at all. Consequently the cost of resources for carrying them out will also be less. The output of this type of MRA will be severely lacking in detail, however it can be sufficiently useful to answer the original question posed and therefore of benefit.

The original format for a qualitative MRA was the ‘risk profile’ (see, for example, Voysey, 2000). This is a paper-based MRA where questions are asked to cover the aspects of the hazard identification, exposure assessment and hazard characterisation steps relevant to the pathogen, food and process being used. A series of tandem questions can be used to gauge the level of uncertainty associated with the answers given to the questions. The questions asked are designed to tease out all the information that is needed to make a judgement by

the performer of the risk profile. It can be useful if the performer of the risk profile considers how standard questions (such as those given in Voysey, 2000, for example), could be interpreted to meet the need of each set of circumstances. All relevant information and data required should be recorded for each question.

If the risk profiler is working at a conceptual stage in product development for example, it can be useful to use a general profile template, and answer the questions on a scale from 1 to 5, varying in severity. Although this exercise will be of limited use, it can be used as a starting point for more detailed consideration. Expert opinion is used extensively in this process. The risk characterisation step of a risk profile consists essentially of identifying the areas of the MRA where the answers suggest that the hazard could be a problem (i.e. lots of 5's) and where questions cannot be answered with any degree of confidence (i.e. high uncertainty).

The risk profile is a useful means for carrying out an 'outline MRA' before the proper MRA is carried out. It helps the practitioners to appreciate what information and data will be needed, to allow a proper MRA to be performed and indeed, to determine if there is a need to perform a full MRA study. Typical descriptors or outputs, which could be deduced from a qualitative MRA, are that the risk associated with this pathogen in the food is 'high', 'low' or 'negligible'.

7.4.2 Semi-quantitative outputs

Microbiological risk assessments need to be carried out with the most up to date and relevant information and data available. It is likely that in most situations where it is considered that an MRA is required, that there will not be some quantitative information available which could be useful to the MRA. In this circumstance, qualitative and quantitative inputs need to be combined in the MRA process. The output of such an MRA can be expected to have a more precise output than a qualitative MRA and less than a quantitative MRA.

7.4.3 Quantitative outputs

Codex (1999) defines a quantitative MRA as 'A risk assessment that provides numerical expressions of risk and indication of the attendant uncertainties.' While the representation in Fig. 7.1 is intended to include qualitative and semi-quantitative relationships (e.g. heating reduces contamination levels), a quantitative risk assessment requires these relationships to be expressed numerically (e.g. equation 7.2).

$$N_T = N_0 10^{-t/D}$$

$$D = D_R 10^{(T_R - T)/z} \quad 7.2$$

where:

N_T = contamination level after heating for time t at temperature T

N_0 = initial contamination level

D_R = decimal reduction time at the reference temperature, T_R
 (a characteristic of the pathogen)
 z = a characteristic of the pathogen

A typical MRA involves many such interacting relationships and the only practical means of representing, linking and calculating them is on a computer.

Spreadsheet programs make it easy to develop, link and visualise relationships. However spreadsheet models may evolve rather than be designed, leading to unforeseen relationships and interactions, and can be difficult to document and validate. Guidance on avoiding these problems is available and should be followed, (Read and Batson, 1999). Other computer programs allow the iterative definition of series of functions, one in terms of the other. These environments make formal design and documentation a more natural part of the model-building process but require more experience in their use and are generally only used by specialists.

However it is undertaken, the results of this initial stage of model building are models, often called 'deterministic' models, which produce single outputs from single sets of input values. If all the input factors (e.g. N_0 , T and t in equation 7.2) had no variability, and those factor values, the model (e.g. the form of equation 7.2), and the model parameters (e.g. D_R and z in equation 7.2) had no uncertainty, then the resultant risk could be calculated from the deterministic model and would have no variability or uncertainty. This is not the case for any realistic risk assessment. Variability in the input factors results in variability in risk. Uncertainty in the parameters describing the variable input factors, in the nature of the models and their parameters, results in uncertainty in the parameters describing the variable risk. Variability and uncertainty, usually represented as frequency distributions, must be added to the deterministic model to produce a model, often called a 'stochastic' model, which gives risk distributions from input distributions.

In principle, if the deterministic model was very simple and the input distributions were amenable, it would be possible to deduce the output distribution algebraically. In practice this is not possible for real situations.

Monte Carlo modelling

The most common approach is Monte Carlo modelling which provides a frequency distribution of the output by making many deterministic calculations, known as iterations. At each iteration a single random value is generated for each of the stochastic inputs and parameters, resulting in a single calculated risk. If the distribution of randomly generated input values is appropriate then the distribution of calculated values represents the distribution of risk. There are a number of computer software packages dedicated to Monte Carlo modelling (e.g. @Risk, Palisade Corporation; Crystal Ball, Decisioneering, Inc.) or it may be implemented in any of several statistical packages by those expert in their use. Although Monte Carlo modelling is relatively simple to understand and implement and is by far the most widely used technique, it is not without its dangers.

The validity of the output distribution (risk) depends entirely on the validity of the input distributions. Vose (2000) presents a 'cardinal rule', 'Every iteration of a risk analysis model must be a scenario that could physically occur'. The distributions representing the inputs must be realistic. 'However, experience indicates that what is important is to choose distributions based on properties such as whether the distribution is skewed or symmetric, if it should be truncated or not, and whether extreme values should be allowed' (Smith, 2002). It is important to include correlations between the input values. Failure to do so may break Vose's cardinal rule as input values are used which are feasible individually but not in combination. This applies to all stochastic elements, uncertain parameters as well as variable factors. It is important that sampled input values cover a wide range of the input values. For simple random sampling this can require a great number of iterations. 'Latin Hypercube Sampling' is the most common approach to achieve a wide spread of random values representing the chosen distribution.

Separating uncertainty and variability can be burdensome. The most common approach is 'second order simulation'. One set of distributions describes the uncertainty in model parameters and estimated values, a second set of distributions represent variability. A single simulation uses one set of values sampled from the uncertainty distributions and many samples of the variability distributions to produce a result incorporating variability without uncertainty. Multiple simulations are run, each with a fresh sample from the uncertainty distributions, producing an uncertainty distribution of results. This is conceptually simple and can be straightforward to implement, especially with Crystal Ball. However, a single simulation often requires many iterations to produce an adequate representation of variability. A second order simulation dramatically increases the time required and is often performed with relatively few simulations, limiting the reliability of the uncertainty estimates.

It can be difficult to represent variability and uncertainty in categorical values, especially in choices such as model selection. The many numbers and graphs resulting from a typical Monte Carlo simulation can give a misleading impression of precision and a temptation to ignore sources of variability and uncertainty which have not been explicitly and quantitatively included in the model. It is important that the conclusions are considered and expressed with due regard to all sources of uncertainty, including those in the underlying assumptions. The reported risk estimate should be accompanied by an indication of 'the dispersion of the values that could reasonably be attributed to the estimated value'.

Other approaches

Although Monte Carlo modelling is by far the most common means of including variability and uncertainty in a model there are others, albeit as yet rarely used except in theory or demonstration. As mentioned above, classical statistics and algebra are impractical for all except the simplest problems. However they do give rapid, reliable conclusions and they should be used when possible, even

within a Monte Carlo simulation. If a part of a model can be solved and represented algebraically within a simulation, then this should be done.

The Bayesian approach to statistics, in which information modifies a 'prior distribution' to generate a 'posterior distribution', is becoming a more popular approach to combining qualitative or semi-quantitative expert opinion with data. There can be substantial conflict between proponents of classical and Bayesian approaches to statistics, often relating to the meaning of the fundamental term 'probability'. The authors of this chapter do not take a position in this conflict, regarding classical and Bayesian approaches as complementary, each with their own advantages and appropriate in different circumstances. Where possible we avoid the contentious issues, preferring to use the terms 'frequency', 'relative frequency' and 'confidence' where these are more appropriate than 'probability'.

Techniques such as expert systems and neural networks are also being adapted to the incorporation of expert opinion into stochastic models, see for example (Barker, 2000). However they have not yet been used in major, published MRAs and their application to MRA must be regarded as 'work under development', whose potential is not yet proven.

7.5 Risk characterisation in practice: some examples

When chemists consider the risk characterisation step, they identify two different approaches. The first of these is adopted when the nature of the hazard and the dose-response data indicate the existence of a threshold. In this case a 'safety evaluation' is carried out and the risk characterisation is used to determine risk relative to parameters such as the acceptable daily intake (ADI) of the chemical. The second alternative relates to toxic effects that appear not to be thresholded, or where the existence of a threshold cannot be assumed. In this case, the risk characterisation may take the form of a quantitative risk assessment (Walker, 2000). This second approach is similar to that taken for the risk characterisation step in MRA.

With the advent of the Codex Alimentarius papers on risk assessment, there is a much more structured and universally accepted format for the undertaking of risk characterisation. In particular, the issues of sensitivity and variability are being addressed more thoroughly, thus allowing higher levels of confidence in the analysis of various mitigation strategies for reduction of pathogens at different stages of the food chain. The series of FDA/USDA risk assessments (e.g. *Salmonella* in eggs, *Vibrio parahaemolyticus* in shellfish, *E. coli* in ground beef and *Listeria* in various ready to eat foods) are extensive studies and indicate both the breadth and depth of investigation which may be necessary to 'accurately' estimate risk. In the following section some key features are highlighted for a small number of risk assessments which have recently been published.

7.5.1 Study 1: Risk assessment to public health from foodborne *Listeria monocytogenes* among selected categories of ready-to-eat foods (US DHHS/USDA, 2001)

In this study, the risk assessment linked the probability of exposure to *Listeria monocytogenes* from the consumption of food in 20 food categories with adverse health outcomes. The primary focus was on a prediction of relative probability of contracting listeriosis from the consumption of a single serving of food in one of the 20 food categories. Additional predictions considered the extent of the annual consumption of various foods and the predicted contribution of each of the individual food categories to the number of listeriosis cases nationally. The study was based on contaminated foods at retail level and included both sporadic and outbreak cases.

This study, right at the start of the risk characterisation process, importantly considers the limitations of modelling. In particular, because listeriosis is such a rare event, straight Monte-Carlo modelling was unable to provide adequate characteristics with the tails of the distribution in the model. The risk characterisation was developed in two stages. Firstly a simulation on exposure assessment calculations that produced the number of annual servings for each of three sub-populations (perinatal, elderly and intermediate age) at designated dose levels for each food category. This included population variability and uncertainty due to lack of information. The second step calculated predictions of the relative risk of listeriosis to each sub population from each food category. Previous work has focused on highly virulent strains in a single population group. By including human susceptibility variation and pathogen virulence variability there is a substantial reduction in risk estimation associated with a particular dose. The study recognises that most exposures to *L. monocytogenes* are unlikely to result in listeriosis, even among highly susceptible segments of the population.

The study showed substantial differences in risk among the different food categories. For example the median predicted relative risk between pâté and meat spreads and ice cream and frozen dairy products differs by almost a million-fold. The 5th and 95th percentile values were calculated for the three sub-populations thus enabling an estimation of the variability and uncertainty. It is recognised that five key factors had a profound influence on the results of the exposure assessment and the subsequent risk characterisation including storage before consumption. This study also recognised that data on actual consumer storage practices were not available and data was therefore based on expert judgement and USDA recommended practices. In reality, it is likely that actual consumer storage times of food are longer than USDA recommendations. In most cases, foods with a high risk based on servings had a high risk based on a per annual consumption basis but this was not always the case. For example, risk of illness with vegetables and pasteurised fluid milk was relatively low on a per serving but higher on a per annum basis.

7.5.2 Study 2: Draft risk assessment on the public health impact of *Vibrio parahaemolyticus* in raw molluscan shellfish (USFDA, 2001)

This study describes the probability of illness caused by consumption of oysters harbouring pathogen *V. parahaemolyticus*. The study was divided into three modules, harvest, post harvest and public health. In the harvest module, salinity was not considered an important variable and the module was therefore based solely on water temperature. The post harvest module addressed the simulation of oyster handling practices and effects of various mitigations. The public health module looked at the destruction of potential illness in different regions and seasons. The post harvest mitigation strategies investigated were

- mild heat treated (5 min at 50°C),
- freezing (-30°C) and
- rapid cooling immediately following harvest.

All three had a substantial effect on the distribution of the probable number of illnesses. The effect of mild heat treatment was found to reduce the mean risk of illness per serving to susceptibility to less than 1 in 100,000.

FDA had advised that *V. parahaemolyticus* in shellfish should not exceed a level of 10,000 viable cells per gram. This risk assessment did allow the workers to address the question of what would be the predicted impact on the incidence of disease if one could exclude oysters at the time of harvest that had a certain level of *V. parahaemolyticus* in the Louisiana Gulf Coast summer harvest. The simulation results suggest that 15% of illness are associated with consumption of oysters that contain greater than 10^4 *V. parahaemolyticus* per gram at time of harvest. The corresponding fraction containing greater than 10^4 per g was 5%. Therefore, a large proportion of the harvest contains lower numbers, but a significant associated level of risk.

Additional simulations were performed to examine the effect of uncertainty and variability parameters on the variance of the distribution of illnesses obtained by simulation. The influences of three parameters were examined:

1. relative growth of *V. parahaemolyticus* in oysters versus broth model
2. combination of variability and uncertainty in the overall percentage of *V. parahaemolyticus* that is pathogenic; and
3. variation of water temperature.

These three factors are considered to account for approximately 45% of the total variation in risk per serving. Individually, the uncertainty in growth rate proportionality and percentage pathogenic account for 26% and 12% of the total variation respectively. Water temperature, which is variable, accounts for 22% of total variation. Thus of all factors, the variation would be reduced most by additional information on growth in oysters versus broth. An additional and important source of uncertainty associated with the predicted distribution of illness is that associated with the extrapolation from illness in feeding trials.

7.5.3 Study 3: *Salmonella enteritidis* risk assessment: shell eggs and egg products (USDA, 1998)

The first major formal risk assessment undertaken in the USA was a very large study. The work programme commenced in 1996 in response to the increasing number of illnesses associated with the consumption of shell eggs. The risk assessment model consisted of five modules, egg production (estimating number of eggs infected with *Salmonella Enteritidis*), the shell egg module, the egg products module, the preparation and consumption module and the public health module. The latter calculated the incidents of illnesses associated with four degrees of clinical outcome, recovery without treatment, recovery with treatment, hospitalisation and mortality. The baseline model for shell eggs simulated an average production of 46.8 billion shell eggs per year in the US, 2.3 million of which with *Salmonella Enteritidis*, resulting in 661,633 human illnesses per year. The study then examined mitigation elasticity which is a measure of how changes in module variability affect model outputs. It was observed that combinations of mitigations may potentially be more effective in reducing total human illnesses. Each of the 5 modules was subjected to a sensitivity analysis.

7.5.4 Study 4: Quantitative microbiological risk assessment: principles applied to determining the comparative risk of Salmonellosis from chicken products (Brown *et al.*, 1998)

In this paper models were constructed in accord with Codex Alimentarius principles, to provide a quantitative risk assessment (QRA) of Salmonellosis from frozen poultry products. The QRA addressed three types of information: occurrence and distribution of *Salmonella*, sensitivity of populations to infection and the effect of cooking (in the factory or home) on levels of *Salmonella* and hence the risk of infection. The paper contains interesting data on the issues associated with thermal inactivation and heat transfer. The models compute the chance of infection from a chicken portion (possibly contaminated with Salmonellae), subjected to a specified heat treatment and ingested by an individual who may be sensitive. The program allows users to produce risk estimates without extensive data on the dose response within populations. A facility has been built into the program to find the value of a chosen variable that gives rise to n people per million units at risk of infection. The authors discuss the issues associated with statistical sensitivity and the implications for risk estimates.

7.5.5 Study 5: Quantitative risk assessment for *Escherichia coli* O157:H7 in ground beef hamburgers (Cassin *et al.*, 1998)

The authors introduce the term process risk model (PRM) for the integration and application of QRA methodology with scenario analysis and predictive microbiology to provide an objective assessment of the hygienic characteristics of a

manufacturing process. In the PRM, one submodel described the behaviour of *Escherichia coli* O157:H7 throughout the production, handling and consumption chains. The second submodel is a dose-response model to estimate illness risk. Monte Carlo simulation was used to assess the effect of the uncertainty and variability in the model parameters on the predicted human health risk. The model predicted probability of haemolytic uremic syndrome and mortality. The efficacy of three mitigation strategies were also explored. The authors give a very clear account of importance analysis, i.e. examining the sensitivity of an outcome to a factor and the uncertainty and variability associated with that factor.

7.6 Current problems and future trends

Inasmuch as the risk characterisation synthesises the results of previous stages its problems and future reflect those of the previous stages. Many of the problems arise because MRA is a new and rapidly developing discipline. Practitioners have limited experience, in years and in range of technique and application. While a consensus is building on fundamental principles and terminology, helped by the Codex document (1999), this is not yet complete. It is to be hoped and expected that more formal definitions will be laid down and widely accepted, reducing misunderstandings between practitioners and confusion of audiences.

Increased experience of MRAs by those audiences, the ‘customers’ of the risk analyst, will increase their understanding of the process and conclusions and reduce pressure on the risk analyst to use approaches, such as worst case assumptions and the ‘precautionary principle’, which are incompatible with MRA as presented here. We will not discuss such approaches here except to note the Codex principle that ‘There should be a functional separation between Risk Assessment and Risk Management’, and that risk assessment estimates the frequency, not the possibility, of harm.

MRA was developed and has predominantly been applied for governmental purposes. It is already clear that the techniques typically used for governmental MRAs, when regarded as a ‘toolbox’ to be adapted to the situation, can help achieve industrial objectives. However, the relevance and relative importance of different philosophies and techniques to different circumstances will only become evident over time and no doubt specific tools will be developed.

One factor distinguishing governmental and industrial MRAs is their scope. Typically a governmental scope is very broad both in terms of product, covering a generic product group, and the food chain, from farm to fork. An industrial scope is much narrower, commonly restricted to a single brand, or even a single production line, and often concentrating on that part of the chain under the control of the company. The reduced scope has benefits and disadvantages. The range of variability to be considered is much reduced, especially in categorical

rather than numerical factors such as processing method, resulting in reduced model complexity and uncertainty. There is often substantial directly relevant monitoring data available reducing the uncertainty in estimating values, and in extrapolating from the samples measured to the population considered by the MRA. However, the limited scope reduces the extent to which the conclusions of the MRA can be applied. This reduces the value of the MRA, and thus the resource which can be justified. There is a balance between, on the one hand, ambitious objectives and wide scope leading to wide applicability but high uncertainty and, on the other hand, tight objectives and a narrow scope leading to narrow applicability but increased precision. It is not yet clear which industrial objectives can be reasonably achieved at what cost. This hampers the cost benefit analysis which, at least informally, precedes any MRA. Once again, experience will clarify the objectives and appropriate scopes which can be achieved cost effectively and within time scales appropriate to industry.

Turning from the purpose of the MRA to the information collection and synthesis stages, the principal problem is undoubtedly the quantity, quality and relevance of the information. Most of the scientific data used in MRAs has not been produced with MRAs in mind. As MRAs become more important it is to be expected that data, especially that from government funded work and including that not produced directly for MRAs, will be more suitable for MRA use. There are already initiatives to build collections of information and other resources so that they are readily available to MRA practitioners.

Much of the available and relevant information is, and will remain, non-numeric, qualitative, expert opinion. Such information is not easily handled by Monte Carlo simulation, at least not with appropriate handling of uncertainty and variability. The techniques referred to above and others should be developed into practical tools which can be combined with each other and Monte Carlo simulation to give a broad range of flexible tools capable of handling and synthesising 'fuzzy' as well as numeric information.

MRA is often constrained by the limits of scientific knowledge, especially on the behaviour of pathogens and the mechanism of infection and disease processes. Progress on such fundamental issues will be slow, but MRA must be ready to incorporate new knowledge as it becomes available. The requirement for MRA to use the most current information and understanding will militate against the re-use of MRA modules. The limited number of complete MRAs performed to date have generally been independent of each other. Although each has been modular in itself the modules have not been directly compatible between MRAs. This is likely to remain the case for some time. The number of extant MRAs is so small, and information and techniques available are developing so rapidly, that it is generally inappropriate to re-use major portions without careful consideration, and probably substantial modification. Nevertheless, prior MRAs are already easing and accelerating the production of later MRAs, and this trend can be expected to continue.

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8

Risk communication

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8.1 Introduction

Communication is one of the most basic of human activities, yet so often it goes wrong. Experts can feel exasperated when non-experts (i.e. consumers, the food industry and politicians) fail to understand expert pronouncements on food safety risks and consequently fail to follow expert advice on the proper practices needed to eliminate or mitigate those risks. They feel that non-experts are at fault because they are technically illiterate. Their solution is that more and better education is needed. On the other hand non-experts are equally frustrated when experts (i.e. public health professionals and scientists) apparently fail to see their point of view and come up with what appears to them as ludicrous and patronising advice. They feel that experts need to get out more and live in the real world. Clearly, there is a wide gulf between these opposing points of view. Something is needed to bridge this gap. The answer is risk communication.

Expressed in simple terms, risk communication is the two-way exchange of information and opinions on how the risks have been assessed and can be managed (Mitchell, 2000). In technical terms, it was defined by the Codex Alimentarius Commission as 'an interactive exchange of information and opinions concerning risk among risk assessors, risk managers, consumers and other interested parties' (FAO/WHO, 1997). However, the perception of 'risk' is heavily influenced by a range of 'outrage factors' that can trigger in people psychological responses that may be out of step with the risk expressed in purely technical terms (Section 8.4.2).

Accordingly, a FAO/WHO Expert Consultation on the Application of Risk Communication to Food Standards and Safety Matters (1998) recommended that

the Codex definition should be modified by inserting the words ‘and risk-related factors’ so that the definition would read

Risk communication is the exchange of information and opinions concerning risk and risk-related factors among risk assessors, risk managers, consumers and other interested parties.

8.2 The concept of risk

Almost every aspect of human existence carries with it an element of risk. In order to survive, human beings need to assess each risk, decide whether or not it is acceptable and develop strategies for managing it.

An understanding of risk communication is predicated by an understanding of the concept of risk itself, not least because the concept of risk encompasses a large element of human psychological responses and because non-experts often perceive risks in ways very different from experts.

8.2.1 Different uses of the word risk

The first barrier to effective risk communication is that the term ‘risk’ can take on a variety of very different meanings. There are a number of ways in which this can lead to confusion:

- To many experts risk means ‘probability’; to others it means ‘severity of the hazard (harm)’; to others it is a combination of the ‘probability and severity’ together.
- Some languages do not discriminate between ‘hazard’ and ‘risk’. For example, in French the same word ‘*hasard*’ can cover both terms, and in German they have both been translated as ‘*risiko*’.
- The context of the term ‘risk’ is heavily qualified by the terms that precede or succeed it. Precedent terms include, for example, ‘relative’, ‘acceptable’, ‘high’ and ‘low’, each of which imbues a very different meaning to the context. Similarly, successor qualifying terms include ‘factor’, ‘assessment’, ‘analysis’, ‘management’, ‘communication’, ‘averse’, ‘perception’, ‘ratio’ and ‘behaviour’.
- The hazard component referred to can vary. For example, it can refer to ‘risk of illness’, ‘risk of illness per thousand servings of a product’, ‘risk of illness per hundred thousand of the population’ or the ‘risk of loss of business or loss of sales’.
- The meaning of ‘risk’ changes depending on who is affected by it. It can be the risk ‘to me’, ‘to the population as a whole’, ‘to vulnerable groups within that population’ or as before ‘to my business’.

The key to overcoming this particular barrier is to be very specific. For successful risk communication it is vital to be quite detailed when describing

risks, almost to the extent of using, where appropriate, statements in the form of: the risk 'of what' to 'whom'. This should avoid many of the arguments about risk that are caused by an incomplete description of risk.

8.2.2 Technical expression of risk

Historically, experts have tended to think of risk purely in terms of the probability of an adverse event happening. (This was very much true in relation to risk management strategies like the hazard analysis and critical control point (HACCP) system where the resulting harm was described as the hazard.) The Codex Alimentarius Commission now 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' (Codex Alimentarius Commission, 1998). However, it can be argued that the general population, and sometimes experts, do not truly understand probability.

Probability can be defined as 'the number of desired outcomes divided by the number of all possible outcomes'. However, this can be of limited meaning in determining the public's behaviour. A simple example is the UK National Lottery where one has to select 6 balls from a combination of 49. There is only one combination in any draw whereby these 6 balls will be chosen, the probability of which is 1 in 14 million. To put this probability into context, if you spent £50 a week on the lottery, then you could expect to win the jackpot by matching 6 balls roughly once in 5000 years. Further details on the behaviour of the public in relation to probability and lotteries across the world are available from Haigh (1999).

The failure of the general public and experts to understand even simple probabilities is one of the many factors that promote misunderstanding between perceptions, estimates or communication of risk between experts and the general public.

Table 8.1 is taken from Morris and Bate (1999). It shows the risk of dying from a variety of causes. Tables such as this can be attractive and have often been used by experts to communicate risk to the public at large. However, their practical usefulness is limited because the public experience difficulty in interpreting them in context. Very few people have been struck by lightning so how can the rest of the population use this as a measure of their chances of being infected by salmonella from poultry?

Historically, expert thinking on how to communicate risks has been somewhat outdated and ineffective. It appears that many food safety experts seem to think that all they have to do is (Fischhoff, 1995):

- Get the numbers right.
- Inform the public of the numbers.
- Explain what we mean by the numbers.
- Show them that they have accepted similar risks in the past.
- Show them that it is a good deal for them.

Table 8.1 The numerical risk of dying from various causes

Cause of death	Risk of dying
Smoking 10 cigarettes a day	1 in 200
All natural causes age 40	1 in 850
Violence or poisoning	1 in 3300
Influenza	1 in 5000
Accident on the road	1 in 8000
Accident at home	1 in 26 000
Accident at work	1 in 43 500
Radiation working in radiation industry	1 in 57 000
Homicide	1 in 100 000
Salmonella infection from poultry	1 in 5 000 000
Struck by lightning	1 in 10 000 000
Nuclear power station radiation leak	1 in 10 000 000
Beef on the bone	1 in 1 000 000 000

- Treat them nice.
- Make them partners.

This attitude is patronising, relies heavily on numerical estimations of risk and will fail to work in light of the outrage factors outlined below.

An appreciation of how the general public understands, or fails to understand, risk and probability is absolutely critical to successful policy-making by government and experts in terms of how they should anticipate the public response to hazards and risks. Furthermore, this awareness is critical to improving risk communication between experts, lay people and the decision makers. Without this understanding the best efforts of experts and government will fail.

8.3 Risk perception

People's attitudes to risks are determined by more than numerical expressions of probability alone. Risk is not just about science. There is a human factor. In other words, human psychology plays a fundamental role.

8.3.1 The human element and outrage factors

Human beings are not machines. They do not process information like computers but are subject to emotions and other psychological influences. Not surprisingly their perception of risk is heavily motivated by these psychological factors. The consequences for risk communication are enormous. Various psychological techniques have shown how the general public perceives risks. Studies have shown that the public's reaction to any given risk can be motivated, just as much if not more, by these emotional reactions than by the particular

hazard (in terms of severity and probability) associated with that risk (e.g. Fife-Shaw and Rowe, 1996). Indeed some authors (Sandman *et al.*, 1993) express this in the equation:

$$\text{Risk} = \text{hazard} + \text{outrage}$$

No matter how serious the risk (in technical terms) and no matter how much technical detail is used to explain it, it is the degree of outrage that will determine much of the public's response to the risk. Psychological studies have shown that there are number of outrage factors:

1. **Choice.** Is the risk voluntary? Some authors have expressed this crudely as the difference between skiing and being pushed down a mountain with two planks of wood attached to one's feet – the risk is the same but reaction is markedly different depending on whether or not one has chosen to participate. In food terms, an example would be that consumers in the UK apparently prefer to be exposed to the quantifiable and demonstrable risks associated with pathogens in raw milk than to the as yet unquantifiable risks associated with genetically modified (GM) foods.
2. **Control.** Arguably, the driver and passengers in a car are exposed to the same risk yet the driver is more comfortable by virtue of feeling in control. It can be argued that consumers are more willing to accept the presence of salmonella in poultry because they have the potential to cook and handle the product in such a way as to negate the risk associated with it. They do not feel such control with GM foods.
3. **Fairness.** People are more willing to accept risks if they perceive that everybody is equally affected by them. Press reports about GM foods having been banned by the caterers supplying Monsanto, the UK Houses of Parliament and the European Parliament can have done little to reassure the public at large (BBC, 1999).
4. **Trust.** Is the organisation responsible for managing the risk trustworthy? Trust is multidimensional and appears to be linked with perceptions of accuracy, knowledge and concern for public welfare (Frewer *et al.*, 1996). In the UK public trust in the Ministry of Agriculture Fisheries and Food and to some extent the Department of Health was seriously eroded by the bovine spongiform encephalopathy (BSE) crisis. Largely as a counter to this, the Food Standards Agency (FSA) was set up as an independent food safety watchdog to protect the public's health and consumer interests in relation to food. The FSA has been working hard to ensure that it is the UK's most reliable source of advice and information about food. To this end the FSA's guiding principles are: putting consumers first; being open and accessible; and being independent.
5. **Morality.** Is the risk moral? To many people, including Prince Charles, GM foods are immoral in the sense that the associated manipulation of genetic material is tantamount to playing God with these foods.
6. **Familiarity.** People are more comfortable with those risks that they have

lived with from day-to-day than those which they feel they know nothing about. A recent survey of consumer attitudes (FSA, 2001) revealed that, despite concern about hygiene standards in takeaways and fast-food outlets, two-thirds of people in the UK visit them on an occasional or regular basis.

7. **Memorability.** Does the risk stick in the mind? Health scares in general, and food scares in particular, can be remarkably memorable. Emotive newspaper headlines such as '*Listeria* hysteria' and 'Frankenstein foods' are designed to attract attention and are unforgettable.
8. **Catastrophe.** Outrage is elicited where a large group of people are affected at the same time in the same place. Train and aeroplane crashes receive much prominence even though the deaths associated with them are rarer and fewer compared to the daily death toll on the roads. Each year in England and Wales there are more than three times as many laboratory-reported cases of human infection due to campylobacter than salmonella. However, the fact that the salmonella cases tend to be clustered around groups of people, a specific restaurant or a specific event means that this organism attracts more attention than campylobacter, where the vast majority of cases are sporadic.
9. **Dread.** How terrifying is the risk? Emotive phrases such as 'mad cow disease' or 'Frankenstein foods' can very easily induce fear in the minds of the general public.
10. **Benefits.** It is a fundamental truism that we are happy to take risks if we perceive some benefit from doing so. Consumers expect food that is cheaper, tastier or more nutritious. It appears that they are more willing to accept risks with products with these attributes.
11. **Impact on vulnerable groups.** Risks that impact on vulnerable members of society, such as the young, the elderly or pregnant women, are much less acceptable. Exposing children to the risks from verotoxigenic *E. coli* O157 is very likely to induce outrage among the general public, particularly when images of children being treated by kidney dialysis or life support equipment are involved.

In total, up to 47 outrage factors have been identified (Covello and Merkhofer, 1994). These include:

- Public understanding of the risks.
- Whether or not scientists actually understand the risks involved.
- Whether or not scientists can state them clearly to the public.
- Media attention.
- Whether or not the risk can be reversed.
- Whether someone could be blamed or identified as being at fault.

Outrage factors are more complex than this sequential one-dimensional list suggests. Psychologists have used psychometric techniques to determine people's responses to combinations of outrage factors. One approach is the factor-analytic representation shown in Fig. 8.1. It depicts the results obtained when peoples'

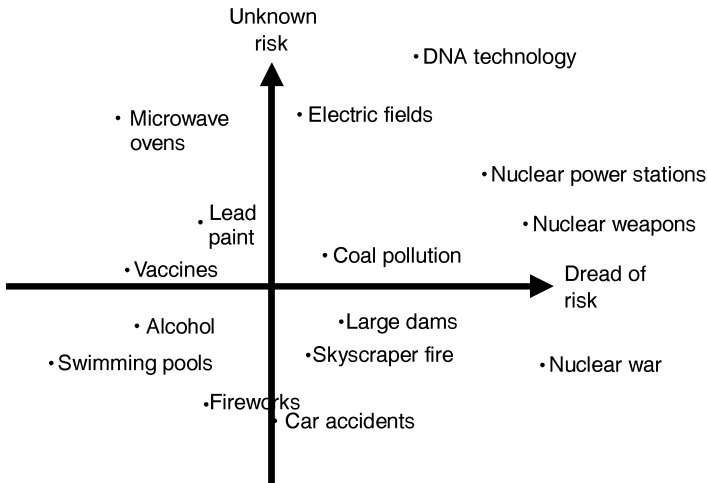


Fig. 8.1 Risk factor analysis for general risks. (After Slovic, 1987.)

responses to dread factors and unknown risks are represented on a two-dimensional basis (Slovic, 1987). Dread factors are a measure of whether or not the risks are controllable, global, catastrophic, of high risk to future generations or involuntary. Unknown risks are those that are not observable, are not recognised by those affected, have delayed effect, are new or are unknown to science.

Risk factors that have the greatest effect on the general public such as nuclear power stations and DNA technology appear in the top right hand corner of the graph. These are rated highest in terms of both dread factor and unknown risk and are also those that people feel most require government intervention. In contrast the opposite corner consists of those factors that are demonstrably more risky in terms of death or illness but are relatively known and dreaded less. Thus, the general public appears to be much less concerned about the consumption of alcohol or the use of swimming pools even though they are palpably more risky. An equivalent study carried out on food related risks in the UK by Sparks and Shepherd (1994) found a markedly similar picture (Fig. 8.2). Fife-Shaw and Rowe (1996) report comparable results. In the light of the results, public fears about GM foods and food irradiation are perhaps unsurprising.

8.3.2 Expert perception versus public perception

A fundamental explanation for 'risk mis-communication' is the evidence that suggests experts and non-experts can perceive the same risk in vastly different ways.

Studies of 'expressed preferences' have shown that perceived risk is quantifiable and predictable. Table 8.2, derived from Slovic (1987), shows the results when various groups of people were asked to rank up to 30 hazards in terms of their 'riskiness'. An activity with a score of 1 was perceived by that

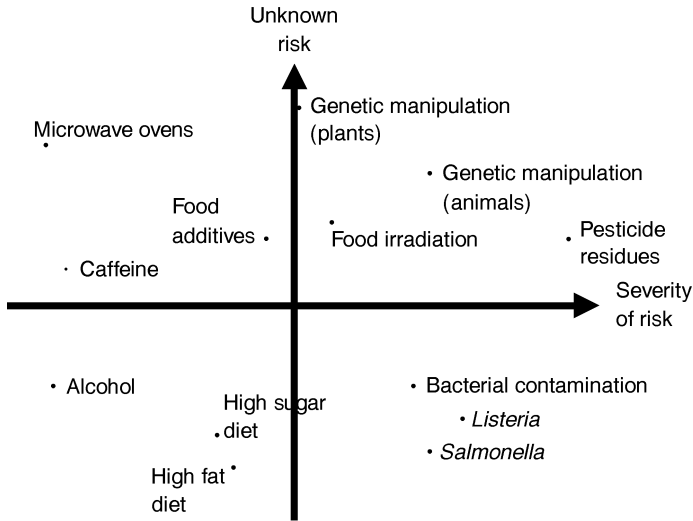


Fig. 8.2 Risk factor analysis for food risks. (After Sparks and Shepherd, 1994.)

group as being the ‘most risky’ while a score of 30 was seen as being the ‘least risky’. Students were used as examples of the general public; activity club members were used as examples of those people who would either participate in a particular activity or use the technology associated with it; experts were used as examples of the experts. Not all the answers are shown here but it is clear that each of the different groups rated the various hazards in a markedly different manner. For example, students ranked nuclear power as being the most risky activity whereas the experts gave this the lowly ranking of 20.

Further evidence for this risk-perception dichotomy is obtained when the factor-analytic representations shown in Figs 8.1 and 8.2 are recalculated and redrawn: the responses of experts are vastly different from those of non-experts (Slovic, 1987; Sparks and Shepherd, 1994; Fife-Shaw and Rowe, 1996). For example, whereas the general public tend to consider risks like nuclear power stations or food irradiation to be ‘unknown and severe’, placing them in the top right hand quadrant, experts tend to consider such risks to be ‘known’ (perhaps

Table 8.2 Risk ranking by different social groups (1 = highest risk)

Activity or technology	Students	Club members	Experts
Nuclear power	1	8	20
Motor vehicles	5	3	1
Handguns	2	1	4
Smoking	3	4	2
Motorcycles	6	2	6
Alcoholic beverages	7	5	3
General aviation	15	11	12

not surprisingly) and less ‘severe’, placing them more towards the bottom left hand quadrant. Further, experts tend to consider quantifiable risks like alcohol or a high sugar diet to be more ‘severe’ and place them further to the right hand side of the representation than do the public at large.

Psychometric studies such as these explain why the risks from technologies such as GM foods can elicit differing reactions from experts compared with the general public and why the general public is so concerned with such risks. They highlight the tremendous scope for confusion and misunderstanding if experts do not recognise and appreciate that the general public can perceive risks in a different manner. Many issues and many problems in risk communication, not just in food safety, stem from this dichotomy in perception.

8.4 The concept of communication

The *Oxford English Dictionary* defines communication as ‘the imparting or exchanging of information by speaking, writing or by using some other medium’. In the context of risk communication, perhaps a more useful definition is ‘The two way process whereby one party exchanges a message, idea, action or intention to another’ (Mitchell, 2000).

The three components of communication are: the audience with whom one wishes to communicate; the message one wishes to impart; and the medium by which it is conveyed. Communication is a two-way process. As such, it will fail unless it determines the needs of the audience, adjusts the message to reflect those needs, and then confirms that the correct message has been received.

8.4.1 The audience

Consumers and other customers are sensible. They know, often by intuition, when they are being talked down to, patronised or lied to. Nevertheless, some experts wittingly or unwittingly still try to pull the wool over their eyes. The Food and Nutrition Alliance has published a list of warning signs that consumers should look for when evaluating claims made about foods and food safety. These are the ‘10 Red Flags of Junk Science’ that should immediately raise suspicions about any food safety or risk communication claims (Bruhn, 1998):

- Recommendations that promise a quick fix.
- Dire warnings of danger from a single product or regimen.
- Claims that sound too good to be true.
- Simplistic conclusions drawn from a complex study.
- Recommendations based on a single study.
- Dramatic statements that are refuted by reputable scientific organisations.
- Lists of ‘good’ and ‘bad’ foods.
- Recommendations made to help sell a product.
- Recommendations based on studies published without peer review.

- Recommendations from studies that ignore differences among individuals or groups.

8.4.2 Different types of audience

Risk communication is complicated by the fact that ‘the audience’ does not comprise one homogeneous group whose members would all receive ‘the message’ in the same way. Different groups within a population (e.g. health practitioners or parents or the elderly) can have different information needs. Consequently within the same risk communication strategy it may be necessary to deliver different messages targeted at each population subgroup. The social context within which messages are received is also crucial. For example, people of a lower socio-economic status tend to receive health information from a few, local community-based sources (National Research Council, 2001). Almost any criterion that can be used to divide up the population can produce subgroups that might perceive risk messages differently and will therefore need to be taken into account, e.g. gender, age, health status or ethnic background (Fischhoff and Downs, 1997; Breakwell, 2000).

Further, psychologists have identified at least four different types of people, each of whom perceives risks differently and as a consequence will react differently to the same risk message.

1. **Egalitarians.** This group perceives the balance of nature as fragile, distrust expertise and strongly favour public participation in decisions.
2. **Individualists.** Such people see nature as robust and want to make their own decisions.
3. **Hierarchists.** These see nature as ‘robust within limits’ and want well-established rules and procedures to regulate risks.
4. **Fatalists.** These see life as capricious and attempts at control as futile.

Rarely will any risk communication exercise be aimed at any of these groups individually. Any risk message aimed at the population as a whole will generate a range of markedly differing responses influenced by the characteristics listed above. A spectrum of responses should be expected from any such exercise. As an added complication, the public’s response can fluctuate as risk messages evolve.

8.4.3 The message

Most people judge messages not by their content but by the credibility of the messenger. If the messenger is not credible then the message is likely to be disregarded, no matter how technically correct it is, how well intentioned and well delivered. Indeed, some research (e.g. Frewer *et al.*, 1996) suggests that well-presented arguments from distrusted sources actually have a negative effect. It can appear that the sender is not only untrustworthy but also devious.

In practice the risk messages that consumers receive will comprise multiple messages, from many sources (Trautman, 2001). Individual issues can comprise

difficult and complex ideas, yet preparing even a single risk message can be difficult. It may require choosing between a message that is so extensive and complex that only experts can understand it and a message that is more easily understood by non-experts but is selective and thus subject to challenge as being inaccurate or manipulative (National Research Council, 1989). There is no easy answer.

Important points to remember about risk messages are as follows:

- Messages are usually judged first by whether or not their source is trusted.
- Intentional communication is often only a minor part of the message actually conveyed.
- Responses to messages depend not only on content but also on manner of delivery, especially emotional tone.
- Experts no longer command automatic trust, no matter how genuine their expertise.
- Trust is generally fostered by openness, both in avoiding secrecy and in being ready to listen.

8.4.4 Risk comparisons

Experts often try to communicate risk by means of risk comparisons (Table 8.1). The underlying philosophy is that by numerically comparing a new risk to a known risk then the non-expert can perceive the new risk in its proper context. The flaw in this approach is that people seldom react to risks in such a cool logical fashion (Section 8.4.3). Indeed, it has been suggested that use or over-use of risk comparisons can damage the credibility of the messenger (Department of Health, 1998).

Guidance for using comparisons include:

- Avoid comparisons.
- Do not exaggerate the risk of rare events.
- Using comparisons to imply acceptability is dangerous.
- Compare like with like.

Nevertheless, in the absence of better information on microbiological risks in foods, risk comparisons may be the only method of risk communication available for the foreseeable future.

8.4.5 The medium

Experts communicate with each other by means of peer-reviewed publications, specialist fora and conferences. These tend not to be available to the general public. The vast majority of people receive their information about risks in foods from the media. Indeed this is often the first and only source of information about risks for many people. The media have two objectives: (a) to educate and inform, and (b) to make a profit. It is unavoidable that sometimes the media tend

to exaggerate or sensationalise issues in order to attract customers. As a result, the media can sometimes act as ‘amplifiers’ of risk messages, bringing them to a wider audience and increasing public concern.

In order to be prepared for these events it is necessary to know the ‘triggers’ that stimulate or amplify media interest in a story. A possible risk to public health is more likely to become a major story if the following are prominent or can be made to appear prominent (Health and Safety Executive, 1998):

- Questions of blame.
- Alleged secrets and cover-ups.
- Human interest through alleged heroes, villains, dupes, etc.
- Links to existing high-profile issues or personalities.
- Conflict, particularly between experts or between experts and others.
- Story is a sign of further problems.
- Many people exposed to the risk, even at low levels.
- Strong visual impact, e.g. pictures of the victims.
- Links to sex or crime.
- Reference back to other stories.

8.5 Risk communication

Risk communication is a highly specialised form of communication. To be effective it needs to take account of all the facets, technical and human, described above. The Codex Alimentarius Commission currently defines risk communication as ‘an interactive exchange of information and opinions concerning risk among risk assessors, risk managers, consumers and other interested parties’ (FAO/WHO, 1997). In conjunction with risk assessment and risk management, risk communication constitutes the Codex microbiological risk analysis paradigm. It follows that risk communication needs to be based upon a sound assessment of the risk under consideration. Further, some might consider that, in practice, risk communication is a critical component of risk management.

8.5.1 The benefits and uses of risk communication

The benefits and uses of risk communication are largely self-evident. Risk communication allows one party to communicate risk to another in order to:

- Demonstrate that a proper risk assessment has been conducted and that risk management procedures are in place.
- Justify any costs, alterations or restrictions that might be required to implement the risk management procedures.
- Communicate the actions that need to be taken to accomplish the risk management procedures, e.g. avoid certain products or ingredients, alterations to pasteurisation requirements or even the withdrawal of product from sale.

There may be other benefits and uses but they will tend to be subsets of the three listed above. Indeed the risk communication process and its benefits will tend to be the same for government, enforcers and health professionals and industry: only the messages and the medium will change.

In 1998 an FAO/WHO Expert Consultation on the Application of Risk Communication to Food Standards and Safety Matters set out the goals of risk communication in more detail (FAO/WHO, 1998):

1. Promote awareness and understanding of the specific issues under consideration during the risk analysis process, by all participants.
2. Promote consistency and transparency in arriving at and implementing risk management decisions.
3. Provide a sound basis for understanding the risk management decisions proposed or implemented.
4. Improve the overall effectiveness and efficiency of the risk analysis process.
5. Contribute to the development and delivery of effective information and education programmes, when they are selected as risk management options.
6. Foster public trust and confidence in the safety of the food supply.
7. Strengthen the working relationships and mutual respect among all participants.
8. Promote the appropriate involvement of all interested parties in the risk communication process.
9. Exchange information on the knowledge, attitudes, values, practices and perceptions of interested parties concerning risks associated with food and related topics.

8.5.2 Proactive and reactive risk communication

Basically the risk communication process will differ depending upon the reason for doing it. *Proactive* risk communication is easiest primarily because one has time to plan and test the mechanisms involved. Indeed it is an integral component of overall risk analysis planning and implementation. It can be greatly improved by having a risk communication strategy (see below).

Reactive risk communication is required when problems arise with specific foods or a sector of the industry and may be required to reassure others that everything possible is being done to minimise or eliminate the risk. Although the problem might be unforeseen it is a relatively safe bet that any organisation will face problems from time to time. In a crisis, a great deal can be gained from having at least the elements of risk communication planned in advance.

8.5.3 An example of a risk communication strategy

It is possible to be proactive and plan in advance to have a strategy for risk communication. Table 8.3 is based upon the Pointers to Good Practice for Communicating about Risks to Public Health published in 1998 by the

Table 8.3 Good practice in communicating about risks (Department of Health, 1998)

Anticipating public impact

1. Responses to risks will be amplified by outrage factors and media triggers.
2. Knock-on effects are often caused by responses to the original risk. Plan in advance for potential indirect economic, social and political consequences.

Planning a strategy

3. Clear aims are essential:
 - What do you want to achieve or avoid?
 - Who do you need to agree them with in advance?
4. Identify the key stakeholders:
 - Not only the intended audiences but others who may react or who can affect what happens.
 - What do they stand to gain or lose from different outcomes?
5. Consider how they may perceive the issue:
 - Can this be investigated or influenced?
 - What can be done to enhance trust?
 - What other issues may stakeholders be responding to?
6. Check for apparent inconsistencies with previous messages or other actions:
 - If unavoidable, these need to be explained.
7. Keep all the above (including aims) under review as the situation develops.

The process of communication

8. Plans must determine who needs to be involved at each stage of message preparation and release. It might be a good idea to draw up standard lists in advance.
9. Ensure that:
 - Choices are consistent and defensible.
 - Any lack of openness is both necessary and well-explained.
 - Mechanisms for involvement are made clear to others.
10. Check *what else is being done* to deal with the risk. What counts is the overall impression conveyed.

Content of communication

11. Be careful to address audiences' values (e.g. perceived fairness, or a need to vent anger), as well as providing factual information. Keep checking the emotional tone used.
12. Acknowledge uncertainties in scientific assessments.
13. In giving statements about probabilities:
 - If relative risks are cited (e.g. 'the risk has doubled'), the baseline risk must be made clear
 - Any risk comparison ('the risk from X is less than from Y') should be relevant to actual choices.
 - Avoid comparisons that may seem unfair or flippant, e.g. juxtaposing voluntary and involuntary risks.
14. If alternative options have benefits as well as risks, ensure that both are fairly spelt out. In any case bear in mind framing effects of wording (e.g. 'lives lost' versus 'lives saved').

Monitoring decisions and outcomes

15. At the start of an episode, set up procedures to monitor events and actions.
 16. Afterwards, review the strategy taken and outcomes reached – desirable or otherwise – and disseminate lessons for future practice.
-

Department of Health. The checklist can be used to identify difficult cases in advance and to guide reaction to incidents as they occur.

8.6 The future of risk communication

The science of microbiological risk analysis in foods is still in its infancy. Consequently, risk communication in this field has yet to develop to its full potential. Examples of good practice would be extremely useful, but to date it is hard to find any that are widely, or even narrowly, acknowledged as being suitable models for others. Clearly, much research and sharing of good practice are required.

An indication of the areas of research and procedures that need to be developed further can be gleaned from the reports of two expert consultations, one on risk communication and the other on strategic planning (FAO/WHO, 1998; WHO, 2001):

- If risk communication is to be effective, then key issues dealing with the process itself must be addressed. These include the involvement and interaction of all interested parties; the use of persons trained in risk communication; an assurance that the risk communication is received and understood; and the fostering of transparency during the entire process.
- Practitioners of food safety risk analysis should seek to involve and gain input from all interested parties. This input will help risk assessors and managers to become aware of and consider valid issues and concerns other than science.
- Persons with training and experience in the application of the principles and procedures of risk communication should be part of any crisis management team involved in a food safety issue. Training programmes in the principles and practices of risk communication should be established for both risk assessors and risk managers.
- Communications between and among risk assessors, risk managers and other interested parties should use language and concepts that are readily understood by the target audience. This includes clearly identifying what is science, what are value judgements and what benefits, if any, are involved.
- Risk analysis practitioners should use risk communication procedures to make the risk assessment process and the resulting risk management decisions as transparent as possible. This will increase the likelihood of both public understanding and acceptance of the risk management option(s) selected.
- Generic communication strategies need to be developed based on these recommendations. They should take into account local differences and information needs. Constant refinement of the risk communication message and process, following feedback from evaluation activities is essential.

Finally, communication of microbiological risks in foods is clearly still in its infancy. Nevertheless, if food microbiologists and other parties conducting

microbiological risk analysis in food begin to take account of the factors described in this chapter, then a vitally important first step will have been taken.

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Part II

Implementing microbiological risk assessments

9

Implementing the results of a microbiological risk assessment: pathogen risk management

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9.1 Introduction

The aim of a microbiological risk assessment (MRA) is to provide risk managers with answers to one or more questions that may enable them to make better informed decisions. For example, risk managers may have encountered a problem and wish to know how big it is in order to decide whether control measures are needed. They may also want to know the potential options available to control the problem. Perhaps they merely want to be assured that the problem is a one-time accident rather than a continuous threat to public health. Sometimes, microbiological risk assessors can answer a question very rapidly. Based on profound experience and common sense, they come to a conclusion and make recommendations. On the other hand, an MRA may be very elaborate; it may take several months and be carried out by several experts. Examples of elaborate risk assessments include those carried out in the USA for *Salmonella enteritidis* in eggs (FSIS, 1998) and *Listeria monocytogenes* in ready-to-eat foods (FSIS, 2001). The MRAs carried out by the FAO/WHO experts are other examples of very detailed assessments (FAO/WHO, 2001).

Whatever the depth and sophistication of the MRA may be, it provides risk managers with data or recommendations, which help them to make the appropriate decisions. According to the Codex document on microbiological risk management (CAC, 2001a), risk managers should consider various options for control measures. In order to provide data on the effects of these options, risk assessors may be asked to simulate scenarios to determine the possible outcome of implementing several control options. Although all stakeholders in the food chain, in practice, could apply this risk management model according to the Codex

Alimentarius, it is mainly applied by governments or intergovernmental bodies such as Codex. Food industries use during the development of new products, a similar approach, but the aim and outcome are different.

A governmental risk assessment deals with all kinds of similar products in the market made by different producers. The risk assessment will provide risk managers with a risk estimate which can be, for example, an estimation of the number of people that may get a type of illness as a consequence of consuming a particular food containing a (certain level of a) certain microorganism. When different scenarios are studied, the risk estimates may change according to the control options considered. Clearly, those control measures that will result in a lower estimate of the number of illnesses will be evaluated for implementation and, when appropriate, considered for inclusion in generic hazard analysis critical control point (HACCP) plans.

In the food industry, food safety managers do not normally express the outcome of the simulation of different control measures as an estimated number of cases of illness. They are more likely to estimate the level of a certain microorganism in the food to be marketed, and to compare this with a similar food with a good safety record. In the food industry this is called food safety benchmarking. Well-established good hygienic practices (GHP) and HACCP are the basis of the safety record. When new formulations, new technologies and new equipment are going to be used, their effect on the safety of the final product will be estimated. This process is part of the hazard analysis in the HACCP system. Food industries do not determine how many more, or how many fewer, people may become ill after the consumption of the new food; the target is to prevent illness. In performing this hazard analysis the same methodology can be used as is used in the product/pathogen/pathway analysis in MRA. Predictive models, Monte Carlo simulations, etc. can be useful, but the end-point will be an exposure assessment rather than a risk characterisation.

It is important to make the distinction between a governmental MRA and an industrial hazard analysis (HA). There are several differences between the implementation of the results of a governmental MRA and the results of an industrial HA. Industrial HA starts with an assessment of their raw materials and their suppliers. An estimate of the initial level of contamination with the hazard of concern may thus be obtained. This forms the basis of the elaboration of the product formulation, processing conditions, shelf-life and shelf-life conditions, as well as instructions for preparation and use necessary to obtain the required level of safety. If a supplier is not able to deliver what is needed to produce a safe product, another supplier is found or another technology applied. Thus one of the first activities of industrial food safety managers is to determine the level of safety they want to achieve and to ensure that this will be achieved. Frequently this level is regarded to be 'as low as reasonably achievable' (ALARA), but in practice it is often the benchmarking mentioned earlier. Safety is 'built-in' and hazards are 'engineered out'. However, incidents and unforeseen events still happen occasionally during all steps of the food chain.

Governmental risk managers have to determine the level of risk they are willing/prepared to accept or tolerate in order to comply with the WTO/SPS (sanitary and phytosanitary measures) agreement (WHO, 1997). Establishing such a level of risk is a complex exercise, and while science should be the starting point, consumer preferences, costs and feasibility all play a role in decision making.

A product submitted for import may be rejected if it endangers the appropriate level of protection (ALOP) also called the 'acceptable level of risk'. Instead of the latter term, the expression 'tolerable level of risk' (TLR) is preferred because while consumers may tolerate food safety risks, they are reluctant to accept them. Moreover, risk assessment is mentioned in the SPS agreement as a tool in setting an ALOP.

An ALOP is defined as:

the level of protection deemed appropriate by the Member [State] establishing a SPS measure to protect human life or health within its territory.

A food put on a market in another country should not endanger this appropriate level of protection: imported foods should not lead to an increase in the number of diseases caused by a certain microorganism in a certain food.

An ALOP and a TLR may both be expressed as an annual number of illnesses per 100 thousand of a population caused by a certain pathogen in a certain food considered to be appropriate or tolerable. In theory, an MRA would be necessary to determine whether a food would be acceptable for importation if this is in doubt. If the outcome of the MRA were a risk estimate lower than TLR, the food would be accepted. If, however, the risk assessment resulted in a risk estimate higher than the TLR, the food would be rejected.

Clearly, this procedure would hamper the trade unnecessarily (which is against the objectives of the WTO), and thus another way of dealing with the SPS agreement had to be found. The food safety objective (FSO) concept has been proposed to deal with this: it converts a 'level of illness' into a 'level of a hazard' (ICMSF, 1998). An FSO expresses the maximum frequency and/or concentration of a microbiological hazard in a food at moment of consumption that provides the appropriate level of health protection (CAC, 2001b).

9.2 Establishing food safety objectives

MRAs serve as a tool for risk managers to select or reinforce control measures that will provide consumers with the appropriate level of health protection. The Codex document on microbiological risk management (CAC, 2001a) specifies the assessment of various options as one of the key elements of risk management:

The primary objective of microbiological risk management options assessment is an optimisation of the interventions necessary to prevent and

to control microbiological risks. It is aimed at selecting the option or options that achieve the chosen level of public health protection for the microbiological hazard in the commodity of concern, in an as cost effective manner as possible within the technical feasibility of the industry. Available options may be identified at national, regional or international level in the context of international trade agreement provisions.

There might be many different options for reducing microbiological risks, such as:

- avoiding foods with a substantiated history of contamination or toxicity;
- preventing contamination and/or introduction of pathogens at any stage in the food chain, including reducing the level of specific pathogens in primary *production*;
- preventing growth of pathogens by the combined action of extrinsic factors (e.g. chilling or freezing) and/or intrinsic factors (e.g. adjusting pH, A_w ; adding preservatives; employing microbiological competition);
- destroying pathogens (e.g. cooking, irradiation);
- establishing regulatory requirements and/or creating incentives for changes in attitudes that will contribute to risk reduction;
- labelling products with consumer information that either instructs regarding safe handling practices or warns regarding microbiological hazards that are likely to occur and for which adequate controls were unavailable;
- educating/informing the population at large or affected sub-groups about the steps they can take to reduce risks;
- establishing microbiological standards or other criteria and enforcing compliance;
- establishing microbiological food safety objectives (FSOs);

Usually, a combination of options will be more effective in reducing risks.

All these options need careful consideration, and which ones are chosen depends largely on the product, the pathogen, the population at risk, technical, economic and other societal considerations. For this reason, the following text will not deal with most of them. However, the concept of FSOs will be explained, because all risk management options and selected control measures should result in a certain level of health protection.

The FSO concept was developed because it is difficult to assess whether an ALOP or TLR will be achieved. An FSO converts the ALOP/TLR into parameters that can be controlled by food producers and monitored by government agencies. The ALOP/TLR is an expression of a public health risk, while an FSO expresses the level of a hazard in relation to this risk. The FSO can be defined as:

the maximum frequency and/or concentration of a microbial hazard in a food at the moment of consumption that provides the appropriate level of health protection.

An example of an FSO is <100 *L. monocytogenes*/g in a serving of food at the moment of consumption. The estimated level of protection achieved by meeting this FSO is that the chance of someone getting ill from eating a food that contains this concentration of *L. monocytogenes* would be 10^{-12} (FAO/WHO, 2001). An FSO should be met through the implementation of GHP and HACCP systems as well as correct food preparation and use practices. This is in line with the Codex definition of food safety: 'assurance that food will not cause harm to the consumer when it is prepared and/or eaten according to its intended use' (CAC, 1997a). Since FSOs define the level of a hazard at the moment of consumption other criteria have to be used to define the level of a hazard that is expected for other points in the food chain. Such criteria have been called performance criteria and can be described as: 'the required outcome of a control measure or combination of control measures that can be applied to assure that an FSO is met' (ICMSF, 1998). In Section 9.3 this concept will be further developed and a proposal for a distinction between the terms 'performance criteria' and 'performance guidelines or standards' will be made.

Establishing an FSO is a risk management activity and not the result of a risk assessment. It is a decision, based on scientific input, feasibility assessment, and a judgement of the acceptability by stakeholders such as consumers and industry. Ideally, an FSO would be based on the frequency or concentration of a pathogen in a food that would not cause illness. This would be equivalent to finding a no-effect dose, the value that is used for setting tolerable levels of daily exposure for acutely toxic chemicals. Certain foodborne pathogens have clearly definable threshold levels below which they pose no risk to the consumer. For example, for certain toxigenic foodborne pathogens such as *Staphylococcus aureus* a threshold concentration of cells can be estimated below which the microorganism does not produce sufficient toxin to cause a measurable adverse health effect (Jablonski and Bohach, 2001).

For infectious pathogens such a threshold is often assumed to be one viable cell. Currently, most risk characterisation models are based on this assumption (Whiting and Buchanan, 2001). An important outcome of an MRA is the establishment of a relationship between the level of a hazard (frequency and/or concentration) in a food and the incidence of the illness it causes in a given population, which may be represented by a hazard characterisation curve. The slope of this curve is specific to the hazard, the food, the illness and the category of consumers for which the curve has been determined. If such a curve is available for the incidence of illness for a specific pathogen–food combination, the selected ALOP can be positioned on the *y*-axis and the corresponding level of the hazard (FSO) can be obtained on the *x*-axis (see Fig. 9.1). Thus, the curve describes the relation between the level of a microbiological hazard in a specific food and its effect (for example the

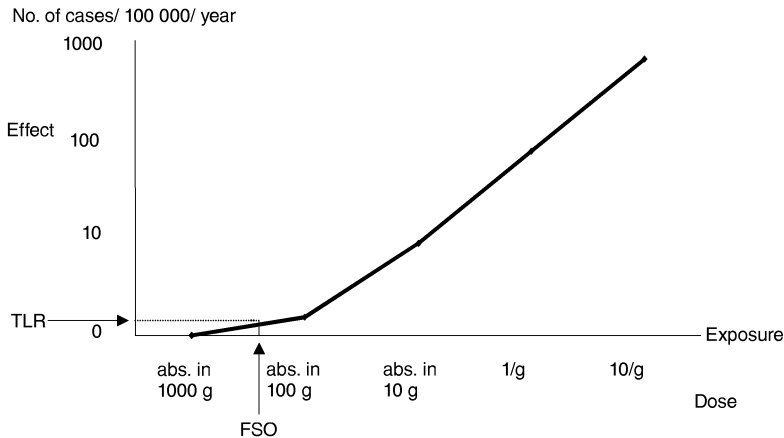


Fig. 9.1 Hypothetical risk characterisation curve.

number of cases of diarrhoea) on the general population. When the TLR has been set, the FSO can be determined.

Even when no ALOP is determined and the risk assessment does not provide the necessary information, FSOs can still be established. Investigations of foodborne illnesses and epidemiological surveillance programmes provide information about which foods have caused adverse health effects and which pathogens were implicated. Industry records are in principle another important source of information. Many foods processed for safety have an excellent history of providing an appropriate level of health protection. When such foods have been implicated in foodborne illness this is usually caused by deviations from good manufacturing/hygienic practices or accidents that were not detected in time. A good example is the safety record of industrially produced shelf-stable canned products. By analysing the production of such a food, an estimate can be made of the level of a potential hazard that may remain in the food. This level may then be used to establish a performance criterion/standard or an FSO.

Risk managers must seek to provide evidence that the proposed FSO is technically achievable through implementation of good hygienic practice (GHP) and HACCP. If the FSO cannot be achieved, then the product, process and/or the FSO should be modified. When this is not possible, or if the public does not accept the modified FSO, the consequence may be that the products, processes or foods need to be banned. An exporting country may encounter the same problem, i.e. that meeting the FSO is technically not achievable. This would mean that the product could not be exported. Thus FSOs could play an important role in providing the transparency and equivalence mentioned in the SPS agreement.

9.3 Developing food safety management strategies

9.3.1 Definitions

From the information provided in a FSO, regulatory authorities and food operators can select appropriate control measures to achieve the intended results (ICMSF, 1998). A control measure is ‘any action and activity that can be used to prevent or eliminate a food safety hazard or reduce it to an acceptable level’ (CAC, 1997b). One or more control measures may be necessary at each step along the food chain to ensure that a food is safe when consumed. In order to design control measures it is necessary to establish what needs to be achieved (the performance criterion) and how it will be achieved (the process and product criteria). Control measures should be established according to GHP and HACCP (CAC, 1997a, b).

In order to prevent confusion concerning parameters describing what should be achieved, where and how, the following terminology will be used:

- **Food safety objective:** the level of a hazard at the moment of consumption.
- **Performance standard:** the level of a hazard at any other point in the food chain. NB: the use of the word ‘Standard’ does not imply that the specified level of the hazard would be a regulatory mandatory requirement.
- **Performance criterion:** the outcome of a process step or a combination of steps (decrease or increase in the level of a microorganism or microbial toxin).
- **Process criterion:** a control parameter (e.g. time, temperature, pH, a_w) at a step that can be applied to achieve a performance criterion.
- **Product criterion:** a parameter of a food that is essential to ensure that a performance standard or food safety objective is met.
- **Microbiological criterion:** the acceptability of a product or a food lot, based on the absence or presence, or number of microorganisms including parasites, and/or quantity of their toxins/metabolites, per unit(s) of mass, volume, area or lot.

When designing and controlling food operations it is necessary to consider initial pathogen contamination (H_0), reduction (R), growth (G) and possible recontamination (RC). These events can be represented by:

$$H_0 - \sum R + \sum RC + \sum G \leq PS$$

in which the PS stands for performance standard, the \sum indicates that several of these events may occur and should be summed. This is based on the ICMSF equation:

$$H_0 - \sum R + \sum I \leq FSO$$

in which I stands for increase, i.e. both RC and G (ICMSF, 2002).

Since a PS can be at any point of the food chain, Fig. 9.2 may serve as an example of a more complete picture. The level of the hazard in raw materials, intermediate product and end-products may change along the food chain (‘from

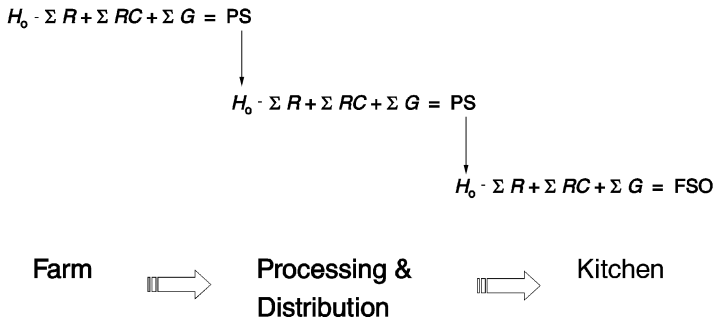


Fig. 9.2 Picture showing factors influencing food safety.

farm to fork') due to all kinds of influences. At various stages a raw material or product may become contaminated (RC), the microorganism may grow (G) and may also be reduced in number (R). This may occur several times and the resulting effects are summed (Σ). The PS of one stage is the H_0 of the next stage, the last PS (that of the preparation in the kitchen and further events before consumption) becomes the FSO. To give an illustration, the hypothetical fate of *Listeria monocytogenes* in a soft cheese will be considered. At the farm the milk is contaminated with 1 cell per ml (C). The receiving dairy factory does not accept milk containing >10 *L. monocytogenes*/ml (the dairy's H_0 and the producer's performance standard). The time and temperature during storage at the farm and transport to the dairy plant should thus limit the multiplication to a factor of 10 or three generations (G). At the plant multiplication before thermal treatment should again be limited to a factor of 10 (G). The thermalisation of the milk should achieve at least a 10^{-5} reduction (R) so that a level of 10^{-3} cells/ml is obtained. Cheese making means that a 10-fold increase is reached after heating by draining of the whey and expressing the level in cells per gram. Growth during cheese making cannot completely be prevented, but should again be limited to a factor of 10 (G). The frequency of recontamination (RC) is kept under control by GHP and does not exceed 1 cell per 10 g and thus the PS of $\leq 10^{-1}$ cells/gram (used by the dairy plant) is met. The FSO has been set at < 100 *L. monocytogenes* at the moment of consumption, thus growth during storage and distribution should not exceed a factor of 10^3 (ΣG) but would preferably be less than this figure.

The equation is a good example of using the result of the product/pathogen/pathway analysis performed during MRA or the results of the hazard analysis performed in a HACCP study.

9.3.2 Performance standards

The term performance standard (PS) is chosen because in trade these criteria play an important role. The FSO sets the level of a hazard at the moment of consumption, a stage of the food chain where foods are no longer traded. An FSO for *Salmonella* in poultry meat may be 'absence in a serving'. Currently

broilers in most countries contain this pathogen, and a government may want to limit the contamination by setting a PS of 'not more than 15% of broilers may be contaminated'. Proper cooking and application of GHP during preparation should ensure that the FSO is achieved, while the market is not unreasonably challenged by a PS equal to the FSO, which in many countries is not achievable.

When a stable ready-to-eat (RTE) food is dealt with, the FSO and the PS may be the same, but frequently a producer may want to build in a 'safety factor', in order to be 'on the safe side'. This takes into account that some abuse may occur during further handling and that this should not lead to illness. The magnitude of this 'safety factor' may be the result of an analysis of distribution, sales, preparation and use practices carried out during the hazard analysis in a HACCP study or an exposure assessment of an MRA. When microbial growth will occur after a product leaves the factory, the PS is more stringent than the FSO; for example, certain RTE products with extended shelf-life in which *L. monocytogenes* can multiply. Obviously, the PS can be less stringent than the FSO when a product needs to be cooked before consumption and when the performance criterion of this preparation step, in combination with the H_0 , would ensure that the FSO would be met. The case of *Salmonella* in broilers is a good example of this. An MRA can estimate whether a certain PS will meet the targeted health protection.

It should be mentioned here that a PS can be set at any point in the food chain and that it is identical to the 'acceptable level' to be achieved at a critical control point (CCP). A CCP is defined as: 'a step at which control can be applied and is essential to prevent or eliminate a food safety hazard or reduce it to an acceptable level' (CAC, 1997b).

9.3.3 Performance criteria

In the original ICMSF concept (ICMSF, 1998) no distinction was made between a PC expressed as the level of a hazard and a PC expressed as a *D*-value or another outcome of a process. This has led to some confusion and therefore the term performance standard was introduced to express the level of a hazard. An example of a PC is a 6*D* kill of *Salmonella* when cooking ground beef, or < 15% of freshly slaughtered broilers contaminated with *Salmonella* as mentioned above.

A PC does not only refer to a reduction in numbers, it may also be used to limit recontamination and growth. For example, if the FSO for *L. monocytogenes* in a non-stable RTE food is less than 100/g and the PS after a cooking step during production is absence in 10 g, then the PC for recontamination (*RC*) could be less than 1/g and the PC for growth (*G*) less than 10².

Validation is an increasingly important aspect of food safety management (ILSI, 1999; CAC, 2001b). It is defined as: 'obtaining evidence that the elements of the HACCP plan are effective' (CAC, 1997b). Setting PCs based on performance standards is an excellent means of ensuring that the system becomes transparent and it will serve to obtain evidence of the equivalence

mentioned in the WTO/SPS agreement. It helps the shift from the old system of compliance with processes and process criteria to compliance with objectives. The consequence of this is, of course, that evidence needs to be provided that the required PS is achieved with the PC applied. Validation can be performed through challenge studies, by analysis of samples, by calculation, e.g. using *D*- and *z*-values, etc.; a discussion of the merits of the different approaches is outside the scope of this chapter. Validation is used to provide evidence that certain data used in the MRA were correct; results of MRA cannot be used to validate PCs in the food chain.

9.3.4 Process criteria

Process criteria are the control parameters (e.g. time, temperature, pH, a_w) at a step, or combination of steps, that can be applied to achieve a PC. For example, the control parameters to achieve at least a 10^{-6} reduction of *L. monocytogenes* in milk are 71.7°C for 15 s (ICMSF, 1996). Process criteria are identical to critical limits (CAC, 1997b) when the control point is a CCP in a HACCP plan.

Correctly applied process criteria for the preparation of food prior to consumption is very important. Cooks have no means of checking whether an FSO is achieved. They can, and should, monitor parameters such as time and temperature. Providing other information concerning the importance of good kitchen practices is part of risk communication, and initiating active information and education programmes was already mentioned in Section 9.2 as a risk management option.

In the Codex document on General Principles of Food Hygiene (CAC, 1997a) the following text refers to this:

governments should provide health education programmes which effectively communicate the principles of food hygiene to industry and consumers'.

This document also mentions that:

Industry should ensure that consumers have clear and easily-understood information, by way of labelling and other appropriate means, to enable them to protect their food from contamination and growth/survival of foodborne pathogens by storing, handling and preparing it correctly.

And moreover it is stated that:

consumers should recognize their role by following relevant instructions and applying appropriate food hygiene measures.

9.3.5 Product criteria

Once products are ready for distribution and sale, care is necessary to ensure that they do not become unsafe due to multiplication and/or toxin formation by

pathogens. Parameters in foods that are used to prevent unacceptable growth of microorganisms are called product criteria. Multiplication and/or toxin formation are dependent on the formulation, composition and ‘environment’ in the food. Parameters such as pH, a_w , temperature, structure, additives, competitive flora and gas atmosphere are used to control growth. For example, to prevent *L. monocytogenes* reaching levels above 100/g in a RTE food during distribution sale and storing at home, it may be necessary that a food has a pH < 4.6 or an $a_w < 0.92$. Process criteria deal with treatments used to render foods safe; product criteria are used to keep them safe.

9.4 Establishing microbiological criteria

9.4.1 Sampling plans

One risk management option is to establish microbiological criteria or standards, which serve various purposes in the trade of food. In principle they are intended for the assessment of foods based on microbiological analysis. A Microbiological Criterion (MC) for food defines according to Codex (CAC, 1997c):

the acceptability of a product or a food lot, based on the absence or presence, or number of microorganisms including parasites, and/or quantity of their toxins/metabolites, per unit(s) of mass, volume, area or lot.

This document describes further how these criteria should be established and applied:

A Microbiological Criterion consists of:

- a statement of the microorganisms of concern and/or their toxins/metabolites and the reason for that concern
- the analytical methods for their detection and/or quantification
- a plan defining the number of field samples to be taken and the size of the analytical unit
- microbiological limits considered appropriate to the food at the specified point(s) of the food chain
- the number of analytical units that should conform to these limits.

In the establishment of MCs, FSOs or PSs can be useful and an MC for a food should be related to its FSO. An MC that is excessively stringent relative to an FSO may result in rejection of food even though it has been produced under conditions that provide an acceptable level of protection.

According to the Codex document, in order to decide whether or not an MC should be established and what the content should be, consideration should be given to the following:

- Evidence of actual or potential hazards to health (epidemiological evidence or the outcome of an MRA).

- The microbiology of raw materials (H_0).
- Effect of processing (R).
- Likelihood and consequences of contamination (RC) and growth (G) during handling, storage and use.
- The category of consumers at risk.
- The cost–benefit ratio of the application.
- The intended use of the food.

These considerations are of a very general nature and apply to all foods. When dealing with specific foods, decisions must be made where criteria are to be applied in the food chain and what would be achieved by applying them.

Microbiological criteria differ in function and content from FSOs (see Table 9.1). However, occasionally the limit in a criterion is the same as an FSO or a PS as, for example, in the case of the FSO for *L. monocytogenes* in a stable RTE product. An FSO will normally not prescribe a sampling plan. For MCs it is essential that such a plan is developed, because that will assist in achieving the transparency and equivalence mentioned in the WTO/SPS agreement.

The Codex document specifies that, in developing sampling plans, the severity of the hazard and assessment of the likelihood of its occurrence must be considered, but for more guidance the document refers to ICMSF Book 2 (ICMSF, 1986). The first part of this book that deals with the scientific rationale for the development of sampling plans has been revised and published as ICMSF Book 7: *Microbiological Testing in Food Safety Management* (ICMSF, 2002).

Table 9.1 Characteristics of FSOs and microbiological criteria

Food safety objective	Microbiological criterion
A goal upon which food processes can be designed so the resulting food will be safe	A statement that defines acceptability of a food product or lot of food
Aimed at consumer protection	Confirmation that effective GHP and HACCP plans are applied
Applied to food at the moment of consumption	Applied to individual lots or consignments of food
Components: <ul style="list-style-type: none"> • Maximum frequency and/or concentration of a microbiological hazard 	Components: <ul style="list-style-type: none"> • Microorganism of concern and/or their toxins/metabolites • Sampling plan • Analytical unit • Analytical method • Microbiological limits • Number of analytical units that must conform to the limits
Used only for food safety	Used for food safety or quality characteristics

The ICMSF approach distinguishes three categories of hazards based upon the relative degree of severity of their effects:

1. Severe hazards, life threatening.
2. Serious hazards, incapacitating but not life threatening.
3. Moderate hazards, severe discomfort of short duration.

This categorisation and the examples presented in Table 9.2 were based on the best epidemiological data available at the time of publication, but may need to be reviewed when new data become available.

The other factor to be considered is the likelihood of occurrence of an adverse effect, taking account of the anticipated conditions of use. Here the ICMSF again recognises three categories:

1. Conditions that would reduce the risk.
2. Conditions that would increase the risk.
3. Conditions that would not cause a change in risk.

Combining the three levels of severity of a health effect with the categories of likelihood of occurrence leads to different levels of concern called 'cases' by the ICMSF, case 7 being of lowest concern to food safety and case 15 of the highest.

Taking into account the likelihood of a health effect, cases 9, 12 and 15 represent the highest levels of concern because they refer to situations where pathogens can multiply in the food under expected conditions of handling, storage, preparation and use. Cases 7, 10 and 13 represent the lowest levels of concern, because they refer to intermediate situations of concern where the level of the hazard is likely to be reduced before consumption, for instance during

Table 9.2 Categories of hazards with some examples. (Based on ICMSF, 2002.)

1. Moderate, severe discomfort, short duration	<i>S. aureus</i> <i>V. parahaemolyticus</i> <i>B. cereus</i> <i>C. perfringens</i>
2. Serious, incapacitating, not life threatening	<i>Salmonella</i> (non-typhi) <i>Yersinia enterocolitica</i> <i>Shigella</i> (non-dysenteriae I) <i>Listeria monocytogenes</i>
3A. Severe, life threatening for general population	<i>C. botulinum</i> <i>V. cholera O1</i> <i>S. typhi</i> Enterohaemorrhagic <i>E. coli</i>
3B. Severe for restricted populations	<i>Campylobacter jejuni</i> Enteropathogenic <i>E. coli</i> <i>Listeria monocytogenes</i>

preparation. Cases 8, 11 and 14 refer to situations where the level of the hazard would remain the same between the time of sampling and the time of consumption.

Based on these nine cases, the ICMSF developed two-class sampling plans in which n indicates the number of sample units to be tested and c the number of defective sample units that can be accepted. These sampling plans are summarised in Table 9.3. The plans direct more of the available resources for analysis towards those situations with a high level of concern.

Often 25 g or ml of the samples taken from a lot is analysed, but a smaller or larger weight or volume can be used to decrease or increase the stringency of the sampling plan. Using 25 g analytical units means that in Case 10 *Salmonella* would be 'absent' (not detected) in 125 g, and in Case 15 in 1.5 kg. When pathogens are homogeneously distributed throughout a lot, or when samples are taken at random, statistical methods can be used to express the likelihood of contamination of the lot. Finding no *Salmonella* when applying Case 10 would mean that 90% of the lots containing 2% defectives would be accepted (with a probability of 95%). For Case 15 it would mean that 30% of such lots would be accepted. However, in many cases the distribution of contaminants is not homogeneous and random sampling is most of the time not possible. This clearly illustrates that examination of batches, lots or consignments of products for the presence of pathogens has only limited value as a control measure.

Table 9.3 Plan stringency (Case) in relation to degree of health concern and conditions of use. (Based on ICMSF, 2002.)

Degree of concern relative to expected health effect	Conditions in which food is to be handled and consumed after sampling in the usual course of events		
	Conditions reduce degree of concern	Conditions cause no change in concern	Conditions may increase concern
1. Moderate, severe discomfort, short duration	Case 7 $n = 5, c = 2$	Case 8 $n = 5, c = 1$	Case 9 $n = 10, c = 1$
2. Serious, incapacitating, not life threatening	Case 10 $n = 5, c = 0$	Case 11 $n = 10, c = 0$	Case 12 $n = 20, c = 0$
3A. Severe, life threatening for general population and 3B. Severe for restricted populations	Case 13 $n = 15, c = 0$	Case 14 $n = 30, c = 0$	Case 15 $n = 60, c = 0$

n = the number of sample units tested.

c = the number of defective sample units which can be accepted.

9.4.2 Establishment of microbiological criteria based on FSOs

The FSO states the level of a hazard at the moment of consumption; this is normally not the point in the food chain where samples are taken and tested for the frequency and/or the concentration of a pathogen. Therefore, the MCs have to be related to other points in the food chain, i.e. to PSs. The nature of this relationship will depend on whether the level or concentration of a certain microorganism or a group of microorganisms (indicators) are measurable or not.

The proposed FSO for *L. monocytogenes* in a stable RTE food is less than 100/g at the moment of consumption. This concentration can be determined with classical microbiological procedures such as a plate count or most probable number (MPN) technique. An MC could be directly related to this concentration, because in a stable RTE food, the level of *L. monocytogenes* would not change. The number of samples to be taken would reflect the safety factor that a government or a company applies. If the RTE food is not stable, then it will depend on when the sampling is done, how much time is envisaged between sampling and consumption and what the conditions for growth are expected to be during this time. If a 100-fold increase were envisaged, then the criterion at the moment of sampling would be absence of *L. monocytogenes* in 1 g of a given number of samples of the product. This would still be measurable. However, if a 10 000 fold increase is foreseen, the criterion should be absence in at least 100 g, which would become much more difficult to determine.

If the FSO for *Salmonella* in dried egg was less than 1/10 kg, testing for compliance would become impossible. In such case, a criterion could be based on the concentration of an indicator group of microorganisms such as Enterobacteriaceae. When the initial number of *Salmonella* (H_0) in raw egg would be 1/g, a 10^5 reduction should be obtained (PC) in order to achieve the FSO (assuming a 10-fold increase in numbers due to the evaporation of water during drying). The group of Enterobacteriaceae has more or less the same heat resistance as *Salmonella* (Cox *et al.*, 1988). This means that in order to achieve the FSO, the number of these indicators should also be reduced by a factor of 10^5 . Assuming that the initial level of Enterobacteriaceae in raw egg is 10^5 then the criterion would be absence of these indicators in a number of samples of 1 gram. This criterion is again measurable.

Indicators that have a relationship with measures to control a pathogen are not always available. For example, for the sterilisation of a low-acid canned product, a so-called 'bot cook', is applied. This means that the product receives a thermal treatment that reduces the concentration of spores of *Clostridium botulinum* by a factor 10^{12} . Even if an indicator group such as 'total viable spores' could be used to check whether a heat treatment was performed, it would not be able to determine the presence of spores in a sufficiently large quantity of food to check whether the PC was met.

In many cases, microbiological criteria cannot be directly based on an FSO or a PS because of the low level of the pathogen to be achieved and the absence of relevant indicators. In these cases, the ICMSF approach to use a form of primitive risk assessment as basis for the selection of 'cases' and the suggested

sampling plans is still recommended. By using the appropriate criteria for the selection of the cases, the best use of available resources is achieved. Moreover, the reason for choosing the stringency of the sampling plan becomes consistent and transparent, which is important in the context of the WTO/SPS agreement.

9.5 Problems in implementation

The results of an MRA are often difficult to interpret. During the assessment, many assumptions have to be made, many data are lacking and hazard characterisation curves are not available. Although a risk estimate should include attendant uncertainties, the magnitude of these uncertainties is often difficult to establish.

Risk managers may find it difficult to understand clearly the implications of the implementation of certain control measures. Decision making is further complicated by the fact that stakeholders such as consumers and industries should be involved in the decision making process. The exchange of ideas and perceptions are part of what is called risk communication, i.e. the third element of risk analysis. Risk communication not only pertains to communicating the decisions to the public and the affected industry; it also refers to the interactive communication during risk management (FAO/WHO, 1998). How industries, consumers and other interested parties might participate in governmental risk management activities is still not apparent (Renn *et al.*, 2001). Often, this communication is carried out in so-called hearings and consultation processes during which interested parties may comment on proposals and where they may ask pertinent questions. The effectiveness of these procedures, and whether this will help the acceptance by the public of certain decisions made, may need to be studied further.

One of the main problems regarding the safety of food products is the public perception of the magnitude and the severity of the effects of certain hazards in foods. Even when it was clearly demonstrated scientifically that the use of alar in the cultivation of apples would have no adverse public health effect, still its application had to be stopped because of the public reaction against it. The public became scared because of an anti-alar campaign that was supported by a well-known Hollywood actress. Many other examples can be given where scientific evidence was not sufficient to influence public acceptability of a governmental decision (Groth, 2000a).

For the industry, public perception is as important as the outcome of scientific risk assessments. A genetically modified product may be considered safe by risk assessors and governmental risk managers. However, if the consumer does not buy such a product, the industry has little interest in putting it on the market. One of the main problems in the implementation of the results of MRA will remain how to prepare the consumer for the acceptance of certain risk management decisions based on these risk estimates.

9.6 Future trends

MRA will develop into a powerful risk communication tool. It will show what is known and what is not known. It will make the pathogen–product pathway transparent and will show the differences in food safety that can be achieved by various control options. Further refinement of many MRAs will be necessary (FAO/WHO, 2000). For example, the MRA of *L. monocytogenes* in RTE foods carried out in the USA did not differentiate between pâté recontaminated after the heat treatment and in-pack pasteurised pâté. Obviously the risk of the last product is negligible, while the first product has been involved in a major foodborne outbreak (McLaughlin, 1996).

Since many data are currently lacking, the ‘precautionary approach’ will most probably be advocated by consumer organisations (Groth, 2000b) or countries that want to protect their own production. ‘Worst-case’ scenarios are often reported by the media. How to deal with uncertainty in the estimations needs to be agreed upon, in order that MRA becomes an effective part of the risk management process.

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10

Tools for microbiological risk assessment

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10.1 Introduction

Microbial risk assessments are usually carried out by a team of assessors with expertise in such areas as food microbiology, epidemiology, food engineering and product development. Such a team needs to keep up to date with all aspects of risk assessment. As knowledge in this area is rapidly increasing, it is very hard to keep track of the latest developments in such areas as risk assessment methodology, data on microorganisms and new outbreaks, for example. This growing volume of information and the complexity of decision making makes the use of computers a logical tool in microbiological risk assessment. Such tools provide support at each stage. Databases provide background information on pathogens such as physiological characteristics, growth kinetics and means of inactivation. Computer models help to predict the behaviour of microorganisms in processes, products and the environment. They can help calculate the impact of corrective actions on shelf-life, product safety and consumer health.

In microbiological risk assessment various stages can be distinguished in the decision making process. The first stage is making an inventory of product and process characteristics and collecting microbiological data. Processes are usually described in terms of process variables that influence the introduction, increase or inactivation of microorganisms. Products are also described in terms of supporting the growth, survival or inactivation of microorganisms. Consumers can be described in terms of their susceptibility to infection. At this stage databases containing information on microorganisms and their interactions with products, processes and consumers can be very useful. This information provides a basis for modelling and predicting the behaviour of microorganisms in response to product, process and consumer characteristics. In Fig. 10.1 the

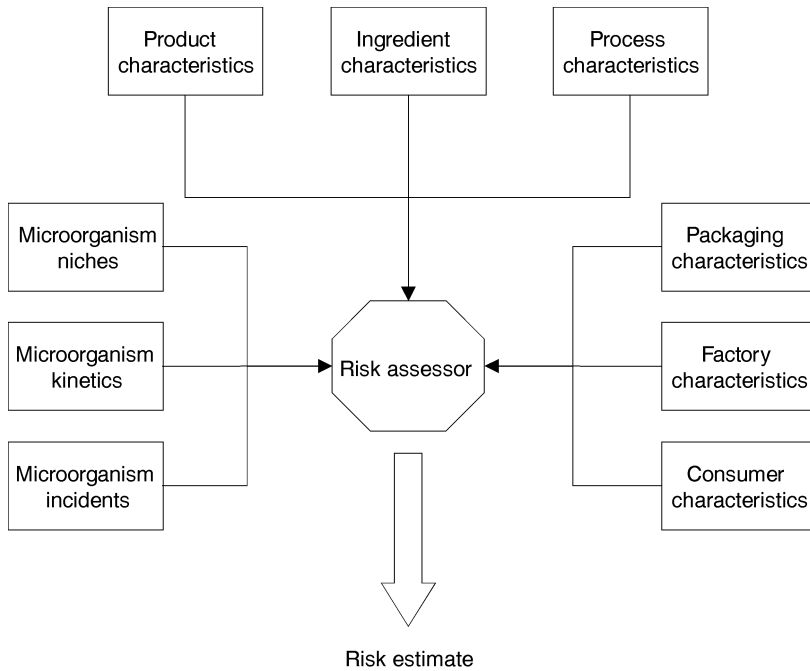


Fig. 10.1 Information sources for a risk assessor.

required information sources are depicted graphically. Each of the boxes in the figure represent a database or a set of tools that could be used.

Tools for microbiological risk assessment can be divided into two groups:

1. Qualitative tools dealing with risk assessment in words rather than numbers.
2. Quantitative tools dealing with the numerical prediction of the microbiological risk.

Qualitative decision making can help risk managers decide which microorganisms are of concern, and hence their characteristics and behaviour. Quantitative tools then help to calculate the extent of the risk involved. Qualitative interpretation of risk relies on heuristic knowledge. Heuristic knowledge exists in the form of facts and expert opinion. This knowledge can either be diffused among a range of sources or it can be collected and organised systematically in databases. The quality of this database information relies on the care with which the data were gathered, the sources and accuracy checked, and the skills in organising the database coherently and keeping it updated. Quantitative tools can be divided into deterministic tools, yielding fixed values, and tools based on quantitative probabilistic models where outcomes are probabilities and distributions.

10.2 Qualitative tools for risk assessment

In what has been called the information age, one would expect a dedicated knowledge base in the area of microbiological risk assessment. At present, however, there are relatively few central information sources available. Much information is distributed among individual experts and organisations, journal articles, books and conference proceedings.

Internet information resources can be divided into so-called portal sites and content sites. Portal sites provide a gateway to other information resources, usually not as part of the actual portal domain. Portals are useful for identifying and accessing a range of content sites. An example of a good food safety portal site run by the US Government is: <http://www.foodsafety.gov>. It provides links to a range of non-commercial food safety information resources covering food safety issues for the US food industry.

There are now a number of sites that contain information on microbiological risk assessment methodology. The Food and Agriculture Organisation (FAO) and the World Health Organisation (WHO) list key activities and reports (www.who.int/fsf/mbriskassess/index.htm and www.fao.org/waicent/faoinfo/economic/esn/pagerisk/riskpage). The US Department of Agriculture (USDA) has also compiled a helpful bibliography on food safety risk assessment (www.nal.usda.gov/fnic/foodborne/risk.htm).

Content sites containing dedicated information on microbiological risks are still relatively rare. A good example is the so-called 'bad bug book' compiled by the US Food and Drug Administration (FDA). This database, which is available electronically through the FDA's website, provides information on individual pathogens, conditions for growth, and epidemiology. The content of the site is updated on a regular basis (www.cfsan.fda.gov/~mow/intro.html).

Table 10.1 lists examples of portal and content sites currently available. It is necessarily a snapshot of a landscape that is evolving on a daily basis with new sites regularly coming on stream. There are also a number of microbiological databases and disease surveillance systems set up by national governments, many of which are also available electronically. Examples of these include:

- USA: The Center for Disease Control and Prevention (www.cdc.gov).
- USA: Center for Food Safety and Applied Nutrition (www.cfsan.fda.gov which includes the bad bug book).
- UK: Public Health Laboratory Service (www.phls.co.uk).
- Australia: Communicable Diseases Centre (www.health.gov.au/pubhlth/cdi/cdihtml.htm).

There are moves to try to share and standardise microbiological data. Several forums have proposed the creation of data 'clearing houses', which are already established in the chemical and pharmaceutical industry. In the USA a microbial food safety risk assessment 'clearing house' is established within the Joint Institute for Food Safety and Applied Nutrition (<http://www.foodriskclearinghouse.umd.edu/>) to 'capture' data generated and collated within risk

Table 10.1 Internet sites

Information source	Description	Quality
http://www.cfsan.fda.gov/~mow/intro.html	Bad bug book; excellent background material on behaviour of microorganisms. Appendices are useful reading.	+++
www.foodsafety.gov	Portal to US safety information	++
www.who.int/fsf/	WHO on food safety	++
www.fsis.usda.gov	USDA food safety site	++
www.foodhaccp.com	Lot of background material on hazards, HACCP, etc.	++
www.fda.gov	FDA site; contains, e.g., bad bug book	++
www.cdc.gov	Centre of disease control and prevention	+
www.safetyalerts.com	This site provides recent recall information in the USA. A lot of information on food and allergens. Per notice a short description is given on the background.	+

assessments so that they are more readily available for subsequent assessments. Eurosurveillance system has been also developed to share data within the EU (www.eurosurv.org). The WHO/FAO (2000b) also recommended that the feasibility of establishing an international repository for microbial food safety risk assessment data be investigated.

10.3 Predictive modelling

Quantitative risk assessment relies heavily on the use of predictive microbiology models. These models use information on pathogen, product and process characteristics to predict inactivation, survival and growth of microorganisms. These models are usually developed for a particular microorganism under specific, well-controlled environmental conditions. Most models relate the kinetics parameters governing the behaviour of a microorganism to changes in environmental conditions such as temperature, pH, water availability and activity, or concentration of organic acids. These models are usually developed using sample products or model media from which experimental data are derived.

Predictive models use both static and dynamic models of microbiological behaviour. Static models describe the kinetic parameters of microorganisms under fixed, non-changing, environmental conditions. As an example, one temperature value is set and the growth of a microorganism is followed in time. Static models do not take into account *changes* in the environmental parameter such as temperature changes. These models are explicit functions of the kinetic parameters as a result of the environmental conditions. An example of such a model is the Gompertz model, which is given below (Zwietering *et al.*, 1991):

$$\ln\left(\frac{N_t}{N_0}\right) = A \exp\left\{-\exp\left(\frac{\mu_m e}{A} \exp[\lambda - t] + 1\right)\right\} \quad 10.1$$

where N_t = numbers of organisms at time t

N_0 = initial number of microorganisms

A = maximum level of microorganisms

μ_m = maximum specific growth rate at a specific value of, e.g.,
temperature

λ = lag time at a specific value of, e.g., temperature

Among the approaches more commonly used are the modified Gompertz equation, the Baranyi equation and the logistic equation (Baranyi *et al.*, 1993; Gibson *et al.*, 1988). Combinations of linear models for exponential, lag and exponential or lag, exponential and stationary phases have also been used (Buchanan *et al.*, 1997) though the last of these is controversial (Baranyi, 1997; Garthright, 1997).

Dynamic models attempt to relate changing environmental conditions to the kinetic parameters of microorganisms. Changes in microbiological behaviour are, for example, monitored against changes in temperature over time. These models usually have the form of (a set of) differential equations. An example of such a set of differential equations is the first order exponential growth model with time-delayed growth:

$$\text{For } t < \lambda : \frac{dN}{dt} = 0 \quad 10.2$$

$$\text{For } t \geq \lambda : \frac{dN}{dt} = \mu N$$

All the parameters are as described above. In this equation two things strike the eye. First, for two different times (t) there are two different models: one for times shorter than the lag time (λ) and one for times longer than the lag time. The second important part are the 'd' in the equation. A d mathematically stands for a change; so dN represents a change in numbers (N). The denominator (dt) represent a change in time. So the left hand side of the equations work out as a change of numbers in time. The right hand side of the upper equation equals zero, so when time is shorter than the lag time there is no change in numbers in time. The right hand side of the lower equation equals μN . This is the standard first order growth model. Static models provide a foundation for the building of dynamic models of microbiological behaviour.

10.3.1 Model development: empirical models

Most available models are empirical models based on experimental data. The development of an empirical model takes place in different stages (Legan *et al.*, 2002). The first stage is the selection of the organism, the reference product and the parameters that will be studied. This planning stage should include a

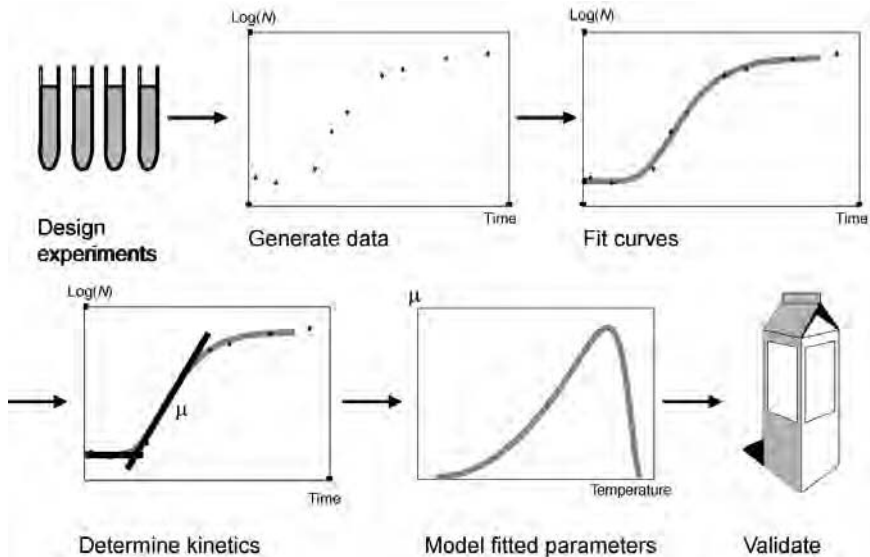


Fig. 10.2 Stages in the development of an empirical predictive model.

literature study to identify available data and existing relevant models. Where appropriate, it may be more cost-effective to make use of an existing model, providing the assumptions on which it is based match the conditions that are to be modelled. Some existing models are described in Section 10.5.

Based on the objectives set out for the model and the parameters to be studied, and taking into account existing data, an experimental design is set up (Fig. 10.2). Several design techniques exist, ranging from factorial to minimal designs and so-called craftsmen designs. Several authors have given detailed descriptions of experimental designs for modelling in food microbiology (Davies, 1993; McMeekin *et al.*, 1993; Ratkowsky, 1993). After deciding on an experimental design, the experiments themselves are carried out. Depending on the type of model, environmental conditions are set and the kinetic parameters of the microorganisms are followed in time. In both dynamic and static modelling, microbial numbers in time are measured. Measuring changes in microbial numbers is the most laborious part of model development. Guidelines for data collection and storage from experiments have been put together by the protocols group of the UK Food MicroModel programme (Kilsby and Walker, 1990) and discussed by Walker and Jones (1993).

Measuring microbial numbers over time usually produces so-called growth curves. In a growth curve the natural logarithm of the counted number of microorganisms (y -axis) is plotted against time (x -axis). At this stage of the model development, through a process of statistical regression called fitting, the parameters of the curve are determined. Since static models attempt to describe the behaviour of microorganisms at a single value of the controlling environmental parameters, a growth curve usually has a sigmoid shape (Fig.

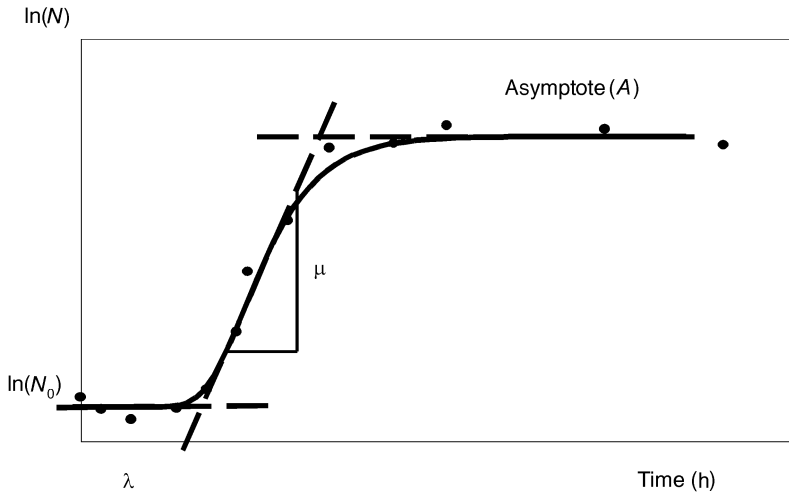


Fig. 10.3 Bacterial growth curve.

10.3). In this graph, the kinetic parameters are shown as in equation 10.1. A sigmoid growth curve consists of four stages. The first stage is characterised best as an adjustment period. Cells have to adjust to their new environment. This stage is called the lag-phase. Microbial numbers stay constant during this stage. After a while, when the microorganisms have adapted to their new environment, the log-phase starts. The microorganisms make maximal use of the nutrients present and reach a maximum specific growth rate. This phase is characterised by a rapid increase of cells. Later again, nutrient depletion occurs and the rate of growth slowly declines. In the end, the asymptote is reached. Cells no longer divide because of a lack of nutrients, a too low pH or too high concentrations of other growth-inhibiting substances. Usually, foods are long spoiled when the asymptote is reached. Long after the asymptote is reached, cells start to die and microbial numbers become less and less. This stage is called the death stage and is not shown in Fig. 10.3. Each of these stages has its kinetic parameters. The lag phase has the so-called lag-time (λ). The log-phase has the maximum specific growth rate (μ) and the asymptote has the asymptotic level of organisms (A). These parameters can be used to describe an entire growth rate curve.

Since a growth curve is measured at one single value of a controlling variable, a large number of growth curves need to be measured. This again results in an equally large number of fitted growth rates, lag times and asymptotic values. In the next stage of model development, the values for the kinetic parameters (μ , λ and A) are related to the value of the controlling environmental parameters. This results in an explicit mathematical equation for lag time (λ) or growth rate (μ), as an example, as a function of pH, temperature or water activity, for instance. An example of such an equation is:

$$\mu = b(T - T_{\min})^2 \times (\text{pH} - \text{pH}_{\min})(\text{pH} - \text{pH}_{\max}) \times (a_w - a_{w,\min}) \quad 10.3$$

where μ = maximum specific growth rate at a specific value of, e.g.,
temperature

b = regression coefficient

T = temperature (Celsius)

pH = negative log of $[H^+]$ concentration

a_w = water activity

T_{\min} = lowest temperature at which growth ceases

pH_{\min} = lowest pH at which growth ceases

pH_{\max} = highest pH at which growth ceases

$a_{w,\min}$ = lowest water activity at which growth ceases

When all parameters in these models have been determined by means of statistical regression, the models can be used for prediction. However, before these models can be used with confidence, they need to be validated. The accuracy of the model predictions needs to be verified against the dataset that was measured. Several strategies exist for performing a good model validation. For a simple model validation a statistical package should be used that is able to perform non-linear regression as well as generate 95% prediction intervals for single point predictions of the model (Baranyi *et al.*, 1999). Examples of such packages are SAS and SPSS, but less sophisticated packages such as Tablecurve 2D are also able to calculate these intervals.

The basic approach to validate a model is to divide an entire dataset into two subsets. One subset is used to determine the parameters of the suggested model, while the second subset is used for validation. The fitted model based on the first subset of the data is used to predict the remaining part of the dataset (second subset). The predictions of the data can be compared with the actual data. If the 95% confidence intervals of the second subset overlap the predictions of the first subset, the model describes the data accurately. This validation strategy works well under laboratory conditions.

The ultimate test for a model is performance under field conditions. Model predictions should be validated against relevant data on real foods. In some cases it is possible to extract validation data from the literature. Unfortunately, data in the literature are often too incomplete to use and it is necessary to resort to experimentation to compare actual growth data points with predicted growth curves (Fig. 10.4). It is less critical to catch the points of inflection than it is with the model-building experiments and four to six well-spaced points per curve can be enough. However, more points can allow growth parameters to be derived from the food data and this can facilitate comparison with the model predictions. Good agreement between predicted and observed responses helps to build confidence in the model. The comparison is often shown as a plot of observed against predicted values (Fig. 10.5) in which the responses observed in foods should be no faster than those predicted by the model for maximum confidence. Methods and issues in validation are discussed in Baranyi *et al.* (1999).

Once it has been validated, the model can be used for prediction. Models, in general, can be used only for interpolation. This means that models should never

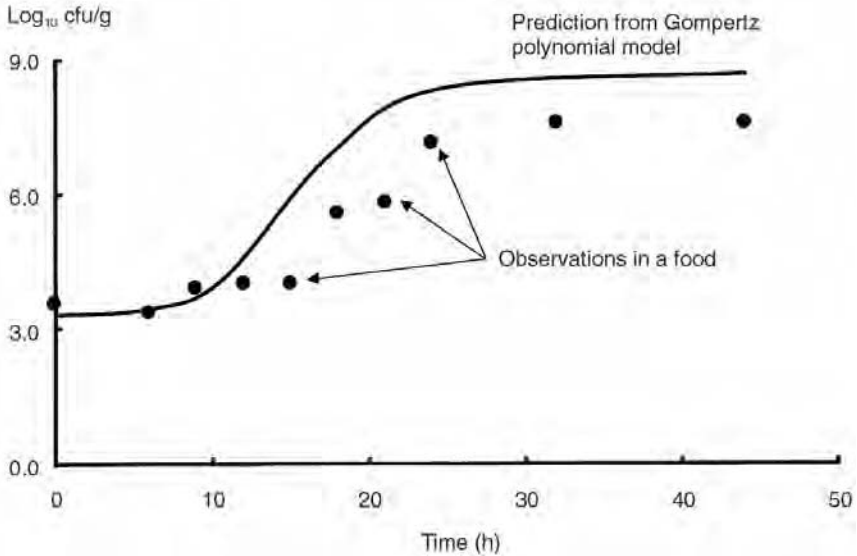


Fig. 10.4 An example of food validation data plotted against a predicted growth curve. Predictions and observations were for *Bacillus licheniformis* in custard at pH 6.14, NaCl 0.3% and 28°C. The prediction is from the Food MicroModel *B. licheniformis* model and the data were from J. D. Legan, P. A. Voysey and P. S. Curtis (unpublished observations).

be used outside the range where data were gathered. In some cases it is very hard to distinguish the areas where confident predictions can be made from the areas where there is no supporting data. Some statistical packages provide for an estimate of the confidence of single point predictions, using a similar process to validation. However, instead of using the 95% prediction interval, a 95% confidence interval is calculated for each prediction. The less confidence for a single prediction, the larger the confidence intervals. Confidence intervals for a single prediction will increase dramatically when predicting outside the measured data range.

10.3.2 Mechanistic modelling

The previous section discussed empirical models that describe experimental observations as a mathematical relationship but have nothing to say about underlying physiological or physical processes. Experience has shown that such models are adequate for many practical purposes in food safety management, but they provide no secure basis for extrapolation outside the range of the experimental data.

Mechanistic or deterministic models are built upon a theoretical understanding of microbiological behaviour. They have the potential to give more accurate predictions than empirical models and can explain why microbiological

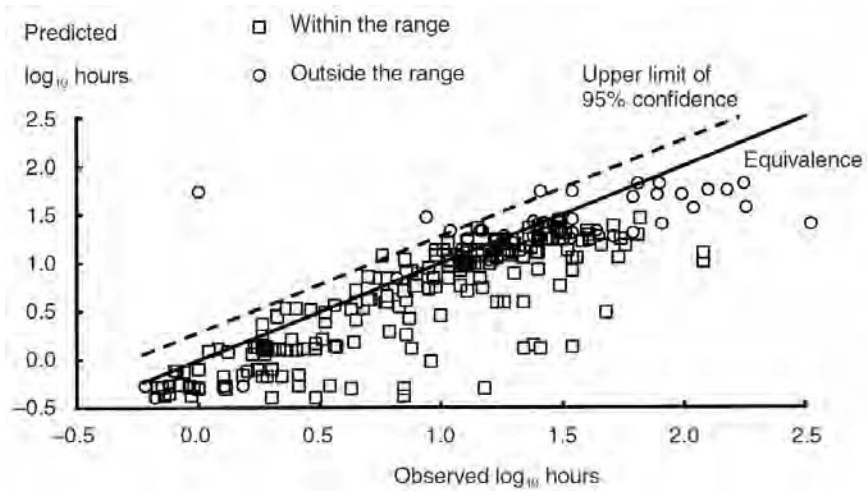


Fig. 10.5 An example of model validation across a range of conditions for predictions from Food MicroModel for growth of *L. monocytogenes* compared with literature data (adapted from McClure *et al.*, 1994).

behaviour varies. Mechanistic models also provide a better basis for extrapolation outside the range of the experimental data because it is the mechanism controlling the response that provides the foundation for the model. This added predictive capability is extremely valuable, but extrapolation without validation may still be dangerous because the mechanism itself may change, or prediction errors may become very large (Box *et al.*, 1978).

Many 'quasi-mechanistic' models have developed (Bazin and Prosser, 1992; McMeekin *et al.*, 1993; Ross, 1999) and have certainly proved useful for developing and testing hypotheses. The mechanisms postulated include rates of reaction between enzymes and nutrients, rates of protein denaturation in response to temperature changes and rates of enzyme synthesis by ribosomes. These models have all indicated linkages between the putative mechanisms and the observations of growth responses used in empirical models. However, in all cases the 'key enzyme' is unknown and a 'mechanistic' model whose parameters cannot be determined experimentally cannot be considered truly mechanistic (Heitzer *et al.*, 1991). Despite much progress, the observation by van Dam *et al.* (1988) remains essentially true:

Much is known empirically about rates of growth and substrate consumption for different microorganisms growing on various substrates. At the same time the biochemistry and molecular biology of the organisms is known in considerable detail. However, the question of how growth (and death) kinetics are related to the physiology of microorganisms is generally not well understood.

A rare example of a truly mechanistic model linking these elements is the work of Cayley *et al.* (1992) that relates the growth rate of *Escherichia coli* K12 under

osmotic stress to the intracellular accumulation of betaine and proline and the thermodynamics of osmoprotection.

Box *et al.* (1978) commented that judgement is needed in deciding when and when not to use mechanistic models. They indicated that a mechanistic approach is justified whenever a basic understanding of the system is essential to progress or when the state of the art is sufficiently advanced to make a useful mechanistic model easily available. Clearly the latter is not yet true in microbiology, but basic understanding is being actively pursued. As Cole (1991) observed: 'researchers in the field of predictive microbiology are striving to develop models for microbial life and death based upon an understanding of cell variability and physiology and that could be used to extrapolate to other conditions'. Truly mechanistic models will be developed in time as these activities help to develop our understanding of the links between microbial physiology and growth (and death) responses to environmental conditions.

10.4 Tools for modelling, prediction and validation

This section looks at the following types of software:

- Decision support in hazard identification.
- Packages that can be used in model development and validation.
- Current off-the-shelf models.
- Decision support systems.

10.4.1 Decision support in hazard identification

There are a number of decision support 'tools' to assist in determining whether a pathogen is, or could be, an important hazard in a given food/food process combination. These include various semi-quantitative scoring systems, decision trees and expert systems (see, e.g., Notermans and Mead, 1996; Todd and Harwig, 1996; ICMSF, 1996; van Gerwen *et al.*, 1997; van Schothorst, 1997) such as the one in Fig. 10.6. Decision trees enable the experience of others to be shared and can assist in decision making by presenting a structured series of questions relevant to the decision being made. In essence, the structured approach of risk assessment offers the same assistance for more complex decision processes.

10.4.2 Model development and validation

General statistical packages such as SAS and SPSS are useful in model development in such areas as experimental design, data handling, and establishing prediction and confidence intervals. While there are still no integral packages dedicated to the whole process of modelling microbial behaviour, there are a number of packages which are helpful in model design. A widely used tool for performing probabilistic modelling is @RISK. This package is a

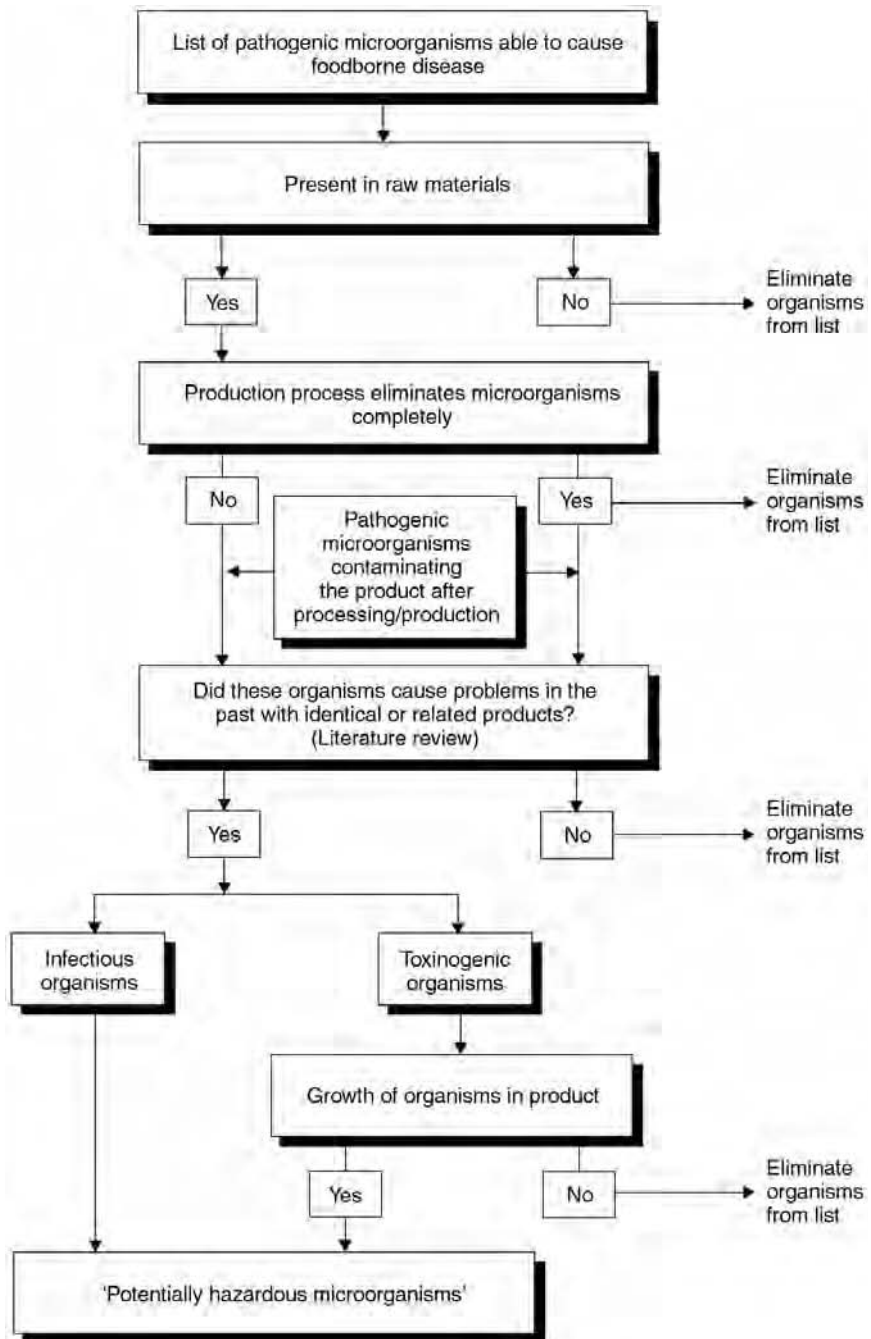


Fig. 10.6 A decision tree to aid identification of microbial hazards in finished foods. Reproduced from Notermans and Mead (1996).

risk analysis and simulation add-in for Microsoft Excel[®] or Lotus[®] 1-2-3. The package uses the technique known as Monte Carlo simulation to allow an assessment to be made of all possible outcomes. Uncertain values in a spreadsheet are replaced with statistical distribution functions that represent a range of possible values. The package recalculates a spreadsheet hundreds or even thousands of times, each time selecting random numbers from the distributions that were entered. The results are distributions of possible outcomes and the probabilities of getting those results. These results not only calculate the outcome in a given situation but also the likelihood of it happening. Packages such as BestFit are able to fit statistical distribution functions to measured data. These functions can then be entered into a package such as @RISK to perform simulations. As these packages are integrated into standard spreadsheet packages such as Microsoft Excel[®], they are easy to install and use. Two packages specifically designed to help create predictive models have been developed by the Institute of Food Research (IFR) in the UK: Microfit and DMFit. These are downloadable from the IFR website (www.ifr.bbsrc.ac.uk). Both help to fit, plot and analyse growth curves from microbiological data. The first one fits the model of Baranyi and Roberts (1994) to measure concentrations of growing bacterial population. The user can carry out a significance test to compare the specific growth rates of different growth curves. The second one, DMFit, is an Excel add-in, fitting, plotting and analysing many growth curves simultaneously.

10.4.3 Off-the-shelf models

Most of the models available have been developed as research tools rather than for commercial applications. The disclaimers of these sorts of software usually mention that these tools can be used for obtaining estimates rather than absolute predictions about shelf-life, stability or safety of products. The packages can give product and process developers a broad indication of what might happen with the products or processes that are assessed.

A good example of a package of this kind is the Pathogen Modelling Program, developed by the US Department of Agriculture (USDA), and available free over the Internet. This predictive microbiology application program was designed as a research tool for estimating the effects of multiple variables on the growth or survival of foodborne pathogens. It consists of both growth and inactivation models for a number of pathogens. Although most of the models are based on observations of microbial behaviour in broth cultures, some are based on observations in specific foods. Microbial behaviour in foods is similar to broths having comparable compositions. However, the user must be aware of additional factors in other environments that may affect microorganisms which are not within the experimental design parameters of the models. Available models include the following:

- Growth models for *Aeromonas hydrophila*, *Bacillus cereus*, *Clostridium perfringens*, *Escherichia coli* O157:H7, *Listeria monocytogenes*, *Salmonella* spp., *Shigella flexneri*, *Staphylococcus aureus* and *Yersinia enterocolitica*.
- Time-to-toxigenesis and thermal inactivation models for *Clostridium botulinum*.
- Non-thermal inactivation/survival models for *E. coli* O157:H7, *L. monocytogenes*, *Salmonella* spp. and *Staph. aureus*.
- Gamma irradiation survival models for *Salmonella typhimurium* and *E. coli* O157:H7.

The growth models for particular pathogens predict bacterial growth curves at user-defined sets of values for temperature, pH, salt concentration and water activity. In the case of some pathogens, the effects of preservatives and atmospheric composition can also be studied.

The *Food MicroModel* was developed by the British Government and is commercially available through the Leatherhead Food Research Association in the UK (www.foodmicromodel.com). After selecting the model for a particular pathogen, and then entering parameters such as temperature, pH, water activity and preservative concentrations, the predicted generation time or reduction time can be calculated. Results may be displayed as tables or graphs. Many of the models are for pathogens, but other models for spoilage microorganisms are being added. This system is considered more flexible and versatile in mimicking bacterial performance in real foods than the Pathogen Modelling Program (Baranyi and Pin, 2001).

The majority of public domain predictive models focus on the growth and survival of pathogenic microbes for obvious reasons. However, it is also important to be able to predict the growth of food spoilage organisms when considering the likely stability and shelf-life of food products. Campden and Chorleywood Food Research Association in the UK has addressed this need by developing a collection of models, the *FORECAST* system, which can be used to assess spoilage rates or likely stability of different product formulations (Betts and Earnshaw, 1998). Models are available for specific spoilage organisms, e.g. *Pseudomonas* species, for groups or organisms, e.g. Enterobacteriaceae, or for a mixture of spoilage organisms relevant to food commodities, e.g. fish and fish products. The models were developed in laboratory growth media and validated by comparison with published growth data and validation in appropriate food matrices.

The majority of models are kinetic growth models that can be used to predict growth rate and lag time, although more recent models have been produced that will predict non-growth or time to growth. The system is still under development and will be expanded to include other product specific models. *FORECAST* is available to potential users via an enquiry service that runs the models on behalf of clients after a detailed consultation with respect to their needs. The consultancy aspect of this approach allows subsequent expert interpretation and consideration of model validation status and there are currently no plans to make

it available as a software package. *FORECAST* is unique among modelling systems in that it is developed by an industry-driven research association and is able to ensure that further developments meet the current industrial microbiological needs. Further information regarding *FORECAST* is available from www.campden.co.uk.

The main advantage of such products as these is that predictions are produced in minutes rather than the days or weeks required for conventional challenge testing. Although they cannot replace challenge testing, the main role of the software is helping to identify when challenge testing is required and then in identifying the most relevant experimental parameters for challenge tests.

10.4.4 Decision support systems

A more recent development is the use of decision support systems for the prediction of product stability and product safety. A well-known system is the MIDAS system developed by the joint Unilever-Bestfood Research Laboratories (Kilsby, 1999). The system contains data on the parameters that influence the microbiological stability and microbial safety of certain foodstuffs together with modelling software. It is usually applied at the product design stage. MIDAS analyses a product's ingredients, processing methods and packaging systems to identify potential microbiological risks. The system is currently being expanded to include toxicological approval.

Wageningen Agricultural University has also developed a decision support called the Food Design Support System (Wijtzes, 1996). The system can be used to simulate a food product. Information on ingredients is combined with data on food processing operations and pathogen growth kinetics. Parameter values of ingredients of foods, such as water activity and acidity, and models for microbial growth and inactivation are used for the prediction of the microbial behaviour in the simulated food system. These values are drawn from the system database. If required information is lacking, reliable guesses of the parameters can be made. As an example, differing food distribution chains can be simulated to assess the impact, for example, of temperature abuse during distribution on food quality. The system can be used in such areas as product and process development and training. In future it will be possible to apply expert knowledge in production and development of foods to improve the quality of prediction.

Another decision support system developed by Wageningen Agricultural University is SIEFE: Stepwise and Interactive Evaluation of Food safety by an Expert system (van Gerwen, 2000). The SIEFE model provides a tool for bacterial risk assessment using various knowledge sources. The main goal of the SIEFE model is to analyse microbial behaviour during individual production processes. SIEFE uses a stepped approach to quantitative risk assessment. Risks are first assessed broadly, using order of magnitude estimates. Variations in process or product parameters can easily be evaluated at this level. These estimates help to highlight the main risk areas, which can then be studied in more detail. Both general and/or specific models, and various scenarios, can be

used to quantitatively describe levels of risk. Thirdly, even more accurate studies can be performed where necessary by using stochastic variables, for instance. All steps in the system are designed to be as transparent as possible, making it easier to assess the accuracy of the results and the assumptions on which they are based.

Several companies now use predictive models as marketing tools to illustrate the effects of ingredients such as preservatives. One of these systems, for example, describes the effect of lactate on bacterial growth and survival of *L. monocytogenes*. It contains simple yet effective models describing the relation between growth rate, shelf-life and product characteristics such as moisture level, salt concentration, pH and lactate concentration.

Ross and Sumner (in press) have developed a novel risk calculation tool to aid determination of relative risks from various product/pathogen/processing combinations. The tool is intended to assist those without extensive experience in risk modelling to provide a first estimate of relevant risk and for food safety risk management prioritisation (see Fig. 10.7). The user mouse-clicks on the appropriate descriptor in each box in response to 11 questions, and can nominate some specific numerical values. As a value is changed, the risk estimates (lower right) are automatically recalculated. To assist users to make selection, and to improve 'transparency' of the model, some of the weighting factors are specified in the list of descriptors. The underlying model translates these descriptors, using relatively simple mathematical relationships, into a range of risk estimates. Some estimates consider only the probability of illness, while others also consider the severity to estimate the risk of the illness and the numbers affected.

The model is based on a series of multiplicative factors that increase or decrease the estimate of the probability of the hazard occurring or the estimate of risk. Some factors, such as processing or cooking, have been assigned a value of zero, i.e. they are modelled to eliminate the risk. The model also recognises that even if a process completely eliminates the risk, re-contamination may occur, however, and re-introduce the risk. The risk estimate is 'truncated' so that no more than one illness *per* consumer *per* day is predicted. Some of the multiplicative factors are derived from fixed relationships, e.g. the risk of daily consumption compared with monthly or less frequent consumption. Similarly, the risk will depend on the size of the exposed population, and the proportion of them consuming the food. The susceptibility of the population to infection for a variety of hazard is based on epidemiological data. Hazard severity is arbitrarily weighted by factors of ten for each increasing level of severity. The frequency of contamination ('probability of contamination'), concentration of the hazard and the implications of subsequent processing and handling are also considered.

The spreadsheet, while providing estimates of risk, also helps to focus attention on the interplay of factors that contribute to the risk of foodborne disease, and can be used to explore the effect of different risk reduction strategies. Users must remember that some of the weighting factors are arbitrarily derived, however, and that the predicted effect of those management

A. SUSCEPTIBILITY AND SEVERITY	C. PROBABILITY OF FOOD CONTAINING AN INFECTIOUS DOSE													
1 Hazard Severity SEVERE hazard – causes death to most victims MODERATE hazard – requires medical attention or hospital admission MILD hazard – symptoms require medical attention MINOR hazard – patient rarely seeks medical attention 2 How susceptible is the population of interest? GENERAL – all members of the population SLIGHT – e.g. infants, aged VERY – e.g. neonates, very young, diabetes, cancer, alcoholic, etc. EXTREME – e.g. AIDS, transplant recipients, etc.	6 Probability of Contamination of Raw Product per Serving How often (in a 1000): Infrequent (1 per cent) Sometimes (10 per cent) Common (50 per cent) All (100 per cent) OTHER: If "OTHER" enter a percentage value between 0 (none) and 100 (all) <input type="text" value="5.0000%"/>	10 What increase in the post-processing contamination level would cause infection or intoxication to the average consumer? None slight (10 fold increase) moderate (100-fold increase) significant (1000-100 increase) OTHER: If "other", what is the increase (multiplicative) needed to reach an infectious dose? <input type="text" value="7.E+01"/>												
B. PROBABILITY OF EXPOSURE TO FOOD	7 Effect of Processing The process RELIABLY ELIMINATES hazards The process USUALLY (90% of cases) ELIMINATES hazards The process SLIGHTLY (50% of cases) REDUCES hazards The process has NO EFFECT ON the hazards The process INCREASES (10 x) the hazards The process GREATLY INCREASES (1000 x) the hazards OTHER: If "OTHER" enter a value that indicates the extent of risk increase <input type="text" value="1.00E-01"/>	11 Effect of preparation before eating Meal Preparation RELIABLY ELIMINATES hazards Meal Preparation USUALLY ELIMINATES (90%) hazards Meal Preparation SLIGHTLY REDUCES (50%) hazards Meal Preparation has NO EFFECT on the hazards OTHER: If "other", enter a value that indicates the extent of risk increase <input type="text" value="5.00E-02"/>												
3 Frequency of Consumption daily weekly monthly a few times per year once every few years	8 Is there potential for recontamination after processing? NO YES – trace (1% frequency) YES – trace (50% frequency) OTHER: If "OTHER" enter a percentage value between 0 (none) and 100 (all) <input type="text" value="2.90%"/>	<table border="1"> <thead> <tr> <th colspan="2">RISK ESTIMATES</th> </tr> </thead> <tbody> <tr> <td>probability of illness per day per consumer of relevant (Pop = Pop)</td> <td>1.26E-09</td> </tr> <tr> <td>total predicted illnesses/annum in population of interest</td> <td>4.50E+00</td> </tr> <tr> <td>COMPARATIVE RISK* in population of interest (severity * proportion consuming / prob. illness per consumer per day)</td> <td>6.32E-11</td> </tr> <tr> <th colspan="2">RISK RANKING (0 to 100)</th> </tr> <tr> <td></td> <td>42</td> </tr> </tbody> </table>	RISK ESTIMATES		probability of illness per day per consumer of relevant (Pop = Pop)	1.26E-09	total predicted illnesses/annum in population of interest	4.50E+00	COMPARATIVE RISK* in population of interest (severity * proportion consuming / prob. illness per consumer per day)	6.32E-11	RISK RANKING (0 to 100)			42
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RISK RANKING (0 to 100)														
	42													
4 Proportion of Population Consuming the Product all (100%) most (75%) some (25%) very few (5%)	9 How effective is the post-processing control system? WELL CONTROLLED – reliable, effective systems in place (no increase) CONTROLLED – usually reliable systems in place (slight increase) NOT CONTROLLED – no systems, untreated staff (10-fold increase) CRISIS SENSE OCCURS – (e.g. 100-fold increase) WERE THE SYSTEM – changed with significant consequences													
5 Size of Consuming Population Australia ACT New South Wales Northern Territory Queensland South Australia Tasmania Victoria Western Australia OTHER: Population considered: <input type="text" value="19,500,000"/> If "OTHER" please specify: <input type="text" value="270,000,000"/>														

Fig. 10.7 A proposed interactive food safety risk assessment tool developed in spreadsheet software. Details of its use and source are described in the text.

options may reflect only the assumption on which the model is based. Nonetheless, weightings can be changed easily if data are available to indicate a more appropriate weighting.

Ready to use software packages for probabilistic microbial risk modelling do not exist yet. Probabilistic modelling adds a new feature to microbial risk modelling as it helps describing and understanding natural variation in microbial behaviour. The amount of data needed for probabilistic modelling, however, is exponentially larger than the amount of data needed for deterministic modelling. Bringing together datasets from different modelling groups might help overcome this problem.

10.5 Future trends

Databases are useful for storing large quantities of data. A key issue for the future is how to integrate information from a range of databases. As an example, a database containing information on the microbial ecology of particular food stuffs could be connected to a database in which the kinetic properties of microorganisms are stored, which, in turn, could be linked to databases with processing and epidemiological data. If such a linked system of databases were available to a large number of researchers and risk assessors, allowing them to input data, models and knowledge in a structured way, microbiological risk

assessment would have a strong foundation on which to develop. Such a development would be particularly helpful in making the most of epidemiological and dose–response data which remains relatively fragmentary.

The best medium for such a system would be the worldwide web. Examples of such systems do not exist yet, but an outline for such a system is described in Fig. 10.1. Each block contains a database or a set of databases with the relevant information mentioned in that block. The combination of these databases or information blocks requires a so-called inference engine. This engine uses several strategies for combining information from these sources. The decision support systems mentioned earlier make use of a variety of strategies to search out relevant information. One uses product formulations to search for epidemiological data on similar products in order to identify relevant microorganisms. Another uses the kinetic growth properties of organisms as selection criteria, while another combines epidemiological and kinetic data. The selection of the most appropriate model, when several models are available for a microorganism in a certain foodstuff also needs addressing in such a system. Selection criteria might include assessment of the goodness of fit between the model and the problem to be addressed, continuous validation of existing models against new data, or assessment of such performance indicators as the conservatism with which a model predicts. It might be possible to employ several models to identify and take account of differing assumptions. Integrated systems, in which all information comes together, decisions are taken and predictions are made, are not to be expected within the next 10 years. International collaborations need to be forged where gathered information, data and models are put together. A framework as described above should be developed and extended with other initiatives, such as toxicological and epidemiological initiatives.

10.6 Sources of further information and advice

Some helpful guides are provided in the following section. Further information on some of the software packages mentioned can be obtained from:

- FoodMicromodel: Leatherhead Food Research Association, Randalls Road, Leatherhead, Surrey KT22 7RY, UK (www.lfra.co.uk).
- Lactate model: Optiform Listeria Control Model: PURAC America, 111 Barclay Boulevard, Lincolnshire Corporate Center, Lincolnshire, IL 60069, USA.
- SAS: SAS Institute Inc., SAS Campus Drive, Cary, North Carolina 27513, USA.
- SPSS: SPSS Inc. Headquarters, 233 S. Wacker Drive, 11th Floor, Chicago, Illinois 60606, USA.
- @RISK and BestFit: Palisade Corporation, 31 Decker Road, New Field, New York 14867, USA.

- Tablecurve2D: SPSS Inc. Headquarters, 233 S. Wacker Drive, 11th Floor, Chicago, Illinois 60606, USA.
- USDA Pathogen Modeling Program: PMP 6.0: USDA-ARS, 600 East Mermaid Lane, Wyndmoor, Pennsylvania 19038, USA (<http://www.arserrc.gov/mfs/pathogen.htm>).

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11

Microbiological criteria and microbiological risk assessment

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11.1 Introduction

Criteria related to the microbiology of foods may be applied with the intention of ensuring quality or protecting public health. Ideally, criteria are established only in response to a real need and crafted to prevent most effectively some undesirable outcome. This approach implicitly suggests that existing criteria related to food safety represent the outcome of deliberations that had identified a hazard, and the magnitude of the risk associated with that hazard, and points or stages in the farm-to-table¹ continuum that were critical to control of the risk. In practice, approaches to setting criteria have varied (see Chapter 2; Adams and Moss, 2000; Baird-Parker and Tompkin, 2000), creating an impediment to international trade in foods because of inconsistency in regulations among trading nations.

Microbiological risk assessment (MRA) may be considered to have its origins in the development of fair rules for international trade in food. The General Agreement on Tariffs and Trade (now the World Trade Organization) resolved in 1995 that demonstration of unacceptable risk to human, plant or animal health was the only reasonable basis for restriction to trade in foods. Formal risk assessment methods, already widely used in commerce, engineering, and environmental and public health analysis, were advocated as the means for comparing or evaluating those risks.

The potential to quantify foodborne public health risk, and/or to identify rational and optimal strategies to reduce it, offers enormous scope for the design

¹ We use this expression to denote all products from the point of harvest, catch or slaughter to the point of consumption.

of new food safety regulations that are ‘outcome based’, rather than prescriptive. These two applications of microbiological risk assessment were recognised by the Codex Alimentarius Commission (CAC, 1999) who described microbiological risk assessment as ‘a key element in ensuring that sound science is used to establish standards, guidelines and other recommendations for food safety to enhance consumer protection and facilitate international trade’.

Within the context of microbiological food safety risk assessment, this chapter considers the history of the development of both food microbiology criteria, and performance and process criteria. Discussion of the difficulties in establishing meaningful and practicable criteria demonstrates how increasingly risk-based approaches have been used to address those problems, culminating in the use of contemporary risk assessment methods and tools. The use of those approaches in the development of microbiological and process and performance criteria applied to foods is discussed and exemplified, as are potential applications of testing against microbiological criteria as an input to risk assessments.

11.2 Types of criteria

Two types of criteria related to the microbiology of foods can be differentiated. These are ‘microbiological’ criteria and ‘process and performance’ criteria (Baird-Parker and Tompkin, 2000).

11.2.1 Microbiological criteria

The following definitions, drawn from CAC (1997) and ICMSF (1986), illustrate the range of criteria related to the microbiological safety and quality of food.

A *microbiological criterion* for food describes the acceptability of a product or a food lot, based on the absence or presence, or a specified number, of microorganisms, including parasites, and/or quantity of their toxins/metabolites, per unit(s) of mass, volume, area or lot. Microbiological criteria are applied to differentiate food of acceptable quality from food of unacceptable quality. Since the advent of control systems such as hazard analysis critical control point (HACCP), they are usually not considered as routine methods to test individual units of food for compliance but as a means of verifying the performance of HACCP plans.

Microbiological criteria can be further categorised according to the intended application. A microbiological *standard* is a criterion that is part of a law or regulation. A *mandatory* criterion is enforceable by the regulatory agency having jurisdiction. Various national standards exist including those issued by, for example, the US Food and Drug Administration and US Department of Agriculture (NRC, 1985). The Codex Alimentarius Commission and the European Economic Community (NRC, 1985; Brown, 2000; Kumagai, 2000;

Schalch and Beck, 2000) are examples of organisations that set international standards that relate to the microbiology of foods. A microbiological *specification* is a criterion that is applied as a condition of acceptance of a food or ingredient by a food manufacturer or a public or private agency. Foods that do not comply are subject to rejection.

A microbiological *guideline* is a criterion that is used by a manufacturer or regulatory agency to monitor a food process or system. Guidelines aid in determining, for example, whether or not microbiological conditions at critical control points or for finished product are acceptable. Guidelines are usually *advisory* but may be *mandatory* depending on the source of the sample and if set by a manufacturer. A mandatory guideline set by a regulator, i.e. having the force of law is, by definition, a standard.

Microbiological criteria can relate directly to the hazard or to other organisms that, if present, are considered to correlate with the presence of the hazard (i.e. 'indicator organisms'), other properties of the food that are believed to be correlated with the presence of a hazard, or loss of quality suggested by total aerobic counts, or detectable levels of spoilage compounds. The selection of the target organism for use in microbiological criteria is discussed in ICMSF (1986). Examples from EU directives (EU, 2002) of microbiological criteria include the absence (per 1 g) of *Salmonella* in cheeses made from raw and thermised milk (Directive 94/46/EEC), or <300 faecal coliforms per 100 g of live bivalve molluscs (Directive 91/492/EEC), or that no minced meat should contain more than 5×10^6 aerobic mesophilic bacteria or more than 500 *Escherichia coli* per gram (Directive 94/65/EEC).

11.2.2 Process and performance criteria

Performance and process criteria are applied during the production of a food to ensure that the food manufacturing process eliminates, or reduces to acceptable levels, the risks of identified microbiological hazards. They are, thus, akin to critical limits as applied to critical control points within HACCP plans or analogous systems.² Often, the relationship between the criterion and the microbiological basis underlying it may not be transparent. This sometimes creates problems for regulators who have to enforce regulations and have to explain the reason for them to food processors who may see them as no more than bureaucratic impediments to their productivity! A performance criterion has been defined as 'the outcome of one or more control measures at a [processing] step or a combination of steps intended to ensure the safety of a food' (Baird-Parker and Tompkin, 2000). Examples include pasteurisation, or the design of heating processes to achieve a 10^{12} -fold reduction in the probability that a viable *C. botulinum* cell is present in a food (i.e. the

² For example, other preventive food safety programmes that do not necessarily follow the full seven steps of HACCP, such as the 'Food Safety Plan' concept promoted by Australian food regulatory authorities.

'botulinum cook'). In general, time–temperature criteria for thermal processing are established on the basis of their equivalence to the level of inactivation of target organisms at some reference temperature.

In Australia a tolerance of no more than a 10-fold increase in the number of *E. coli* on carcasses between slaughter and delivery to retail is being evaluated as an alternative to the traditional criterion that specifies that the product surface temperature must not exceed 5 °C after chilling. The problem with the latter, and similar, approaches is that even very short periods of temperatures above the 5 °C limit would, legally, render the product non-compliant. In practice, on a hot day, carcase surface temperatures could rise during the short time that it took to unload even a few carcasses from the transport vehicle to the cold room of a retail store (Sumner and Krist, 2002). Clearly, a deviation of few degrees for a few minutes does not render a carcase instantly unsafe, nor would it significantly increase the number of pathogens, if present.

The traditional approach is a process criterion intended to prevent unacceptable increase in *E. coli* or *Salmonella* (B. Shay, pers. comm., 2002), based on their minimum temperatures for growth, while the alternative approach is a performance criterion. To support the alternative criterion, a predictive model was used to define time–temperature combinations that would limit *E. coli* proliferation to less than 3.3 generations. To provide guidance to transporters a table of time–temperature combinations and the corresponding increase in *E. coli* was developed, effectively a matrix of process criteria, to support the performance criterion.

The Process Hygiene Index (Gill *et al.*, 1991) is another example of a process criterion. In this approach, the cumulative effect of time and temperature during processing of meat carcasses was related to potential growth of *E. coli* as determined by reference to a predictive model. Performance criteria, based on various percentile values of levels of performance of existing processing plants, were established and expressed in terms of an index related to the predicted number of generations of growth of *E. coli*. Critical pH and water activity limits proposed to guarantee shelf stability of uncooked fermented meats have been also defined (Leistner, 1995; European Economic Directive, 77/99 in EU, 2002) and are examples of process criteria.

11.3 Key issues in the use of microbiological criteria

Microbiological criteria can be used to design products and processes and to indicate the required microbiological status of raw food materials, ingredients or end-products at any stage of the farm-to-table chain, as appropriate. They can be developed by regulators charged with protecting consumer health and ensuring the quality of foods, or by food processors to formulate design requirements or to examine end-products for verification of a HACCP scheme (CAC, 1997). Thus, the uses of criteria fall broadly into those concerned with the role of regulatory authorities in protecting consumers and stated as legal requirements,

and those of industry in meeting those legal requirements and also for establishing and maintaining internal targets. Thus, industry uses of criteria include purchasing agreements and establishment and verification of HACCP plans.

Baird-Parker and Tompkin (2000) state that they 'are not aware where significant foodborne hazards to health have been reduced through application of microbiological criteria to a foodstuff as the primary means of control'. The oft-cited Sir Graham Wilson opined: 'Bacteriologists are better employed in devising means to prevent or overcome contamination than in examining more and more samples. Processing concerns the whole volume of food, sampling only a minute fraction of it' and that 'control of processing is of far greater importance than examining finished product' (Wilson, 1970). This view, and its application using HACCP or similar approaches, is now almost universally endorsed (EU, 2002; Adams and Moss, 2000).

Microbiological criteria cannot ensure the safety of foods, but may serve a role as reference or target values (Mossel *et al.*, 1995), as tools that can be used in assessing the safety and quality of foods, or as means of assessing the performance of an HACCP programme. Process and performance criteria are tools appropriate for ensuring product safety, and are consistent with the HACCP approach. In international trade, however, microbiological criteria are often used as a means of assessing product safety at the 'port of entry' because usually little is known of the methods of production or the efficacy of food safety systems operating in the country of origin. It is through this application of microbiological criteria that many problems have arisen.

11.3.1 Early uses of microbiological criteria

Baird-Parker (2000) traces modern food law to the nineteenth century, viz. the UK Adulteration of Food Act of 1860, and notes that legislation concerning food *hygiene* was first introduced at the beginning of the twentieth century. Food safety legislation continued to evolve during the twentieth century, including the introduction of the 'botulinum cook', and pasteurisation. Concerns over salmonellae and other pathogens led to development of microbiological standards. As these criteria increased in number it became increasingly apparent that many pieces of corresponding legislation enacted by individual countries were inconsistent, creating difficulties in international trade (NRC, 1985; Baird-Parker and Tompkin, 2000; Pourkomialian, 2000). Moreover, it was seen that many had no objective or scientific basis. For example, NRC (1985) stated that 'lack of sound guiding principles for the establishment of microbiological criteria has, at least in part, been responsible for the large number of standards and guidelines (particularly at the state and local level) that are impractical, unenforceable, and without uniformity'. Additionally, microbiological criteria have been, and largely still are, based on technical feasibility (CAC, 1997; ICMSF, 1998) rather than on an objective assessment of need based on scientific risk assessment (Baird-Parker and Tompkin, 2000). This situation has,

presumably, arisen because the establishment of objective and rational criteria is fraught with difficulty as is discussed below.

While there are situations in which microbiological criteria do have a useful role, such as in providing guidance on limits for safety (i.e. providing a 'line in the sand'), verification of HACCP plans and point of entry testing, NRC (1985) succinctly identified the problem of microbiological criteria: 'When microbiological criteria for foods are not based on definite needs, sound principles, and statistically solid background information, they may become a burden to the food industry, give a false sense of security to the public and lessen confidence in the ability of the regulatory agencies to regulate food supply'. As an example, Adams and Moss (2000) cite regulations introduced in Oregon in the USA concerning the microbiological quality of ground meat. After the regulations had been in effect for a number of years, their effectiveness was assessed. It was found that the standards had produced *no* significant improvement in quality but had resulted in significantly increased costs owing to rejection of material not meeting the standard and the costs of testing, and had effectively resulted in consumers being misled. The standards were eventually revoked.

In the face of growing national and international concern that microbiological criteria for foods often were not based on sound principles, a number of organisations considered how rational and objective microbiological criteria for foods could be established (NRC, 1985; ICMSF, 1986; CAC, 1997). Those organisations addressed the question of how to establish criteria and formulated rules for their development.

11.3.2 Principles for the establishment of microbiological criteria

The Codex Alimentarius Commission (CAC, 1997) presented³ principles for development of microbial criteria for foods that are generally consistent with those of NRC (1985). Given the status of Codex as an international food standards setting organisation under the auspices of the United Nations, their recommendations are described here. The principles expressed for establishment and specification of microbiological criteria implicitly identify the problems in setting them.

CAC (1997) resolved that microbiological criteria for foods should be based on scientific analysis and advice and, where sufficient data are available, a risk assessment of the foodstuff and its use. Thus, to develop a criterion it is necessary to:

- Identify any evidence of hazard to health, whether actual or potential.
- Consider the microbiological quality of the raw materials.
- Understand the effects on those microorganisms of any food processing steps that occur prior to consumption including commercial processing and home preparation.

³ The Codex guidelines were developed jointly with the International Commission on Microbiological Specifications for Foods.

- Establish the likelihood of additional microbial contamination and the consequences of the presence or growth of those contaminants in the food.
- Consider the intended use of the food.
- Consider the relative susceptibilities of expected consumers of the food.
- Establish the costs of implementing a criterion in relation to its benefits.

As has been discussed in earlier chapters, the above list features many of the aspects of a microbiological food safety risk assessment including hazard identification (Chapter 4), dose–response assessment (Chapter 5) and exposure assessment (Chapter 6). Notably, the recommendations do not suggest appropriate levels of protection of public health, or some other target with which the criteria should comply. The above considerations reflect one of the main reasons for the introduction of risk assessment methodology to microbial food safety, i.e. the need to draft objective microbiological criteria to harmonise international trade in food.

11.3.3 Specification of criteria

If consideration of the above objectives indicates that a criterion is desirable and feasible, there are requirements for the unambiguous specification of criteria themselves. These, based on NRC (1985) and CAC (1997), are that the criterion:

- Includes a clear description of the food to which the criterion applies.
- Includes a clear description of the pathogen/toxin of concern.
- Details the analytical methods to be used to detect and/or quantify the pathogen/toxin of concern.
- Details the number and size of samples to be taken and the point in the farm-to-table continuum to which the criterion applies.
- Details the limits to be applied and the proportion of samples that must conform to these limits for the batch to be considered acceptable.

The requirement for each of these elements of a microbiological criterion are discussed in various texts and reviews (e.g. NRC, 1985; ICMSF, 1986; Adams and Moss, 2000). Note, particularly, that the last points consider the number and size of samples, and the proportion of samples that must comply. These requirements point implicitly to the need to consider risk, i.e. the probability of exposure and the likely severity of illness, and are important considerations in specification of sampling plans appropriate to the risk. Note also that the specifications require that the point in the farm-to-table chain at which the criterion applies must be nominated. This points to one of the difficulties of establishing microbiological criteria in comparison to chemical safety criteria, i.e. microbial hazard levels and the attendant risk can increase or decrease dramatically during the normal handling and processing of many foods (ICMSF, 1998; Lupien and Kenny, 1998).

11.4 Dealing with variability, uncertainty and hazard severity: sampling plans

In the 1970s, before the HACCP concept was widely implemented, the International Commission for Microbiological Specifications for Foods considered the needs of compliance testing. In response to the need for objective criteria the Commission developed a series of sampling schemes appropriate to different levels of 'risk' (ICMSF, 1974, 1986). In that process, factors affecting risk were recognised, including the potential for change in the level of the hazard (pathogen or toxin) between manufacture and consumption, the levels of the target beyond which a substantial likelihood of health or 'utility' hazard exists, and the severity of the consequence of exposure to the hazard (e.g. quality issues through to severe illness). In addition, these variations were coupled with *attributes sampling plans* whose probability of detecting a pathogen, if present, in a lot of food could be determined. Thus, the ICMSF scheme to some extent considered both variability and its consequences, and uncertainty in the result of the test. Quantification and differentiation of the effects of uncertainty and variability continue to be areas of concern in microbiological risk assessment (CAC, 1997; Cassin *et al.*, 1998b; Nauta, 2000).

11.4.1 Variability and sampling plans

In testing against a microbiological criterion it is assumed that the analytical results obtained are an accurate reflection of the quality of the whole batch of the food. Microorganisms are rarely distributed evenly or randomly throughout a food. One way to increase confidence in the representativeness of the sample is to increase the size, or number, of samples but this carries an increased cost and requires more product to be consumed in testing. The only sampling plan that can provide 100% confidence requires sampling of the entire batch. Currently, all test methods are destructive, so testing of the total batch is not feasible. All sampling plans are, in consequence, a compromise between what is practicable and yet offers reasonable confidence in the representativeness of the test result. Thus, all carry some probability of an incorrect result, which introduces additional types of risk. The *processor's risk* is that the test result leads to rejection of acceptable product, while the *consumer's risk* is the possibility of unsafe product passing undetected and being released for sale.

The mathematics of sampling plan design is discussed in detail in ICMSF (1986). Two main types of sampling plan are recognised, and are described below.

Variables sampling plans

Variables plans use the full range of numerical data describing microbial loads on the foods of interest and are based on the known mean and standard deviation of log-transformed counts of the product being tested. Consequently, they can be applied only to situations in which the microbial loads are known to be

distributed log-normally. Variables plans are more appropriate to producers who regularly perform microbiological testing of their products. Such information is rarely available to a regulatory authority or a purchaser who, consequently, will usually default to attributes plans.

Attributes sampling plans

Attributes sampling plans test against a single criterion or attribute, such as the presence of *Salmonella* in 25 g or the proportion of sample units that contain greater than 100 cfu g⁻¹ of the target organism. Unlike variables sampling plans, the magnitude of the deviation between the number of microorganisms in the sample and that specified in the criterion is not considered – samples simply either pass or fail. Attributes plans are described as two-class or three-class plans. Both types can be characterised by three elements:

1. n , the number of samples taken from the batch of product being tested.
2. m , the attribute or condition that is being assessed.
3. c , the maximum proportion (or number) of the samples that do not satisfy the requirement (m) but for which the batch is still considered to be acceptable.

In three-class sampling plans a fourth characteristic is needed:

4. M , an attribute or condition which, if exceeded, is completely unacceptable and that if exceeded in any sample leads to rejection of the entire batch.

Sampling plans are usually described in terms of these three or four values. For example, an $n = 5$, $m = 100$ cfu g⁻¹, $c = 2$ two class plan involves testing five samples from a lot. The lot is acceptable if at least four out of five samples have less than 100 cfu g⁻¹. If the results for five samples were: <10, 80, 50 and 150 and 45 000 cfu g⁻¹ the two-class sampling scheme presented would lead to acceptance of the batch because no more than two samples exceeded m . If m were reduced to 10 cfu g⁻¹, or c reduced to 1, or if the sampling plan were extended to a three-class plan with $M = 1000$ cfu g⁻¹, the same batch would be considered defective and rejected. Thus, the specification of a sampling plan dictates the probability of acceptance of a lot and dictates the stringency of a criterion.

As discussed more fully later (Section 11.6) the values chosen for m and M reflect tolerance levels, i.e. levels of the target organism considered to represent an unacceptable level of hazard but ICMSF (1986) notes that for a pathogen m (or M) may be zero or a small number corresponding to the level of detectability in a test. If the target organism represents a health hazard m (or M) values should relate the levels of bacteria to probability or severity of illness using epidemiological or laboratory data in combination, animal feeding studies, etc. ICMSF (1986) also notes that the maximum amount of food likely to be eaten at any one time, and the sensitivity of the group likely to eat the food, should also be considered.

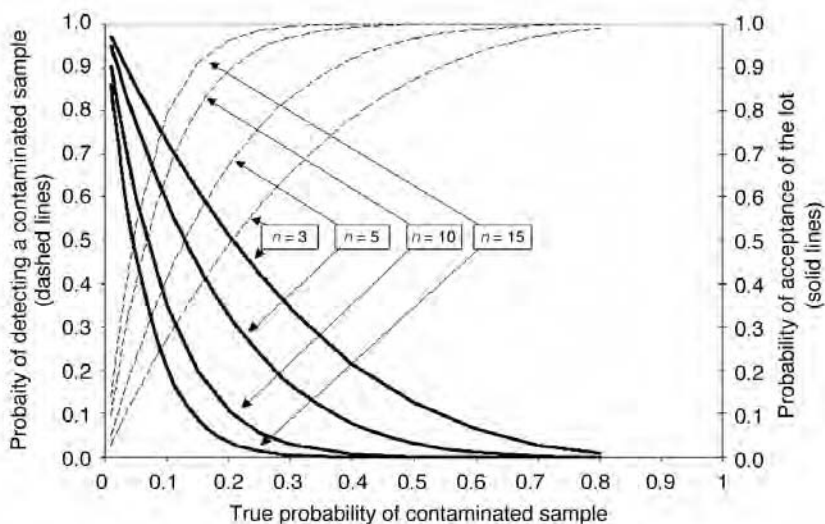


Fig. 11.1. Operating characteristic curve showing the effect of increasing the number of samples, when $c = 0$. The dashed curves relate the probability of acceptance of the batch under a given sampling plan to the true probability of drawing a contaminated sample from the batch.

11.4.2 Reliability of sampling schemes

While a more stringent plan can be expected to characterise more reliably the microbiological status of a given food, unless 100% of the food is tested, no scheme is 100% reliable because microorganisms are not evenly distributed within a food. As sampling plans are an integral part of microbiological criteria, their stringency should be expected to reflect the severity of the hazard. Before considering this point, it is illustrative to consider the probability of ‘success’ of a sampling plan.

The stringency of a sampling plan depends on n and c , i.e. the larger the value of n at a given value of c , the better the food ‘quality’ must be to have the same probability of being accepted by the sampling plan. The performance of a sampling scheme can be described by its *operating characteristic curve*, often abbreviated as *OC curve*. The OC curve relates the probability of acceptance of a lot of given quality as a function of the sampling scheme. An example is given in Fig. 11.1.

Figure 11.1 depicts the effect of the stringency of the sampling scheme on the probability of detecting a contaminated batch. It illustrates that when actual contamination levels in the batch are low (i.e. very few samples would contain a cell of the target organism)⁴ the probability of accepting the batch is always high,

⁴ It must be recognised that the target microorganisms present in a food may not be uniformly and randomly distributed, but may exist in clumps. If non-randomness occurs, an appropriately large sample size may be able to overcome the problems potentially caused. Jarvis (1989) states that only for low-density populations will randomness be a reasonable assumption, but that the calculation

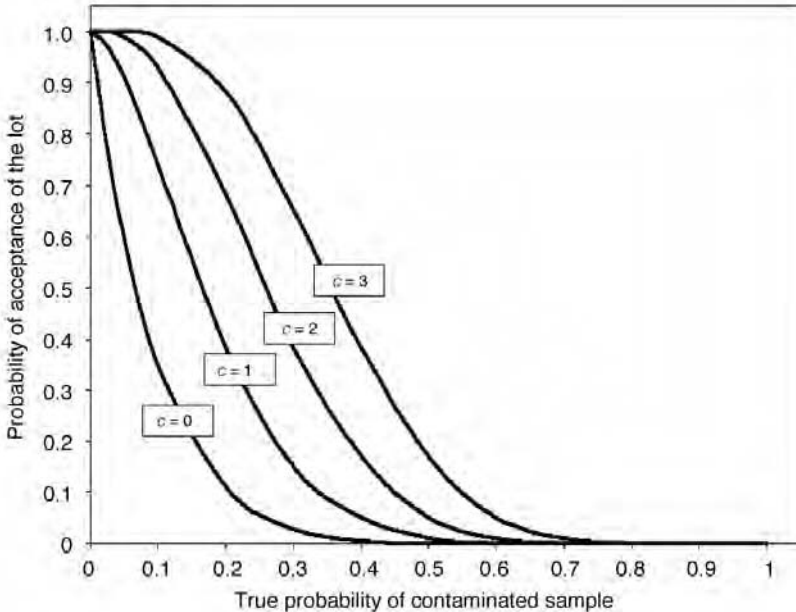


Fig. 11.2 Operating characteristic curve showing the effect of increasing the number of positive samples accepted before rejection of the batch for an $n = 10$ two-class scheme.

regardless of the scheme chosen. This illustrates the difficulty of using end-product testing to manage the threat of low infectious dose pathogens. It also illustrates the futility of end-product testing when very large production volumes are involved. Even if only a small proportion of units are contaminated, the effects can be catastrophic, as a 1998/99 outbreak of listeriosis in the USA demonstrated (Anon., 1999). In that case it was believed that contamination levels were low and sporadic, but because of the scale of production over 100 people became seriously ill over a period of several months before the outbreak was recognised and resolved. Figure 11.2 illustrates the effect of increasing c , the number of 'failures' tolerated before the batch is rejected, and the true level of contamination on the probability of accepting an unacceptably contaminated batch.

These figures illustrate there is no practical method of guaranteeing the microbiological safety of every item of food consumed. Intuitively, however, differences in the processing, distribution, microbial ecology, frequency of consumption and intended use of foods lead to differences in risk. While sampling is not the method of choice for quality and safety assurance of foods at the manufacturing level, in a situation where testing is used to assess the quality of a food (e.g. port of entry), there is a need to acknowledge these differences in

advantages associated with the assumption of random dispersion have often been considered to outweigh the disadvantages of rejecting the hypothesis for randomness.

risk with different intensities of sampling. This need was recognised by ICMSF (1974, 1986) who developed a series of sampling plans.

11.4.3 Sampling plans and risk

ICMSF (1974, 1986) stated that a sampling plan must consider:

- The type and seriousness of the hazards implied by the microorganisms for which the test is made.
- The conditions under which the food is expected to be handled and consumed after testing.

This led them to develop 15 different categories of risk, and to recommend sampling schemes of increasing stringency appropriate to each of them, as shown in Table 11.1.

Table 11.1 is a form of risk-based decision-tree, and its development by the ICMSF represents an early form of semi-quantitative risk assessment. Other schemes have been developed that attempt to include the idea of risk (i.e. probability of exposure to a disease causing dose and severity of illness) to aid

Table 11.1 Suggested sampling plan of ICMSF (1986) based on 15 cases of stringency according to risk-affecting factors

Type of hazard	Conditions in which food is expected to be handled and consumed		
	Reduce degree of hazard	Cause no change in hazard	May increase hazard
No direct health hazard			
Utility (e.g. general contamination, reduced shelf-life and spoilage)	Case 1 3-class $n = 5, c = 3$	Case 2 3-class $n = 5, c = 2$	Case 3 3-class $n = 5, c = 1$
Health hazard			
Low, indirect (e.g. indicator organism)	Case 4 3-class $n = 5, c = 3$	Case 5 3-class $n = 5, c = 2$	Case 6 3-class $n = 5, c = 1$
Moderate, direct, limited spread	Case 7 3-class $n = 5, c = 2$	Case 8 3-class $n = 5, c = 1$	Case 9 3-class $n = 10, c = 1$
Moderate, direct, potentially extensive spread	Case 10 2-class $n = 5, c = 0$	Case 11 2-class $n = 10, c = 0$	Case 12 2-class $n = 20, c = 0$
Severe, direct	Case 13 2-class $n = 15, c = 0$	Case 14 2-class $n = 30, c = 0$	Case 15 2-class $n = 60, c = 0$

microbial food safety decisions (Corlett and Pierson, 1992; Huss *et al.*, 2000; Ross and Sumner, 2002). The latter schemes, however, are directed to toward prioritising risk management actions rather than establishing testing regimes.

11.5 Microbiological criteria and food safety assurance: food safety objectives

Numerous problems with microbiological criteria have been recognised and, as indicated above, remain. Currently, if nations use different management strategies for the control of a common problem, the only way to determine the compliance of imports is some form of point of entry sampling programme. These sometimes lead to disputes between nations. For example, differences in approach to management of the risk of *Listeria monocytogenes* are evident between some European nations and the USA. Some nations impose a 'zero tolerance'⁵ for the presence of *L. monocytogenes* in ready-to-eat foods, while others adopt a more liberal approach.⁶ European companies exporting high-value food products can suffer severe financial loss if their products are rejected at the US port of entry under a more stringent set of criteria than applies in the country of origin.

The wide adoption of the HACCP system promises to obviate many of the criticisms of microbiological standards. In the HACCP paradigm, testing against standards is used only to verify the performance of the HACCP plan, not the integrity of individual units or batches. Just as HACCP offers to obviate the need for compliance testing it was recognised that if the *equivalence* of HACCP, or analogous, food safety assurance programmes used in different trading nations could be demonstrated, the problems and expense of port-of-entry testing could be considerably reduced. Thus, risk assessment techniques were proposed also as a means of demonstrating the degree of equivalence of microbial food safety control measures between nations (ICMSF, 1998; Hathaway, 1999). The needs identified above for objective regulations and for 'harmonisation' of regulations governing international trade in foods, led to calls to apply the principles of formal risk assessment to microbial food safety management (e.g. Royal Society, 1992; ILSI, 1993; CAST, 1994) which were endorsed in the Sanitary Phytosanitary (SPS) Agreement at the conclusion of the Uruguay Round of GATT in 1995.

⁵ Zero tolerance is jargon for a sampling scheme that allows no positive sample for the organism of concern, usually in a relatively large sample unit, e.g. multiple samples of 10 or 25 g.

⁶ Several studies (e.g. CX/FH, 1999) have concluded that the incidence of listeriosis in nations with a 'zero tolerance' policy is not significantly different from those with more 'liberal' approaches. For example Canada and/or Germany, which do not have a complete zero tolerance policy, have about the same per capita incidence of listeriosis as the USA, Australia or Italy, which do have zero tolerance policies for ready-to-eat products that support the growth of *L. monocytogenes*.

11.5.1 Food safety objectives

To establish microbiological food safety criteria, risk managers must determine what constitutes a tolerable risk, i.e. how often will someone become ill, and how badly (ICMSF, 1998; Teufel, 1999). Thus, ICMSF (1998) noted that as techniques in microbial risk assessment develop, risk managers will have to analyse and interpret risk distributions that take into account both the inherent variability of biological systems and the uncertainty of the data available. For example, instead of stating that there is a zero tolerance for a specific pathogen, a risk-based criterion might more accurately indicate that >99% confidence is required that the level of the target pathogen is <1 per kilogram. Importantly, it must not be forgotten that risk is not borne equally by all members of the population. Consideration of this variability, in deliberations about 'tolerable' risk, must also include the risk experienced by those with higher than 'average' exposure or lower than 'average' resistance to the hazard.

That statement of acceptable level and frequency of contamination becomes the 'food safety objective' (see also Chapter 9). A food safety objective (FSO) is defined as a statement of the frequency or maximum concentration of a microbiological hazard in a food considered acceptable for consumer protection. As such, an FSO may be a microbiological criterion.

Implicit, however, in an FSO is the concept of an appropriate level of protection of public health. It is, in theory, possible to translate the FSO into a tolerable level of foodborne illness. The FSO concept was developed by ICMSF (van Schothorst, 1998) who recommend several steps for the management of microbiological hazards in food based on the application of existing Codex documents. The steps include the conduct of a risk assessment and an assessment of risk management options, the establishment of an FSO which should include a quantitative description, and confirmation that the FSO is achievable by application of GHP and HACCP. Only where appropriate is it proposed that a microbiological criterion be established, in accordance with principles outlined earlier. Van Schothorst (1998) also states that FSOs are to be established by government agencies, while elucidation of the complementary HACCP requirements is the province of industry.

Two uses of risk assessment for the assurance of microbial food safety can now be differentiated.⁷ The first of these broadly involves providing decision support for setting of objective microbiological criteria, i.e. limits for the numbers of organisms, or their toxins, or their frequencies of occurrence, in foods that are considered tolerable, and those that are not. A second aspect involves use of the *tools* and approaches of risk assessment to determine where process and performance criteria will most effectively minimise public health risk and to determine what those criteria should be to achieve the FSO.

⁷ Other uses that have been recognised include the identification of risk management options, prioritisation and allocation of resources for food safety management.

11.6 Using microbiological risk assessments to set microbiological criteria

Jarvis (1989) considered that to establish microbiological criteria, a decision has to be made concerning the maximum colony count that could be permitted in any circumstance, i.e. the values chosen for m or M . In the case of food quality, this level is the minimum spoilage level, but in the case of food safety, it was considered to be the minimum infective dose (MID). It is now more widely considered, however, that all infectious pathogens have a MID of 1, i.e. that each cell of a pathogen must be considered to have the potential to cause disease (see Chapter 5; Holcomb *et al.*, 1999; WHO/FAO, 2000, 2001). That potential, expressed as the probability of one cell of the pathogen causing illness in a consumer, is an index of the virulence of a pathogen.

Many factors affect the probability that a single pathogenic cell could cause disease. Thus, to establish meaningful microbiological criteria for protection of consumer health, it is necessary to understand the range of probability and severity of infection for a given dose of microorganisms.

Definition of the dose–response relationship for foodborne pathogens is a complex task. The response to a given dose is affected by the consumer's susceptibility, the strain of the pathogen, the effects of processing and storage conditions on the physiology of the cell, and the interaction of the pathogen, the food that harbours it and the physiology of the consumer at the time of ingestion. In addition, in terms of public health risk, the potential for secondary infections must also be considered.

11.6.1 Dose and hazard severity

The dose–response relationship for a foodborne microbial infection is considered not to have a threshold, i.e. if a pathogen is present there is always a finite risk of foodborne illness. Consumers may be unwilling to tolerate any risk but current consumer preferences for less-processed foods with fewer preservatives creates a paradox. Zero risk would require much *greater* levels of processing to kill or completely inhibit pathogens. As with all risks, there are costs and benefits and the concept of tolerable risk must first be accepted by all stakeholders. Explaining the nature of the costs and benefits, and the magnitude and severity of the risks being discussed, is a perfect example of the need for risk communication (see Chapter 8).

Several groups (Farber *et al.*, 1996; Buchanan *et al.*, 1997; Bemrah *et al.*, 1998; Lindqvist and Westöö, 2000; FDA/USDA/CDC, 2001) have attempted to develop dose–response relationships for *L. monocytogenes*. WHO/FAO (2001) developed an exponential dose–response model that is generally consistent with others presented. It is used here to illustrate the magnitude of risk. Those authors used symptomatic listeriosis as a disease end-point and concluded that, for an average consumer ingesting a single cell of *L. monocytogenes* of average virulence, the risk of infection was approximately 1 in 10^{14} .

To place that estimate into perspective, if an average consumer ingested a 50 g meal containing 100 cfu *L. monocytogenes*. g⁻¹ their risk of infection would be approximately one in 20 000 million. Most consumers eat several meals a day that could potentially be contaminated with *L. monocytogenes*, suggesting that total lifetime potential exposures is in the order of 100 000 meals. Thus, a total lifetime risk of infection – if each of these meals were contaminated at the above level – would be 1 in 200 000. If only one in ten meals was contaminated at that level, the total lifetime risk of listeriosis would be 1 in 2 000 000 people.

As noted earlier, the idea of an average consumer, or average exposure, is misleading and is one of the potential pitfalls of the use of stochastic modelling methods. Often foodborne disease arises from the convergence of unusual circumstances, and identification and estimation of the frequency of these will provide greater insight and be of greater concern than average circumstances. For example, it is known that most cases of listeriosis occur in consumers with identifiable predisposing factors. Some consumers are up to 1000-fold more susceptible to listeriosis than the population average (Peters, 1989; Jurado *et al.*, 1993, Rocourt, 1995). Similarly, inter-strain virulence of *L. monocytogenes* varies by up to 1000-fold (Stelma *et al.*, 1987; Pine *et al.*, 1990, 1991). Thus, certain circumstances could lead to a 10⁶-fold greater risk than estimated by the 'average', indicating both the wide variability in risk, and also the value of representing that variability through the use of stochastic models.

As noted in Section 11.3.2, a microbiological criterion should consider the intended consumer of the food. For example, baby foods or special dietary products for the elderly or immunocompromised should attract more stringent criteria because they are intended for consumers known to be more susceptible to a range of parenteral infections. Consideration of all of these factors should be undertaken in the hazard characterisation phase of microbiological risk assessment.

11.6.2 Developing measures of 'equivalent' food safety risk

The above discussion suggests that, by using the concept of risk, two approaches to setting criteria could be pursued. One would seek to limit the level of contaminants in *any* product, while the other would limit the frequency and level of contamination to achieve the required level of public health protection. The two approaches need not be mutually exclusive. Thus, while the establishment of a microbiological food safety criterion relies heavily on the hazard characterisation step of risk assessment, understanding the routes and probability of exposure to microbiological hazards – the aim of exposure assessment (see Chapter 6) – might also be used to establish criteria. But how realistic a proposal is this?

From the dose–response relationship for a foodborne pathogen it is possible to derive a series of combinations of contamination levels and exposure frequencies that lead to the same *probability of illness* per meal. We will call these sets of combinations 'iso-probabilities', but a more useful measure would

be 'iso-risks' – those combinations of contamination level and severities of illness that are considered equivalent. To compare the severity of the disease resulting from exposure from one hazard with that from another, a common measure of severity is needed.

A useful measure of disease severity is the Disability Adjusted Life Years (DALY) concept that was originally developed by Murray and Lopez (1996) and adopted by the World Health Organization to inform global health planning (AIHW, 2000). The DALY is a measure of the years of healthy life lost due to illness or injury: one DALY is one year of 'healthy' life lost due to sickness or, in extreme cases, death. DALYs are calculated as the sum of years of life lost due to premature death (YLL) and the equivalent years of 'healthy' life lost due to poor health or disability (YLD). The YLD considers the number of years that a disability is endured weighted according to the severity of the disability. Combination of the 'iso-probabilities' with a weighting for disease severity, for example based on the DALY characteristic of the hazard, provides a basis for 'iso-risks'. Were it possible to establish a universal tolerance level for the risk of foodborne illness, the concept of the iso-risk provides a means of setting product- and pathogen-specific specifications that lead to equivalent levels of risk for all foodborne hazards.

Figure 11.3 presents iso-risks for two pathogens with different dose–response relationships⁸ under the assumption that the dose–response relationship is well described by an exponential model. The iso-risk shown represents one illness per 1 million serves of a meal, i.e. contamination levels above the critical value are predicted to lead to more than one illness per million meals for the contamination levels shown. In the example given, the difference in infective dose of the pathogens requires that for an equivalent level of contamination, the pathogen with the lower ID_{50} can only be tolerated at much lower frequency of contamination to achieve the same iso-risk as the other pathogen. Alternatively, for the same prevalence of contamination, higher levels of contamination can be tolerated for the pathogen with the higher ID_{50} .

Use of the iso-risk concept would enable prioritisation of risks and equalisation of regulatory and industry efforts across all pathogen–product combinations to minimise food safety risks. The use of risk-per-serving as the measure of isorisk, however, has a limitation. Even with the same iso-risk, a food that is consumed by most people on a regular basis represents a much greater public health risk than a product/pathogen combination of equal iso-risk that is consumed infrequently by only a small proportion of the population. From a regulatory perspective, however, it is unlikely that iso-risks encompassing consumption patterns could be implemented because consumption could differ between regions and over time. Thus, risk expressed as risk-per-serving appears a more achievable means of comparing the risk of different product/pathogen combinations. The iso-risk concept as described also

⁸ Equivalently, the iso-risks could represent pathogens with equivalent dose–response relationships but with DALY characteristics 1000-fold different.

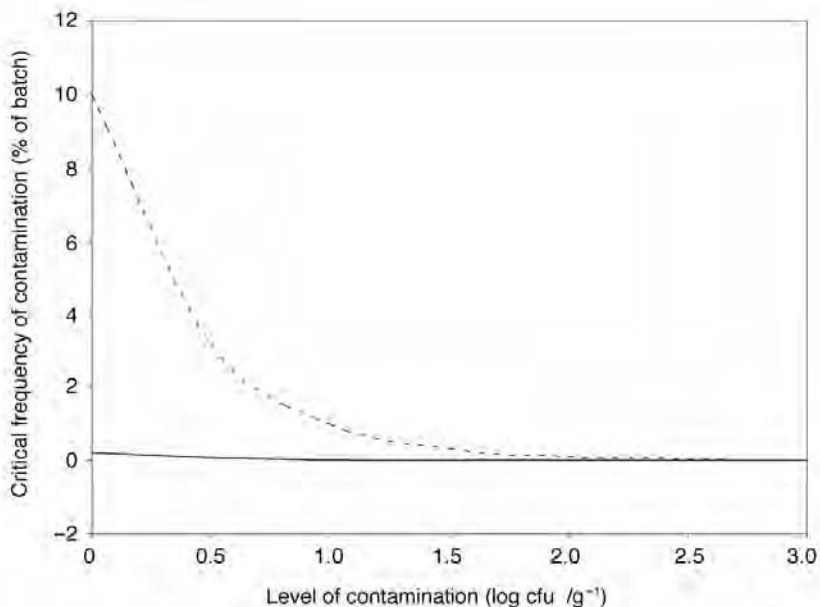


Fig. 11.3 A plot of 'iso-risks', i.e. that combination of dose and frequency that results in equivalent likelihood of illness. In the example shown the iso-risk represents one illness per 1 million meals for two pathogens, each with a different dose–response relationship. The dotted line represents a pathogen whose ID_{50} is $\sim 7\,000\,000$ cfu; the solid line $ID_{50} \sim 140\,000$.

neglects risk management considerations of risk perception such 'outrage' factors associated with particular types of illness or particularly susceptible groups. Furthermore, weighting factors to calculate DALYs for different diseases are not yet agreed. Thus, the iso-risk remains a theoretical concept.

11.7 Using microbiological risk assessments to develop performance and process criteria

There appears to be debate concerning the appropriate use of microbiological risk assessment. Many authors (Foegeding, 1997; Hathaway and Cook, 1997; Cassin *et al.*, 1998b; Buchanan and Whiting, 1998; ICMSF, 1998) have commented on the apparent similarities between risk assessment and HACCP approaches and pointed out that introducing the idea of risk in HACCP planning can differentiate trivial hazards from those genuinely requiring control. Baird-Parker and Tompkin (2000) state, however, that despite the similarities in some aspects of developing a HACCP plan and in performing a risk assessment, that risk assessment should remain the domain of governments, and intergovernment organisations.

Full, quantitative, risk assessment requires expertise in epidemiology, food manufacturing, food microbiology, and statistics and modelling. This expertise is unlikely to be found within any but the largest food companies and, indeed, some multinational food companies have created dedicated, in-house, food safety risk assessment teams. Similarly, in some nations, food industry research organisations have funded food safety risk assessments, sometimes in response to government initiatives.

Clearly, the support that formal risk assessment methods offer to decision making are of benefit to industry in objectively assessing new processes and protocols, and in demonstrating the necessity, or otherwise, of proposed regulations. Industry can also use the mathematical tools of risk assessment to set their own performance criteria to meet other criteria imposed on them. ICMSF (1998) concluded that 'the role of microbial risk assessment is to provide the information HACCP developers need to make more informed decisions'.

11.7.1 Identifying control points

A US Department of Agriculture risk assessment has considered risks from *S. Enteritidis* in egg shells and egg products and another is currently assessing risk from *E. coli* O157:H7 in ground beef. Both these assessments include as objectives the identification of possible strategies to reduce human illness from these product/pathogen combinations and comparison of the effectiveness of alternative risk reduction strategies (USDA, 1998, 2001).

If a stochastic model contains sufficient detail, sensitivity analysis (see Chapter 2) can be used to identify those steps in the farm-to-table chain that have most effect on the predicted risk and, by inference, those steps in a chain where efforts can potentially most effectively be exercised to control the food safety risk. Cassin *et al.* (1998a) considered that sensitivity analysis enabled risk assessment methods to identify potential critical control points, a point implicitly recognised also by Zwietering and van Gerwen (2000) who further considered that sensitivity analysis could be used to identify the main contributions to inaccuracy in the risk estimate.

Whiting and Buchanan (1997) developed a model to assess the risks associated with pasteurised liquid egg. From their analyses both time and temperature of pasteurisation were shown to be important determinants of risk, but temperature of pasteurisation was shown to be much more influential than the time and a deviation of only one degree below the intended pasteurisation temperature greatly altered the estimate of risk.

The use of sensitivity analysis in this rôle was also well illustrated by Cassin *et al.* (1998b) who considered the risk of enterohaemorrhagic *E. coli* in ground beef hamburgers in the north American culture. They termed that assessment a 'process risk model (PRM)' because it explicitly modelled the effects of many steps in the farm-to-table pathway so that the influence of each on the steps on the final estimate of risk could be determined. Using sensitivity analysis of model inputs they concluded that the factors most affecting risk were host

susceptibility, the concentration of *E. coli* O157:H7 in the faeces of those cattle shedding the pathogen, the cooking preferences of consumers and retail storage temperatures of ground meat. The relative success of three risk mitigation strategies was evaluated by modifying the values of the most important factors in the model that affected the risk, and which could feasibly be changed in practice. The new estimates of risk were compared with each other and the original values. The average probability of illness was predicted to be reduced by 80% using a strategy to reduce microbial growth during retail storage by lowering the storage temperature. This strategy was predicted to be more effective than another hypothetical approach that would reduce the concentration of *E. coli* O157:H7 in the faeces of cattle shedding the pathogen, and a third approach based on persuading consumers to cook hamburgers more thoroughly.

It should be noted, however, that the results of a sensitivity analysis are subject to the structure and assumptions inherent in the model, as noted by Cassin *et al.* (1998b). Zwietering and van Gerwen (2000) explain that sensitivity analysis is based upon correlation between *variability* in the output and *variability* in the input factors. For example, if a model predicting the extent of microbial growth included the assumption that temperature were controlled throughout the life of a product within a very narrow interval, the output might not be sensitive to temperature under those assumptions even though temperature is known to have a profound influence on the rate of growth of microorganisms.

11.7.2 Relationship between microbiological and process and performance criteria

Microbiological food safety criteria appear to be focused on the risk to an individual consumer, by specifying limits on the microbiological contamination of an individual unit of food (as adjudged by an appropriate sampling scheme, see below) commensurate with an appropriate level of protection of public health. This, in turn, should be commensurate with some overall level of population risk. Process and performance criteria are management tools, or in the terminology of Cassin *et al.* (1998b) 'risk mitigation strategies', designed to provide an overall level of population health protection. Clearly, these two aspects of microbiological specifications must be complementary: the process and performance criteria should be designed to limit risk and lead to compliance with the microbiological criterion. Performance and process criteria, then, can be considered as mechanisms to achieve an implicit microbiological criterion, though that criterion is often unstated, i.e. it is not transparent.

For example, Australian Standard C1 (ANZFA, 2002) requires a 1000-fold reduction in *E. coli* during the processing of uncooked fermented meats. This performance criterion will not ensure a safe product if the level of enterohaemorrhagic *E. coli* initially present exceed 10 000 cfu g⁻¹ for example and, appropriately, those regulations also require that the raw ingredients must contain <1 000 cfu 'generic' *E. coli* g⁻¹, i.e. a microbiological criterion. Similarly, while

pasteurisation conditions specify time–temperature limits they assume some level of microbiological quality of the raw milk entering the process.

Increasingly, consumers preferences are for less preserved products and food processors will ask questions such as:

- Can less severe processes be developed without increasing consumer risk?
- Are existing process criteria too severe?
- Were existing criteria developed with poorer control systems throughout the chain?

For example, Baker (1993) asked the question whether the thermal treatments to ensure the safety of canned meats against *C. botulinum* were overly conservative. His conclusion was that, given the current levels of production, and the current record of safety, data from more than 1500 years of production would be required to justify that a 12D reduction was needed.

Once a microbiological criterion has been established, it is, in theory, possible to establish performance and process criteria using the tools available in modern stochastic simulation modelling software discussed in Chapter 10. As a simple example, at the time of writing it is proposed that a total level of 100 cfu g⁻¹ *L. monocytogenes* at the point of consumption does not pose a significant threat to public health (ICMSF, 1996; European Commission, 1999; FAO, 1999; Brown, 2000). How can this be translated into a process criterion for foods that permit the growth of *L. monocytogenes*?

If manufacturers had data describing the frequency and level of contamination of their product it is possible using stochastic⁹ modelling tools to estimate a maximum ‘use-by’ period for their product that, under normal conditions of storage, would prevent *L. monocytogenes* from exceeding the microbiological criterion applied.

Using Analytica[®] software, a simple model was constructed that includes the effect of storage temperature, *L. monocytogenes* growth rate on the product, lag times before growth of *L. monocytogenes* commences, and initial level of contamination. Such a model is shown in Fig. 11.4, which is called an ‘influence diagram’. In the model, arrows indicate that the value in one block (representing a step or process) influences the value of the block to which it is connected. For example, storage temperature influences generation time, and generation time and initial contamination levels influence the time taken for the initial contamination level to reach 100 cfu g⁻¹ as does the lag time before growth in the product commences. Using cold smoked fish as an example, representative values of generation times at 5 °C estimated from literature and various predictive models were used. Storage temperatures were assumed to vary between 1 and 10 °C. A relative rate function (McMeekin *et al.*, 1988) based on a simple square root model (Ratkowsky *et al.*, 1982) was used to estimate the generation time at temperatures other than 5 °C. Contamination levels were drawn from the literature. The model was also constructed so that

⁹ As illustrated by Nauta (2000), simple deterministic models are unlikely to yield realistic results.

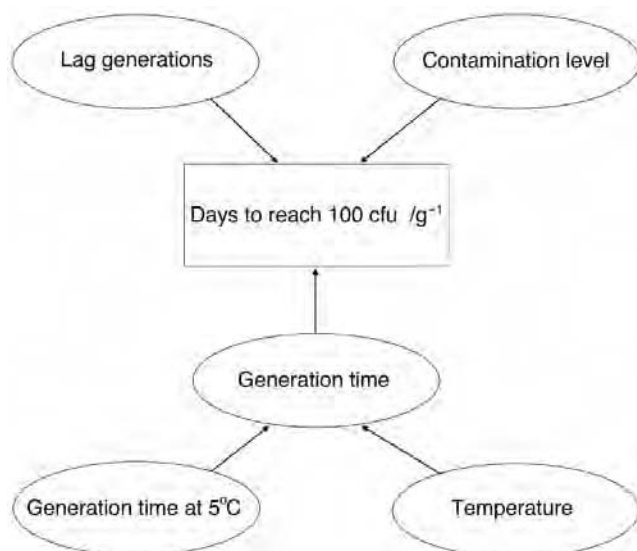


Fig. 11.4 Structure of a simulation model created in Analytica[®] to determine the maximum shelf-life of a product potentially contaminated with *L. monocytogenes* commensurate with not exceeding 100 cfu g⁻¹ at the point of consumption.

the effect of increasing lag times, or reformulating the product to achieve a 20% slower growth of *L. monocytogenes*, or reducing contamination levels by a factor of 10 could be compared. Full details of the model are shown in the Appendix. Estimates of maximum shelf-lives, including the effect of some modification to the product that reduces *L. monocytogenes* growth rate by 20%, by reduction of initial contamination levels by 90%, or by increasing the lag time by 60% are given in Table 11.2, which shows the results for different levels of confidence that compliance will be achieved.

Such an analysis can be combined with an attributes sampling plan to estimate the probability of a non-compliance being detected by testing. Given that the 100 cfu g⁻¹ criterion is applied at the point of consumption, there is no further opportunity for microbial growth. Because of the potential severity of the

Table 11.2 Estimated maximum shelf-life (days) of cold-smoked fish required to prevent product from containing more than 100 cfu g⁻¹ *L. monocytogenes* at the point of consumption at different levels of confidence

Confidence level	Initial values	Reduced growth rate	Increased lag	Decreased Contamination
50	25	30	41	42
90	8	9	11	11
95	11	13	15	15
99	13	15	18	18

disease, a Class 14 plan ($n = 30$, $c = 0$) would be appropriate for a regulatory authority to apply. This scheme delivers a 95.8% reliability when 10% of the batch is contaminated, 78.5% for 5% contamination, but only 26% if 1% of the batch is contaminated. Thus, if a manufacturer was able to ensure 99% of products were compliant, and if the regulatory authority had limited resources and opted for a plan less stringent than Plan 14 (see, e.g., Canadian sampling schemes for *L. monocytogenes*; Brown, 2000) the probability of detection would be low. For $n = 10$, $c = 0$, or $n = 5$, $c = 0$ the probabilities of detection of a non-compliant batch are 9.6% or 4.9% respectively when 1% of all sample units are contaminated at 100 cfu g^{-1} .

11.8 Using microbiological risk assessments to prioritise risk management actions

Another aspect of regulation setting is the prioritisation of regulatory resources, e.g. for inspection and control. Risk assessment methods could, ideally, be used to compare risks quantitatively from different sources. An obvious question is: 'why would one use risk assessment methods when the burden of disease, and hence risk, can be determined more readily from epidemiological data?'

The answer lies in the fact that for many foodborne diseases no data are collected. This may occur because no reporting system exists, because treatments are often instituted without diagnoses, because misdiagnoses occur (e.g. for some microbiological intoxications), or because many foodborne diseases are mild and people affected often do not seek medical attention. Estimates of foodborne disease in Australia (ANZFA, 1999; Sumner *et al.*, 2000) and the USA (Mead *et al.*, 1999) indicate that between one in five and one in ten consumers experiences a foodborne illness each year but acknowledge that these estimates are up to 100 times greater than the number of foodborne illnesses actually reported.

FDA/USDA/CDC (2001) used a risk assessment approach to estimate the contribution of 20 categories of ready-to-eat foods to the observed incidence of listeriosis in the USA. The risk from each category of food was ranked in order of importance, the aim being the development and use of tools to 'evaluate the effectiveness of current policies, programs and regulatory practices that will minimize the public health impact of this pathogenic microorganism'. In Australia, a New South Wales government agency used a risk assessment approach to prioritise risk management needs for that state's seafood industry. A semi-quantitative approach was used to rank the relative public health risk from 10 seafood product/hazard combinations (SafeFood NSW, 2001). A simple risk ranking tool, similar to that described in Ross and Sumner (2002), was used.

11.9 Using criteria in risk assessments

Many practitioners of MRA have found that the estimation of public health risk from microbiological contamination of foods is fraught with difficulty because of apparently intractable problems of estimation of microbial numbers at the point of consumption and characterisation of dose–response relationships for microbial pathogens and toxins (Cassin *et al.*, 1998b; Coleman and Marks, 1998; Lindqvist and Westöö, 2000). The former problems stem from the paucity of relevant data on contamination levels in foods at various times in the product history along the farm-to-table continuum and problems unique to MRA in comparison to risk assessment of foodborne chemical toxins, viz. that of the variability in behaviour and virulence of individual strains of microbial species, and their potential for self-amplification (growth) or complete eradication (e.g. by cooking) from foods. It may be possible to circumvent some of these data needs by recourse to expert opinion or other default assumptions. This section considers the potential use of criteria, or results of testing against criteria, as inputs to risk assessment.

11.9.1 Use of criteria as inputs to risk assessment

Criteria as default hazard characterisation

As illustrated in Section 11.7, which discussed the development of HACCP criteria and limits to satisfy microbiological criteria, in the absence of reliable data from which to derive a dose–response relationship, risk could potentially be assessed using microbiological criteria as default hazard characterisations. Such risk assessments would mainly be used as described in Section 11.7, or to determine the producer's risk. They could also have utility, however, to determine whether predictions of illness from such models accorded with epidemiological data and the results used potentially to assess whether such criteria were realistic and necessary, or not.

Compliance with criteria as default assumptions on inputs

The question can be asked: 'Can the existence of criteria and test results demonstrating compliance with them be used as default inputs to risk assessments?' In our opinion this should only be done using great caution. As was demonstrated in Section 11.4.2, sampling plans are not 100% reliable. The incidence of recalls, and outbreaks traced to in-plant contamination, reinforces that contamination events can pass undetected. (This criticism, however, applies equally to all sources of data that might be used in risk assessment, e.g. retail surveys, epidemiological data). Moreover, it is the frequency and circumstances of those non-compliance events that are likely to be the most important determinants of public health risk.

As was shown in Section 11.7 it is possible from the results of testing programmes, however, to determine the probability that non-compliant product is released for sale, i.e. the consumer's risk. Furthermore, from the results of

attributes sampling schemes it is also possible to infer contamination levels, as described below.

11.9.2 Using results from attributes sampling plans to enrich microbiological risk assessment

A specific problem in MRA has been to obtain data describing contamination levels for hazards that are usually assessed against presence or absence criteria (ICMSF, 1998; Marks *et al.*, 1998). Negative tests may indicate true absence of the pathogen, in which case the risk is zero, or may represent levels below the detection sensitivity of the method and sampling plan. As discussed in Section 11.4.1, there is always some probability of non-detection for any level of contamination. It is possible, however, to infer contamination levels from the results of presence/absence tests in some cases, and Jarvis (2000) provides useful calculations that may be able to be applied.

A two-class sampling plan is essentially a series of replicate analyses that can be considered to be a most probable number determination for a single inoculum level. From this it is possible to generate a most probable number (MPN) estimate of the contamination level. Calculations presented in Jarvis (2000) use the number of negative samples at a single dilution level to derive the probability of occurrence of zero defects. Those calculations lead to the relationship:

$$m = -(2.303/v) \times \log(z/n) \quad [11.1]$$

where: m = true density of organisms in the batch
 v = quantity of material tested
 z = number of sample units assessed by testing as 'negative'
 n = total number of sample units examined

For example, in a series of tests involving 25 sample units of 10 g each of which two were positive, the MPN is 0.0083 g^{-1} .

If no samples are positive, it is possible to estimate the maximum contamination level for various probability levels assuming random distribution of contamination within a lot.¹⁰ Equation 2, derived from the binomial distribution (Jarvis, 2000), gives the true number of defective units at some specified level of confidence:

$$d = 100 \times [1 - \sqrt[n]{1 - P}] \quad [11.2]$$

where: d = actual percentage of defective units in a lot
 P = probability (confidence level)
 n = number of samples examined

¹⁰ Jarvis (2000) notes that this is an unlikely situation, citing the results of Habracken *et al.* (1986) for the non-random distribution of salmonellae in dried milk products.

Thus, for a series of 20 negative results the true number of defective units at 95% probability is estimated by this method to 13.9%. If each test is based on 50 g of product, the maximum likely level of contamination is 13.9% per 50 g, or $0.139/50 \text{ g}^{-1}$, i.e. 0.0028 g^{-1} or 1 cell per 360 g.¹¹ Analogously, if 5 samples of 25 g each were tested and none of the target organism was detected, the maximum likely contamination level would be 0.018 g^{-1} .

From the above equations, it is possible obtain quantitative information from qualitative data.

11.10 Future trends

As demonstrated above, there is a history of risk-based thinking in the evolution of guidelines for setting microbial food safety and quality criteria. Mossel and Drion (1979) also identified components of a risk-based approach to microbial food safety assurance.

In principle, the use of stochastic risk assessment methods offers to revolutionise the establishment of food safety criteria. By determining the range of responses of humans to different doses of microbial pathogens or their toxins it is possible to establish levels of contamination and frequencies of exposure, and to determine the risk associated with different product/hazard combinations at desired levels of confidence, as illustrated in the 'iso-risk' example. Understanding the variability inherent in any system is important in making food safety decisions. This was elegantly demonstrated by Nauta (2000) who showed the different decisions that can result from 'point-estimate' approaches to those from stochastic approaches. Thus, in theory, stochastic and risk-based approaches enable rational and equitable microbiological, process and performance criteria to be established objectively and dispassionately. The establishment of criteria encompassing the concept of probability would also greatly facilitate transparency in the basis of regulations, to the benefit of both producers and consumers. But how feasible is this idealistic approach?

The first impediment appears to be to establish reliable dose–response relationships and, as others have noted (*see* Chapter 5), this is unlikely to be resolved in the near future. The second, even greater impediment, will be to determine what is an acceptable level of risk. The establishment of a microbiological criterion is a risk management problem. A risk assessment can characterise and quantify risk, but the level of risk that is considered *tolerable* is a societal question. This level may differ widely from nation to nation and region to region, depending on local factors affecting the perception of the costs and benefits associated with those sources of risk. The

¹¹ Conceptually it makes no sense to have less than one cell per unit but such values cannot be assumed to be equivalent to zero (ICMSF, 1998). Such results are interpreted as probabilities of finding a cell in that unit. For example, 0.018 g^{-1} would be interpreted one cell in 56 grams of product.

right of nations to set their own criteria commensurate with the level of public health protection they deem appropriate is enshrined under the SPS Agreement, provided that the same criteria are applied consistently to both domestic and imported products. Risk can also have many elements but is generally regarded to include the existence of a hazard, the probability of exposure to it, and the consequences of exposure if it occurs. Metrics for consequences of exposure are not yet well established, and currently limit the ability to compare risks associated with different hazards. The DALY concept begins to address this deficiency. Further, risk encompasses the magnitude of consequences of an exposure, and so is related to levels of production and consumption, i.e. in theory, a tolerable level in one product may not represent a tolerable risk in another, yet to differentiate on this basis seems inequitable.

Thus, in the short term, it is likely that microbiological criteria, or food safety objectives, will default to a set of tolerable, or achievable, frequencies and levels of contamination based on some consensus approach. Cassin *et al.* (1998b) concluded that, given the lack of necessary data and the consequent level of uncertainty in the results of risk assessment models, the most immediate application of risk assessment would be in the area of identification of risk-contributing factors and risk-mitigation strategies through sensitivity and scenario analysis. In other words, in the context of criteria, the most immediate application of risk assessment in criteria setting would be in establishing process and performance criteria.

While the quest for truly risk-based microbiological criteria will continue, it will require the development of new knowledge, and possibly new methods for analysing and integrating data. In the interim, the existing data, approaches and tools can greatly improve the rational development of performance and process criteria to decrease both producers' and consumers' risks.

11.11 Further reading

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Appendix: details of the simulation model used in Section 11.7

Model inputs

Lag generations:	Normal	Normal (5.000e+0, 5.000e−1)
	Shorter	Normal (2.000e+0, 5.000e−1)
Contamination levels:	Normal	10 exp(Beta(1, 10, 1, 100))
	Low	10 exp(Beta(1, 10, 1, 100))
Storage temperature distribution		Beta(4, 10, 1, 12)
Generation time (h) at 5°C:	Normal	Triangular(30, 48, 72)
	Modified product	1.2 * Triangular(30, 48, 72)

Equations in model

Lag generations = lag time/generation time

Time (days) to 100 CFU g⁻¹

$$= \left[3.32 \times \log_{10} \left(\frac{100}{\text{contamination level}} \right) + \text{lag generations} \right] \times \frac{\text{growth rate}}{24}$$

Generation time = growth rate at 5°C × Relative rate function

(based on McMeekin *et al.*, 1988).

Using as an example cold smoked fish, representative values of generations times at 5°C estimated from literature and various predictive models were used and estimated to range from 30 to 72 h with a most likely value of 48 h. Storage temperatures were assumed to vary between 1 and 10°C, with 4°C most likely. A relative rate function (McMeekin *et al.*, 1988) based on a simple square root model (Ratkowsky *et al.*, 1982) was used to estimate the generation time at temperatures other than 5°C, using a T_{min} of -1°C. Lag times were modelled as a function of the generation time at the sampled temperature, with the mean lag time set equivalent to five generation times, with a standard deviation of 0.5 generation times. Contamination levels were drawn from the literature and were described as ranging from 1 to 100 cfu g⁻¹ with a most likely value of 10 cfu g⁻¹.

The model was also constructed so that the effect of increasing lag times, or reformulating the product to achieve a slower growth of *L. monocytogenes*, or reducing contamination levels by a factor could be compared.

The model was executed with 30 000 iterations. Estimates of maximum shelf-lives, including the effect of some modification to the product that reduces *L. monocytogenes* growth rate by 20%, by reduction of initial contamination levels by 90%, or by increasing the lag time by 60% are shown in Table 11.2. Table 11.2 also shows the results for different levels of confidence that compliance will achieve.

12

HACCP systems and microbiological risk assessment

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12.1 Introduction

It is well known that the Hazard Analysis and Critical Control Point (HACCP) system was originally developed by the Pilsbury Company working with NASA and the US Army Laboratories at Natick to assure that food supplied to the manned space programme was microbiologically safe (Anon., 1973a; Bauman, 1974). The limitations of the end-product testing that was in general use by the food industry at that time were recognised by Pilsbury. These limitations included:

- the need to use a significant quantity of products to provide a representative sample for testing;
- the fact that only the tested sample could be completely assured as microbiologically safe;
- the problem that control of hazards was reactive.

A preventative approach to food manufacture was identified as providing a better assurance of food safety. An engineering system known as Failure, Mode and Effect Analysis (FMEA) provided the basis for this new approach. In FMEA potential failures are identified at each stage of an operation. Mechanisms to prevent these failures from occurring are then put into place. The similarities to HACCP are clear. In HACCP systems, potential and predictable food safety hazards are identified at each step of a food manufacturing or handling operation, and effective methods to control these hazards are identified. Those steps determined to be critical to control food safety hazards are managed through the monitoring of critical limits of the control measures, with a predetermined corrective action plan in case of failure to meet a critical limit.

Pilsbury initially used HACCP to assure microbiological safety. Since then HACCP principles have also been applied to physical and chemical safety hazards. HACCP has become internationally recognised as the preferred system to manage the production of safe food. HACCP systems, or systems based on HACCP principles, have been made mandatory by food safety legislation, for example in the European Union, the United States of America and Canada. HACCP has an increasing role to play in international food trade, especially within the concept of equivalence of trade agreements. International guidance covering the development, implementation and maintenance of HACCP as a food safety management system has been provided by the Codex Alimentarius Commission and the US National Advisory Committee on Microbiological Criteria for Food (Anon., 1992; 1997a; 1997b). There is now close agreement on the basic principles and terminology between these two sources of guidance.

12.2 Legal requirements for HACCP systems

Although Pilsbury presented a paper on their management system at a food industry conference in the early 1970s it took time for the potential benefits to be recognised. The 1973 U.S. Food and Drug Administration (FDA) canned food regulations represented the first regulatory use of HACCP principles to identify specified controls (Anon., 1973b). This legislation was followed much later by FDA mandatory HACCP regulations for domestic and imported fish and fishery products in 1995/1996 and the U.S. Department of Agriculture (USDA) HACCP regulation covering domestic and imported meat and poultry products (Anon., 1995a; Anon., 1996). Further U.S. regulations now require HACCP systems for fruit and vegetable juices and eggs. The regulations have brought in new requirements called Sanitation Standard Operating Procedures (SSOPs) that provide a solid foundation and act as prerequisites for the HACCP system.

In Europe, the European Community Directive 93/43 EEC (1993) states that:

Food business operators shall identify steps in their activities which are critical to ensuring food safety and ensure that adequate safety procedures are identified, implemented, maintained and reviewed on the basis of the following principles, used to develop the HACCP (Hazard Analysis Critical Control Point) system.

It then lists at least six of the Codex principles, missing out verification, validation and documentation. In addition there are three product specific 'vertical' directives, Council Directives 91/493 EEC, 92/5 EEC and 92/46 EEC (1991; 1992a; 1992b) covering fishery, meat and dairy products. These directives bring in an 'own check' requirement which includes keeping a written or registered record. The EU plans to harmonise these directives into a single regulation with HACCP as a legal requirement for all businesses covered by the regulations. Mandatory HACCP implementation is also in force or

proposed in a number of countries including Australia, Canada, Cuba, Mexico, New Zealand and Thailand, mostly for seafood products.

12.3 International guidance on HACCP implementation

Two key sources of international HACCP guidance are available from the U.S. National Advisory Committee on Microbiological Criteria for Foods (NACMCF) and Codex Alimentarius Commission (CAC). The NACMCF produced its first guide in 1989, followed by updated versions in 1992 and 1997 (Anon., 1989, 1992 and 1997b). The 1989 guide described seven principles and brought in the concepts of critical limits, corrective actions, record keeping and the HACCP plan. The later guides were modified to make the system easier to use and to reflect the evolution of the HACCP system. The 1997 guide includes a section on prerequisites and is in close agreement with the CAC guidance (Anon., 1997a).

CAC has produced a number of guides, e.g. 1993 culminating in the present guide adopted in 1997. Both the CAC and NACMCF guides identify seven key principles:

- Principle 1 Conduct a hazard analysis.
- Principle 2 Determine the Critical Control Points (CCPs).
- Principle 3 Establish critical limit(s).
- Principle 4 Establish a system to monitor control of the CCP.
- Principle 5 Establish the corrective action to be taken when monitoring indicates that a particular CCP is not under control.
- Principle 6 Establish procedures for verification to confirm that the HACCP system is working effectively.
- Principle 7 Establish documentation concerning all procedures, and records appropriate to these principles and their application.

In the same document Codex also usefully provides guidelines for the application of the HACCP system. These guidelines include a sequence of activities for the application of HACCP principles which are outlined in Table 12.1. In its Technical Manual No 38 Campden and Chorleywood Food Research Association (CCFRA) recommends a similar sequence of steps in HACCP implementation, which is compared with Codex and the standard introduction to HACCP implementation by Mortimore and Wallace in Table 12.1 (Anon, 1997c; Mortimore and Wallace, 1998). This shows that both CCFRA and Mortimore and Wallace put more emphasis on initial preparation and planning. CCFRA suggest a further preparatory stage of defining the terms of reference. This stage has also been referred to as establishing the scope of the study. The HACCP team should clearly define what the study is to cover, whether it is to be a specific product or process line, or a specific range of activities typically called a module. The terms of reference should clearly outline the food safety hazards that are to be considered in the study, whether they will be biological, chemical

Table 12.1 Approaches to HACCP implementation^a

Codex guidelines	Mortimore and Wallace	CCFRA manual
	Stage 1 Preparation and planning	
1 Assemble HACCP team	<ul style="list-style-type: none"> • understanding HACCP concept • identifying and training HACCP team • baseline audit • project planning (incl. improving prerequisite systems) 	2 Assemble HACCP team
	Stage 2 HACCP studies and planning	
2/3 Describe product and intended use	<ul style="list-style-type: none"> • terms of reference • describe product and intended use 	1 Define terms of reference
4/5 Construct and verify flow diagram	<ul style="list-style-type: none"> • construct process flow diagram 	3/4 Describe product and intended use
6 Conduct hazard analysis, identify control measures	<ul style="list-style-type: none"> • hazard analysis • identify CCPs 	5/6 Construct and verify flow diagram
7 Determine CCPs	<ul style="list-style-type: none"> • establish critical limits 	7 Conduct a hazard analysis, identify control measures
8 Establish critical limits	<ul style="list-style-type: none"> • identify monitoring procedures 	8 Identify CCPs
9 Establish monitoring procedures	<ul style="list-style-type: none"> • establish corrective action procedures 	9 Establish critical limits
10 Establish corrective action procedures	<ul style="list-style-type: none"> • validate HACCP plan 	10 Establishing monitoring procedures
	Stage 3 Implementing the HACCP plan	
12 Establish records and documentation	<ul style="list-style-type: none"> • determine implementation method 	13 Establish documentation and record-keeping
11 Establish verification procedures	<ul style="list-style-type: none"> • set up implementation team • agree actions and timetable (incl. training, equipment, record-keeping) • confirm implementation complete • verify implementation through audit 	12 Verification
	Stage 4 Maintaining the HACCP system	
	<ul style="list-style-type: none"> • defined standards and regular audit • ongoing maintenance • data analysis and corrective action • HACCP plan re-validation • update 	14 Review the HACCP plan

^a The sequence of steps given by Codex and the CCFRA has been altered to fit the sequence suggested by Mortimore and Wallace (1998) for ease of comparison. The original sequences are indicated by the numbering of the steps in each case.

or physical hazards or any combination of these. If quality aspects such as microbiological spoilage are to be included, this should be clearly stated. The start point and end point of the study should also be included. Depending on the approach, this could be from raw material purchase through to, at least, onward despatch of the finished product. The role of the prerequisites, if used, should also be clearly stated.

As well as the above guides, there have been a number of publications on the effective implementation of HACCP systems. These include those by bodies such as ILSI (Anon., 1997d) and ICMSF (Anon., 1988) as well as guides such as Corlett (1998) and Mayes and Mortimore (2001), the latter reviewing the experience of those with a background of implementing HACCP systems in practice. The following discussion picks up some of the key issues raised in these guides in the successful implementation of HACCP systems.

Wherever possible the HACCP study should be performed by a multi-disciplinary team with relevant technical/scientific expertise and knowledge of the operation. The team should be able to draw on the skills of a production specialist, an engineer, a quality assurance or control/technical specialist, hygiene management and, if the terms of reference include microbiological issues, a microbiologist. It is very useful to include staff with practical knowledge as well as managers. Typically teams comprising four to six people have been found to be effective. A team leader or chairperson needs to be assigned, and should, ideally, be the production specialist. The team leader is responsible for managing the study and team meetings. In many operations the team leader is the person with specific training and expertise in HACCP principles and implementation. A member of the team needs to take notes from team meetings and to draft the HACCP plan as it emerges from discussions within the HACCP team.

It is recommended that all members of the team receive basic training in HACCP principles. In the UK the Steering Group on HACCP Standards has developed both introductory and advanced level HACCP training standards on HACCP Principles and their Application in Food Safety (Anon., 1995b; Anon., 1999a). Training courses designed to this standard are specifically intended for HACCP team members concerned with developing and implementing HACCP systems. In small businesses it is likely that a team approach will not be feasible. If the study is undertaken by one person, it is recommended that they seek specialist external support or information to ensure the study will be effective. This role may be undertaken by suitably skilled industry consultants. The consultant should not prepare the HACCP plan for the business as it can be a barrier to understanding and ownership of the system by the business (Taylor, 2001). Whoever has been involved in developing the study should be recorded, together with the roles. The commitment of senior management is fundamental to the effective development and implementation of HACCP. The team must receive the resources and backing it needs.

The product(s) to be covered in the study must be fully described and defined in terms of the key parameters that influence the safety of the product. Key parameters could include composition (e.g. formulation, ingredients), physical/

chemical structure (e.g. Aw, pH), processing (e.g. pasteurisation or sterilisation heat treatment, or freezing), the packaging system, storage and distribution conditions and required shelf life. In addition to knowledge about the product the team must have a clear understanding of the expected uses of the product by the end-user or consumer. This should include the target consumer group for the product which may be a vulnerable group such as infants or the immunocompromised.

Prior to the Hazard Analysis it is necessary to examine carefully the product/process under study and prepare a flow diagram. The flow diagram should provide a clear, accurate and simple description of all the operational steps, in sequence, in the process. The team also needs to gather sufficient technical data for the study to proceed. Supplementary information such as site plans, equipment layouts, details of personnel routes, low care/high care separation and waste material flows can be very useful to the team. Transfer of product from one step to the next must not be forgotten. Typically this would be included in a specified step. A commonly found problem with flow diagrams is that product recycling or rework loops are forgotten. The format of the flow diagram is a matter of choice with no universal rules for presentation. It is important that, once the flow diagram has been prepared, it should be confirmed to ensure its accuracy and completeness. This should include confirmation of any variations in procedures during, for example, the night shift or at weekends. The prepared flow diagram must be amended to take into account any deviations identified. The flow diagram will also need to be amended as the process changes over time.

Once these preparatory stages have been fully performed, hazard analysis can begin. Using the flow diagram as a guide the HACCP team should list all the potential hazards that could realistically occur for each step of the process. HACCP teams often use brainstorming techniques to help identify these potential hazards. A hazard analysis must be conducted to determine which hazards must be eliminated or reduced to an acceptable level to assure food safety. Each hazard should be assessed with consideration of the risk of it occurring (i.e. is it realistic?) and the severity of the harm it could cause to the consumer. Considerations should include a combination of the following:

- the likelihood of the hazard occurring;
- the severity of the hazard to the consumer, including the numbers potentially exposed to the hazard and the vulnerability of those exposed;
- if the hazard is microbial, whether and how it survives or multiplies;
- production or persistence of toxins in foods;
- chemical or physical contaminants.

Currently many of the judgements made in hazard analysis are based on qualitative data. Indeed, hazard analysis has been identified as one of the most difficult areas in HACCP implementation (Mayes and Mortimore, 2001).

The HACCP team must then determine how the identified hazards are to be prevented, eliminated or reduced to an acceptable level by appropriate control measures. More than one measure may be required to control a specific hazard,

although, in some cases, one control measure might control a number of hazards. Modification of the process step or the operation may be required in the absence of a suitable control measure. Many physical and chemical hazards may be effectively controlled as part of the prerequisite programme.

The next HACCP stage is the determination of the critical control points (CCPs). CCPs are process steps where control measures are essential to control a hazard. Their identification requires professional judgement and experience which is best provided by a multi-disciplinary team. The use of a decision tree may help to determine the CCP and the reasoning behind it. A decision tree is a logical sequence of questions which can be applied to each hazard at each process step. A number of different versions of the tree have been developed, and training is recommended for their correct use. The application of the tree should be flexible and requires common sense. However, they do promote structured thinking and ensure a consistent approach is taken at every process step. However, they should only be used for guidance when determining the CCPs. There is no limit to the number of CCPs that may be identified in a process. Different businesses producing the same product may have different process steps as CCPs and a different total number of CCPs. Correct identification of the CCPs is essential to enable the business to focus its resources at those steps critical for food safety.

The following HACCP stage is the definition of the critical limits for the control measure(s) at each CCP. The critical limit is the value that separates safe from unsafe. Critical limits may be stated in legislation and codes of practice. In some cases experimental data will need to be collected before the critical limit can be set. Critical limits need to have a definable, achievable level which can be quickly and easily measured or observed through monitoring. Criteria often used for critical levels include measurements of temperature, time and pH. In many instances it is useful to include an operational target level. These levels are set for day-to-day management of the step and are more stringent than the critical limit. They will take into account normal process fluctuations. Tolerances may also be established which indicate the degree of latitude allowable around operational limits.

Monitoring the critical limits of the control measures at the CCPs is the next stage in HACCP development. Monitoring is a planned sequence of recorded checks, either by observation or measurement. It is an essential part of HACCP systems since it establishes that critical limits are being met and that the CCPs are all in control. The procedures used must therefore detect loss of control, or a move towards a loss of control. The frequency of monitoring should be sufficient to enable corrective action to regain control of the process, and ideally should be continuous. Responsibility for monitoring must be clearly defined. Monitors will require specific training to ensure they can perform the task correctly. The records from monitoring provide evidence that safe food is being produced, and must therefore be accurate and genuine. Records will need to be signed by the person responsible for monitoring and reviewed by a responsible reviewing official of the company.

When monitoring indicates a loss of control, and the critical limit has been exceeded, the business must take corrective action. This is another essential stage in the HACCP system. The corrective action plan must clearly state what to do when things have gone wrong to bring the CCP back under control. The corrective action plan should address:

- the identification and correction of the problem;
- the treatment and disposition of the affected product since the last acceptable monitoring;
- the need to record the incident and the actions taken;
- the need to investigate the cause of the deviation and the steps required to prevent its recurrence.

Clear responsibility for taking action will need to be defined. The records should provide evidence that unsafe product did not reach the consumer.

Once the HACCP study has been completed and implemented, it must be maintained and verified. Verification procedures check that the HACCP system is achieving what it has been set up to do, if it is working effectively and whether it is being followed. The Codex guidelines identify three elements in verification: auditing, review and validation. The importance of these elements and the differences between them has been clearly defined in an ILSI publication entitled *Validation and Verification of HACCP* (Anon., 1999b). Validation should be an essential part of the HACCP process and should be performed prior to implementing the plan. It is the responsibility of the business to ensure that the HACCP plan that has been developed is valid. Validation involves checking that:

- the hazards have been correctly identified and that they can be effectively controlled;
- the CCPs have been correctly determined and that critical limits will adequately control the hazards to a safe level;
- the defined monitoring procedures will effectively monitor the critical limit;
- corrective actions will stop unsafe food reaching the consumer if the procedures are correctly implemented.

Validation data needs to be quantifiable and objective.

In contrast, verification can only be performed on an implemented system. Verification is the systematic gathering and evaluation of data to show that the personnel are following the plan and that it has been implemented effectively. In addition, periodic review should be performed to establish if there have been changes to the operation or external factors that mean the HACCP will need to be updated. Typically HACCP teams perform a recorded annual review, with a system in place to trigger automatically a review of the HACCP plan prior to any change.

The final stage in HACCP development is that of documenting HACCP procedures and record keeping. HACCP documentation must include at least the HACCP plan, the written document that shows the application of the HACCP

principles. Typically this would contain information on the preparatory stages, including the terms of reference, team details, product description and intended use and flow diagram, and the HACCP charts detailing the control of the CCPs. There will also be a requirement for supporting information, such as procedures, work instructions, records of HACCP team meetings and prerequisites details. Documentation must be kept up-to date by controlled amendment. Accurate and efficient record keeping is essential to the successful application of HACCP to a food business. Records provide support for a due diligence defence under the UK Food Safety Act. Records need to be retained for an appropriate time and kept easily accessible. Computer software packages are available to help businesses document their HACCP studies. They guide the user through HACCP principles logically and systematically and many have HACCP guidance notes to aid the team. Easier and more controlled amendment of an existing HACCP plan is one major advantage of their use. Although implementation is not a stated principle, it is implied within the Codex text. Essential to successful implementation is the commitment of senior management and staff, the transfer of ownership, training of relevant staff, and maintenance including the verification and the use of a valid plan.

12.4 Problems in HACCP implementation

HACCP has become adopted throughout many sectors of the food and drink chain as the pre-eminent tool for food safety management. It has been endorsed in both national and international legislation and by various bodies such as WHO and FAO. A major attraction of HACCP is its flexibility. Once the principles have been fully understood, it is possible to apply them throughout the food chain. Although presently used mainly by food manufacturers, it can be appropriate for use by caterers, retailers and primary producers. It is a logical system largely based on common sense.

Whilst undoubtedly it has taken food safety forward, there are limitations and potential weaknesses in HACCP systems which need to be addressed. Hazard analysis is difficult without access to the required expertise. The setting of critical limits also requires expertise that may not be available within a food operation. Kane (2001), in addressing the subject of assessing supplier HACCP systems, identified three main areas of weakness which auditors should take account of:

1. Weaknesses in the design of the HACCP plan.
2. Failure to maintain the HACCP system.
3. Very occasionally, management neglect of safety as a priority.

As an example of a design weakness, Kane described an investigation in the mid-1990s involving cases of *Salmonella* illness associated with infant food. He concludes that the possibility of an elevated susceptibility of infants to lower than average *Salmonella* contamination levels had not been adequately

considered in the product formulation or process specification, because it had not been adequately considered in the initial HACCP study of the product, or identified as a CCP. Microbiological Risk Assessment (MRA) could have assisted here by helping make a more informed judgement of the level of risk and hence the need for a critical control point and appropriate critical limit.

It is most important that HACCP plans incorporate new processing and preservation techniques, product development changes and the food safety implications further down the process. As an example, Kane refers to an incident of *Salmonella* food poisoning with snack salami, where in his view, management failed to understand the basic food science and technology changes in moving from a traditional single salami to a snack salami of finger-thick dimensions. This meant that the surface area to mass ratio was different, the salami dried much quicker, water activity fell faster and acidity was incomplete. In this case, management lacked the appropriate microbiological expertise to identify the growth parameters for *Salmonella* and the impact of process changes in removing a traditional control point. MRA would provide more systematic data on the risks posed by pathogens for differing product-process combinations

The lessons to be learnt from HACCP systems that have been implemented in practice have been considered by a number of others, notably Mayes and Mortimore (2001). They identify similar weaknesses to those identified by Kane:

- wrong perceptions of HACCP as a overcomplex and bureaucratic system, resulting in poor motivation in implementing HACCP systems effectively;
- the lack of a proactive culture at all levels of the organisation, leading, for example, to the failure of production staff to take responsibility for critical control points;
- misunderstanding of HACCP methodology, for example in confusing safety and quality issues, or identifying too many control points as 'critical';
- lack of expertise in such areas as hazard analysis.

These weaknesses lead to a number of common failures in HACCP systems, including:

- failure to identify and allow for some hazards in HACCP planning, compounded by poor validation;
- over-complex and unworkable HACCP systems;
- ineffective monitoring and corrective action due to failures in organisational culture, poor training and verification procedures;
- poor documentation and review.

The UK Food Standards Agency (FSA) has an active programme of research focused on improving food safety, and a specific programme on managing microbiological hazards and risks. As part of this programme the FSA has funded projects on HACCP (Anon., 2000). In three projects, the use of HACCP, the necessity for documentation and the degree of verification of HACCP procedures required have been studied. One of these projects focused on meat

product manufacturing and butchers' shops. Significant barriers to the adoption of HACCP were the lack of training and access to expert advice. It was found that the reliance on independent consultants could lead to problems on occasions. A second project involving a range of manufacturing companies showed that most could identify hazards but had difficulty identifying critical control points. There was also considerable confusion regarding the verification of HACCP. The third project focused on the catering and retail sectors and found an excess of documentation in applying HACCP but a failure to identify CCPs correctly.

The FSA Food Research Programmes Annual Report 1999–2000 states that improvements might include:

- improved dissemination of technical information for food businesses;
- emphasis on the differences between quality and safety issues;
- reducing the number of CCPs by expert risk assessment;
- effective identification of general hygiene aspects (GHP) from the precise product/process controls required for HACCP.

The FSA has also started a number of initiatives to overcome these problems, including establishing a documentation system which guides HACCP teams through CCP analysis in order to arrive at valid CCPs (FSA 2000).

12.5 The interaction between HACCP systems and microbiological risk assessment (MRA)

HACCP is a management tool that in many ways can be equated to Risk Management, rather than Risk Assessment. It should be a practical operational system to assure the production and handling of safe food by a particular business, with clear identification of the potential hazards in that operation and the application of appropriate and effective control measures.

In comparison, MRA is a process or design tool enabling the risks from a particular and defined hazard to be identified independently of operational solutions. Increasingly the results of individual MRAs will provide a quantitative analysis of a hazard and its potential effect on the consumer. While it is recognised that full and comprehensive MRAs are only likely to be undertaken by government agencies, research organisations and perhaps some larger food organisations, the principles and tools of MRA will have wide applicability throughout the food chain to businesses of all sizes. The Campden and Chorleywood Food Research Association (CCFRA) has produced a guidance document on the 'Introduction to the Practice of Microbiological Risk Assessment for Food Industry Applications' (Voysey, 2000). CCFRA is currently exploring the possibility of producing an updated and simplified MRA guide also targeted at the food industry.

The CCFRA document entitled 'HACCP: A Practical Guide' (Anon., 1997c) describes 14 stages in the process of undertaking a HACCP study. These 14

stages embrace the seven Codex principles. Below we have attempted to indicate where MRA can assist in developing a more informed and robust HACCP by reference to the 14 stages described in the CCFRA document.

12.5.1 Stage 1: Terms of Reference

It is essential that a HACCP study is undertaken on a specific product/process line. Likewise, a MRA is a highly targeted assessment which addresses specific hazards associated with clearly defined production/processing scenarios. The better defined the questions are then the more valuable the outputs will be. MRAs may help HACCP teams to define clearer terms of reference.

12.5.2 Stage 2: Selecting the HACCP Team

It is recommended that HACCP teams draw on a range of expertise, e.g. quality control specialists, production experts, engineers. Small businesses are advised to seek specialist external support if such expertise is not available in house. By their very nature, MRAs are complex and comprehensive investigations which are generally impossible to undertake without the active involvement of a wide range of specialist skills including clinicians, epidemiologists, mathematical modellers and statisticians. The expertise pool involved in MRA is almost certainly going to be far more extensive than that employed in a HACCP team. MRAs will, therefore, provide HACCP teams with access to a wider pool of expert knowledge.

12.5.3 Stage 3: Describe the product

Both HACCP and MRA should be equally comprehensive in identifying the intrinsic and extrinsic parameters which influence product safety. MRAs will provide a resource in informing this stage in HACCP analysis.

12.5.4 Stage 4: Identifying intended use

In HACCP analysis this stage requires a clear understanding by the manufacturer of the intended use of the product by the consumer and the potential vulnerability of different sub-groups within the consumer population, e.g. infants, the elderly or the immunocompromised. The hazard characterisation step of an MRA will include a dose-response assessment. This will involve an understanding of the nature, severity and duration of adverse health effects associated with harmful agents in food. It will also consider the dynamics of infection and the sensitivity of the host population. As foods become more targeted at different sub-groups within the population, the type of information that can be derived from MRA will become increasingly valuable. At the present time, we are principally dealing with acute illness syndromes. In the future, both HACCP and MRA are likely to address long-term or chronic illnesses.

12.5.5 Stage 5: Construct a flow diagram/Stage 6: On-site confirmation of flow diagrams

A comprehensive HACCP study should create a full process flow diagram. It is unlikely that MRA would add anything further to this stage. It is always important that the flow diagram description is an accurate reflection of what actually happens in practice and should include any night-shift or weekend deviations.

12.5.6 Stage 7: List all potential hazards; conduct hazards analysis and consider measures to identify control measures

This is an activity where potentially MRA has a considerable opportunity to enhance the debate and the judgements made, particularly in relation to the severity of hazards. One criticism of HACCP methodology is that it does not define and measure outcomes for consumer safety (Orris and Whitehead, 2000). This weakness contributes to confusion about what constitutes a hazard and which hazards present the greatest level of risk. MRA provides a systematic analysis of levels of risk for differing pathogens to consumers. Whilst in the past most judgements have been made based on qualitative data, MRA is increasingly introducing quantitative appraisal of data. This of course not only gives greater confidence in data but allows for more objective comparative analysis between data sets. In MRA information on dose–response and exposure assessment is an integral part of the process with rigorous procedures for identifying variability and uncertainty in the data. In MRA the effects of intervention or mitigation strategies can also be analysed to see where the best options for control exist. In HACCP, the need to consider the measures to control identified hazards can only be enhanced by information derived from MRA studies.

12.5.7 Stage 8: Determine Critical Control Points (CCPs)/ Stage 9: Establish Critical limits for each CCP/Stage 10: Establish a monitoring system for each CCP

In HACCP the setting of measurable and meaningful control limits is often the most difficult task and can lead to problems. The real critical limit, the division between safe and unsafe food, is often not known or is based on qualitative data. While some criteria are defined in legislation, e.g. time and temperature for milk pasteurisation, some may need extra data to be collected to determine the critical limit. The target levels and tolerances set for each CCP have to be chosen with care. The benefit of MRA is that techniques are increasingly being developed which can explore the impact of changing parameters i.e. exploring a number of ‘what if’ scenarios. MRAs will thus provide valuable information in setting critical limits.

12.5.8 Stage 11: Establish a corrective action plan/Stage 12: Verification/ Stage 13: Establish documentation and record keeping/Stage 14: Review the HACCP plan

MRA will have limited input on these final four stages of the HACCP process. These are mainly concerned with management and audit control, corrective action, improvement and review.

In summary, the major input of MRA studies will be on the identification of hazards, control measures and the assessment and identification of critical control points. Interestingly, this is the area where there continues to be a level of concern in terms of current HACCP implementation.

12.6 The future relationship of HACCP systems and MRA

Mayes and Mortimore (2001) identified a number of issues that will impact on HACCP in the forthcoming years and promote change. These include:

- the increasing globalisation and harmonisation of trade between countries;
- the changing role of governments and regulatory authorities in the assessment of HACCP;
- the role of HACCP in new science/food safety initiatives such as Quantitative Risk Analysis;
- the need for application of HACCP throughout the supply chain.

A key provision of the World Trade Organisation Sanitary and Phytosanitary (SPS) Agreement is the requirement for countries to provide risk assessments to ensure the safety of food and that standards of safety between exporting and importing countries are equivalent. Mayes and Mortimore (2001) consider that the concept of equivalence is one of the most contentious issues in food safety at the present time.

The International Commission on Microbiological Specifications for Foods (ICMSF) has proposed a scheme for managing microbiological risk for foods in international trade in which the **Food Safety Objective (FSO)** is a functional link between risk assessment and risk management (Legan *et al.*, 2002). An FSO is defined as a statement of the frequency or maximum concentration of a microbiological hazard in a food considered acceptable for consumer protection. FSOs allow for the equivalence of different control measures to be established. The ICMSF has proposed five steps for using FSOs in managing food safety (van Schothorst, 1998):

1. Conduct risk assessment.
2. Conduct risk management option assessment.
3. Establish the food safety objective.
4. Confirm that the food safety objective is achievable through good hygiene practices and HACCP.
5. Establish acceptance procedures.

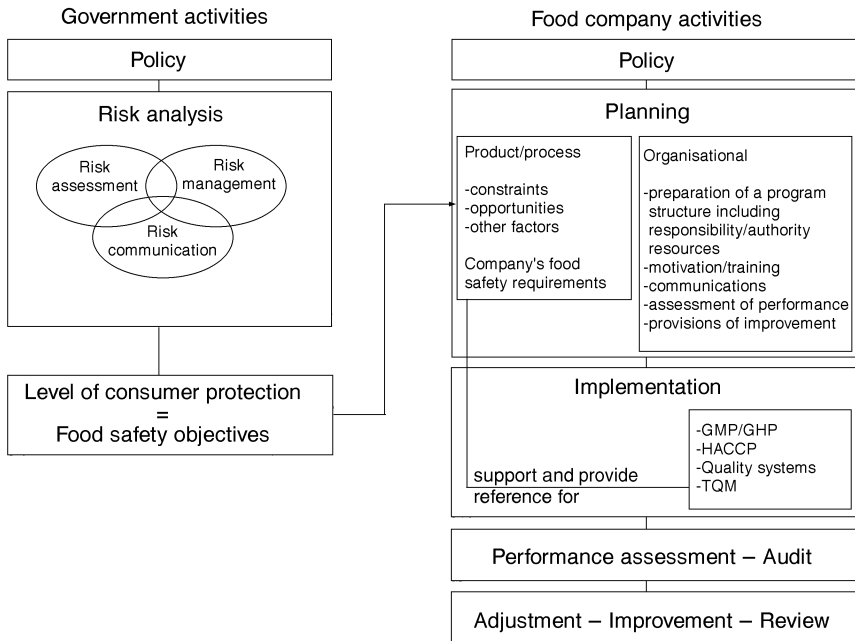


Fig. 12.1 Government and industry responsibilities in food safety management (reproduced with permission of the International Life Sciences Institute).

An example of an FSO could be that the level of *Listeria monocytogenes* in ready-to-eat foods should not exceed 100 cfu/g at the time of consumption. The term FSO and others are slowly being introduced into the food safety management vocabulary. Key terms have been identified and defined by van Schothorst (1998) as follows:

- a performance criterion is the required outcome of a step or a combination of steps that can be applied to ensure an FSO is met, e.g. a 6 \log_{10} reduction in the target organism;
- a step is a points procedure, operation or stage in the food chain including raw materials from primary production to final consumption;
- a process criterion is the control parameters of a step or combination of steps that are applied to achieve the performance criterion, e.g. heating for 2 mins at 70°C.

Risk assessment is very much a science-based activity that provides data for use in risk management decision making. Many scientists and risk managers believe quite strongly that these two processes should be kept quite separate. In that way, objective data is produced based on the best available knowledge. The subsequent process of managing risk is influenced by a number of socio-economic factors. Increasingly, it is being recognised that the outcome of a risk assessment will be a Level of Protection (LOP) (e.g. the estimated number of

cases of *Salmonella* infection per year associated with chicken for 100,000 of the consumer population). It is for the risk managers (government agencies) to decide if this LOP is acceptable or appropriate (Mayes and Mortimore, 2001). Thus the outcome of qualitative risk analysis is an acceptable level of protection (ALOP). Food safety objectives (FSO's) are intended to convert the ALOP (level of risk) to a level of hazard.

Anon. (1998) have produced a schematic diagram which illustrates how risk assessment, as an integral part of risk analysis, leads to the production of food safety objectives (Fig. 12.1). Setting FSOs is a government responsibility. It is for the food industry to embrace these objectives in their food safety management procedures, of which HACCP is a key component. It is clear that several of the tools and approaches used in risk assessment can be of direct benefit to the design, implementation and verification of industrial HACCP schemes.

12.7 References

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13

The future of microbiological risk assessment

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13.1 Introduction

In considering the future of MRA, it is important to recognize the difference between 'hazard' and 'risk', because they pose different challenges and opportunities for risk analysis.

13.1.1 Hazard

A food hazard is a biological, chemical or physical agent in a food with the potential to cause adverse health effects (Codex Alimentarius Commission, 1997; Anon., 1996). There are many microbiological hazards associated with food that can and do cause injury and harm to human health. Millions of people world-wide suffer from 'food-borne' diseases of microbiological origin each year. Microbial hazards are not a static group, but change because of differences in prevalence, eating habits and human sensitivity and the exchange of genetic material between some species of micro-organisms. Hence, reliable identification and characterisation of hazards for any supply chain, food and group of consumers is an essential basis for risk assessment. Providing adequate and credible information for decision-makers will be the major scientific task for researchers, industry and regulators. Similarly it will not be a one-off task, the regular review of which hazards are current, which are emerging with the potential to cause harm, and the severity of their effects, are essential to the future of risk assessment. Accompanying this must be the development and selection of preventive measures, whose severity and nature will be linked to the characteristics and resistance of the hazard and the severity of its effects for humans.

13.1.2 Risk

In contrast, risk is the estimated probability (or perception) and severity of adverse health effects caused by consumption of a hazardous agent in a food. Even if the nature of the hazard itself does not change, demography or other factors, (e.g. increased consumer awareness of health effects or wider geographical distribution of the hazard) can alter its impact. Time and demographic change bring about differences in risk level for various groups of consumers (e.g. those with increased levels of sensitivity – young, old, pregnant, immuno-compromised, which represent growing sections of the population) and need to be considered, along with perceived health impact. Designing products or supply chain conditions to protect vulnerable consumers may impose (unacceptable) costs on other consumers that are not at risk, or may limit their choice, by restricting options for risk management. Ways to manage this have to be found, so that risk management can provide all consumers with ‘real’ protection (from food poisoning) whilst ensuring that any hazard, technology or product provides acceptable (perceived) consequences for everyone affected by it. To help this process, it may be useful to examine the impact of the hazard, and express risk acceptance in terms of performance standards, conveying risk-benefit balances in meaningful terms to consumers, rather than just using technical standards, limited to product, process and microbiological details (e.g. microbiological food safety objectives). This should help consumers to evaluate and compare the performance of control options and may reduce their resistance to technical innovation or calls for changes in behaviour (e.g. cooking of beef meat to eliminate *E.coli* O 157). The most valuable performance standards would allow consumers to use their own direct experience and perception. Risk analysis needs to play a key role in helping consumers confidently accept a balance between technically valid solutions and those based on perception.

13.1.3 Tools for assessing risks

Risk management and communication should structure the information from risk assessments and risk estimates to form a supportable basis for reducing safety risks to an acceptable level. Explaining the link between reducing the level of a hazard in food and the decrease in risk that this causes is essential to providing credible food safety controls, and must be clearly linked to any accompanying increases in cost, or other restrictions. A transparent process for doing this, including the relevant participants in the whole process from the risk profile to the final management actions is a key to reaching valid and acceptable decisions that are supported by consumers and form sustainable solutions to any food safety problem.

Hazard analysis (as part of HACCP) is already established as a key operational means of controlling risks. Lack of rigour in hazard analysis, (an activity roughly equivalent to exposure assessment), has already been seen as a weakness in the HACCP system and more reliable means of hazard

identification and exposure assessment are also needed. In processing operations, there is a progressive move towards making production responsible for quality, with QA and regulatory bodies having a facilitation and monitoring role, rather than their traditional 'control' role. Therefore training should ensure that food industry workers understand their essential role in assuring food safety and maintaining consumer trust. To do this means that they need better training to recognize the importance of risk determining steps, including CCP's.

A different emphasis in the legal framework of various countries places operational responsibility for microbiological safety with producers and regulatory agencies to differing extents. But the level of risk to the world's consumers from food borne microbial hazards is always fixed by the day-to-day control exercised by producers and processors. Official food control authorities are often not fully involved in risk management because of the high costs of participation and the impossibility of them understanding safety aspects all the technologies and supply chains they encounter. Their major activity should focus on improvement in techniques for monitoring compliance with established or new safety principles. Where there is doubt over the acceptability of risks, the question of 'sufficient proof' to show harmlessness, or the effectiveness of control measures needs to be addressed by publicly managed research programmes to prevent undue reliance on precaution and restriction of innovation.

13.1.4 Microbiological safety risk analysis

The systematic analysis of microbiological safety risks is currently an emerging technique with some information sources and some tools. Its process currently comprises three separate tools for the assessment, management and communication of risks, but it lacks any tool for predicting the acceptance of its decisions and actions. The immediate challenge is how to collect and analyse meaningful data and then send out sound messages about safety risks from food, or water, to consumers and trading partners. For these messages to be trusted and acted upon, the information and decision-making processes must be credible. Food safety incidents and scares, resulting from contamination in food have hit trust in areas where it is essential. The content and quality of safety messages has to ensure that they are understood. This will only be achieved by the development of:

- transparent decision-making processes that consumers, producers and scientists understand and trust;
- reliable and pertinent information, including clear identification and handling of knowledge gaps, uncertainties and variability.

In spite of these weaknesses, risk analysis is now widely recognized as a vital analytical process for the development of food safety standards. It is increasingly valued, because its tools can systematically investigate the relevance of hazards and the levels of safety in products and supply chain operations needed to retain consumer safety and confidence.

The fate of micro-organisms in food and human responses to them depend on a number of variables, some of which may be inter-linked; therefore microbiological risk assessment requires handling complex information and predictions. There is rarely good cause and effect data available. Health effects of any agent may be severe in one person, mild in another or completely absent in others. Ideally an assessment of clinical effects and consumer impact would be limited to a technical assessment. But in practice, perceived risk is often a stronger driver for consumer (or regulatory) response to hazards and it is not well covered by current management and communication tools. Especially, consumers express continuing concerns about health effects linked to specific microbiological contaminants (e.g. *Listeria monocytogenes*, *E.coli* O157, campylobacter and viruses), new technologies, uncontrolled or unacceptable food handling practices, or technologies that may introduce or leave microbiological hazards in food. Their assessments and conclusions are often different from those of experts and they give different weighting to the presence or absence of scientific data on hazards, often basing decisions on experience or media material. Safety concerns are most often voiced in the developed world; but improvements in global communication are likely to heighten global interest on them.

To meet these challenges and ensure a balanced response to regulating food safety, the development of risk analysis needs to be managed to handle both 'real' and 'perceived' risks, so that it becomes progressively more widely accepted. And the scientific and transparent assessment of microbiological safety risks builds rather than undermines consumer confidence by providing data that feeds into the channels used by consumers. Risk assessment outputs based on risk level and hazard severity are the best means for risk managers to develop reduction or prevention measures that are scientifically justifiable, consistent and likely to be acceptable to consumers. But perception of their effectiveness or acceptance will depend on presentation and be verified by the subsequent willingness of consumers to accept risks in the form of a product or technology or lobby for change, in the context of their own circumstances. Understanding where the balance lies between technical and perceived risk in various markets can point the way for management strategies and indicate potential problem areas, such as global differences in acceptable levels of safety depending on food availability and the feasibility or cost of control measures. This chapter focuses on future developments and outlines some of the developments, choices, information gaps and process changes that may shape it.

13.2 Information needs for risk assessment

13.2.1 Data needs

Risk analysis needs sound information to produce sound actions. The information flow in risk-based food safety control systems can be summarised as shown below. For any topic, information is available from a variety of

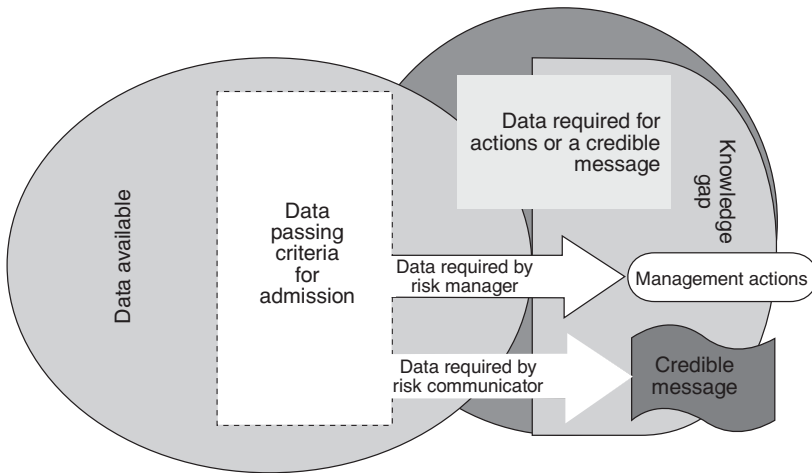


Fig. 13.1 Information flow in risk-based food safety control systems.

sources. Criteria to define the information relevant to the risk assessment should be provided by the risk profile, because this information needs to support both the risk manager and the risk communicator, who may have different requirements arising from their responsibility for technical or perceived aspects of risk. Working backwards from their needs may clarify requirements for a credible message or management actions, and highlight differences between what is needed, what is available and knowledge gaps. Different techniques can be used to fill knowledge gaps, in reliability they range downwards from new data, validated predictive modelling to assumptions (Fig. 13.1).

13.2.2 Data from testing, surveys and clinical, epidemiological or case-control studies

Data on hazards (e.g. infectious or toxigenic pathogens and toxins), routes of contamination, prevalence, geographical or commodity distribution of pathogens, commercial and consumer practices and consumer sensitivity are essential information for microbiological risk analyses and are required, but incompletely available. Limited information is available from many sources, but currently few organisations collect pertinent data or structure it so that it can easily be used by risk assessment studies. Adoption of a risk-based safety control approach by regulatory and other organisations would require co-ordinated development of global or web-based systems for storage and retrieval of microbiological, processing and prevalence information.

Many sources of data already exist because many organisations and companies examine the microbial populations of food and raw materials on a routine basis for comparison with microbiological criteria (regulations, standards specifications or directives) to determine product or process acceptability. Systematic organisation of such data could provide up to date information on the

distribution of pathogens in food and show the actual risks of current products, product designs, supply chain operations and consumer uses (e.g. chilled meals, where there is a continuing debate between expert microbiologists and industry over the risks of botulism). Useful data would cover microbiological levels (e.g. counts of specific types of micro-organisms ~ salmonella absent in 25 g), key process attributes (e.g. heating to 75°C) and product characteristics (e.g. pH \geq 4.6). It could be used to judge the effectiveness of current controls and the implementation of existing risk management actions.

Any proposed microbiological criteria should be compared with accepted criteria and systems (e.g. good manufacturing or safety/quality limits, ICMSF) as these are likely to be widely accepted and based on expert opinion or surveys. Formal risk assessment may help to prevent increasingly tight criteria being forced by uninformed opinion that assumes their value in protecting public health, unsubstantiated by scientific or epidemiological information.

13.2.3 Genomics and bio-informatics

Information on the microbial genome could provide a mechanistic analysis of the different characteristics of micro-organisms that result from their molecular make-up (e.g. acid or heat tolerance or different growth rates, toxigenesis or pathogenicity in response to environmental conditions). At a functional level this tool could be used to predict the activities of any micro-organism present, or growing, in products, provided they and their environment could be adequately characterised. At present microbiological analysis of processes and materials using conventional microbiological methods offer a very intensive and low-resolution approach to determining cause and effect linkages or predicting the fate of food borne pathogens. Because comparative genomics profiles the complete DNA sequence (the genome) it can show capabilities of microbes. Sequencing microbial genomes using gene-transcription will be able provide microbiologists with a genetic parts list of specific pathogens, etc., but not indicate their functionality or potential. Showing this, based on how these parts come together to form functioning micro-organisms is the role of the emerging science of Bio-informatics, which looks at how genes, or groups of genes, work together to produce specific products or determine particular attributes, such as resistance, infectivity or toxigenesis. The combination of techniques would provide a very powerful approach to tracing the origin and risks of bacterial stains and species and would improve the quality of exposure assessments. Genome profiles would provide more complete functional identification, than the current 'fingerprinting' ribosomal rRNA techniques (e.g. PCR amplification, electrophoresis or hybridization).

13.2.4 Predictive modelling

Risk assessments can use predictive models to help reach conclusions and propose actions. At present, model availability and use is patchy and the

usefulness of models for anticipating microbial responses in real food systems is limited. The development, refinement and wide acceptance of predictive models is essential for the development of risk-based food safety control systems. Such models have a tremendous role to play in effective risk management because of their ability to allow 'what if' to be examined without protracted experimental work. Current models are strong at predicting pathogen responses under stable or non-changing conditions (e.g. growth at steady temperatures). But validated ways of dealing with fluctuating temperatures (or other environmental shifts) for example a concept equivalent to the 'z' concept used in death kinetics does not yet exist. Their development is essential for exposure assessment to deal realistically with changes in process or storage conditions (e.g. if a processor wants to determine the potential increase in pathogen numbers during a process run at different temperatures or with different storage patterns). Some models are able to provide and use frequency distributions (e.g. Monte Carlo) rather than single point estimates for risk assessment and this dramatically improves their practical usefulness.

Modelling is currently limited to predictive models for growth and does not cover the range of processing operations that affect microbial levels in food. Models for microbial survival in foods hardly exist, because of the technical difficulty in producing them. On the other hand simple models for the killing of micro-organisms by heat (e.g. D and z) are well established. Although their principles determine the fate of micro-organisms, chemical or thermo-physical models (e.g. acidification of pH buffered foods or heat transfer and penetration into liquid or solid foods) are not currently considered as microbiological models. In spite of obvious theoretical shortcomings (i.e. a log linear interpretation of population death curves that clearly exhibit 'survivor tailing'), simple models have proved effective for predicting heat process lethality, when integration of time and temperature is needed by processors to assess the effects of cooking or heating. Many models are constructed and research programmes undertaken on the premise that mathematical refinement and increasingly accurate predictions are needed.

The practical needs of risk assessors are not really taken into account when software entry procedures or data sets for 'public' models are considered. These models are not offered to potential users with clear indications of their fitness for practical use (e.g. can a model provide a 90% probability estimate to ± 2 minutes (suitable for lethality or cooking calculations), ± 2 hours for process management or hygiene purposes or ± 8 hours or the difference made by a storage temperature rise of 5°C for setting and understanding trade-offs in setting shelf-life conditions). Improved models require a practical explanation of their limitations or scope of use, and in some cases predictions discarded as insufficiently accurate by experts may prove adequate for guiding industrial users. In addition to their practical use in exposure assessment, the public availability of trusted models could provide informed consumers with tools for examining the risks in new foods or new hazards in familiar foods. Hazard characterisation would benefit from reliable tools to predict the extent and

distribution of any hazard, (especially infectious pathogens) and would ideally incorporate epidemiological data to predict the extent and severity of outbreaks for any hazard level in food, based on portion size and the distribution of sensitivity in a population.

Increased availability and acceptance of predictive models by food producers and regulatory agencies would allow businesses without large technical resources, or informed consumers, to examine the safety of food under different scenarios. For example the impact of warm storage of chill-stable foods or the effect of recontamination with subsequent ambient storage of an unpreserved food and reach conclusions on likely harmfulness. This ability would provide a common language for discussing and agreeing the acceptability of risks. The establishment of national and international microbiological models or databases for the growth, death or survival kinetics of infectious (e.g. *Salmonella*, *Listeria*, *E. coli* (including O157:H7), *Bacillus*, *Yersinia*, *Campylobacter* or toxigenic (e.g. clostridia and *Staphylococcus aureus*) pathogens), would improve global ability to trade in safe food and allow trading partners some insight into local risk levels or the effectiveness of HACCP plans or process conditions.

Even producing and agreeing the application and boundaries for use of 'single species' models will be a formidable task. If microbial associations significantly affect the behaviour, or harmfulness to humans, of target species, models of increased complexity with a wider range of variables become essential. Software tools for analysing the behaviour of pathogens in the food chain or prediction of microbial inactivation and growth rates, behaviour in different habitats or in foods of different chemical compositions need to be developed. Ideally models would have a mechanistic base, and in practical terms better validation in food systems would provide a basis for enhanced predictions and indicate limits of validity. The present system of 'curve-fitting' to data points without a mechanistic basis seems to provide effective models, subject to the same limitations as D and z models. Current model outputs need to be validated by limited experimentation, or survey data, on the foods where 'boundary' conditions are in question.

Commercial software is likely to become more fully available and the increasing number of large scale (government published) risk assessments will provide valuable benchmarks or reality checks for less ambitious studies. It is possible to use EXCEL spreadsheet based models for deterministic fixed risk assessments (e.g. scenarios covering best, worst and average conditions or levels). Special software (e.g. @ Risk) is also available using a stochastic (Latin cube) approach to probability distributions for the key variables.

13.2.5 Supporting illustrative or generic studies

Ideally, supporting information for risk management and communication will come from on-site risk assessments. Where output from a direct study is not available, illustrative or generic studies could be used to support choices between risk management options, if alternatives to existing controls are

required. Such guides based on generic studies are already used to support the introduction of HACCP and may help businesses with limited technical resources to get started with risk-based safety management. Generic studies need to provide information for hazard identification and characterisation, e.g. the likely hazardous dose and severity of illness, with illustrative epidemiological or outbreak data. Microbiological reference values (see below) could also be included. A review of information for hazard identification and exposure assessment would need to identify typical contaminants, commodities or supply chains that are problematic and control measures that have worked (e.g. pasteurisation conditions or hygienic manufacturing). Guidance for exposure assessment could focus on process analysis and indicate any likely risk determining steps and provide access to predictive models. Advice on setting acceptable levels of risk for any hazard will help to selection of control options, based on local circumstances and the cost-benefit ratio. Specific guidance on identifying similarities and differences between published studies and user requirements for supporting information would be essential to prevent their misuse. Such guides and data-bases will become feasible as more detailed, quantitative risk assessments become available.

To ensure the long-term effectiveness of such short cuts, regular updating with scientific (e.g. pathogen prevalence and growth, the relative importance and location of pathways of contamination and infection/toxigenesis) and commercial knowledge (e.g. technological changes in food production and the supply chain, storage and distribution) would be needed. Continuing review may lead to the recognition of groups of process systems or sub-systems, sources of failure or common risk determining steps. Consumer understanding and confidence may be improved by making such studies available in publicly accessible data-bases, grouped according to food commodity and presenting data in scenarios based on risk factors at their 'best', 'average' or 'worst' levels. This would improve identification of key risk determining steps and demonstrate the sensitivity of risk level to changes in various factors, such as product cooking or storage.

13.2.6 Microbiological reference values

To promote the use of a risk-based approach, consistency in maximum accepted risk levels to protect human health is needed for particular hazards, based on the severity of their effects. The lack of generally accepted reference values relating hazard level and consumer sensitivity has led to situations where food-products have been declared unfit for human consumption because of non-quantified demonstration of pathogen presence, or in some cases dangerous pathogen levels have passed unchallenged. For example, the detection level for *L. monocytogenes* is far below the threshold value for harm, and detection does not always indicate hazardous food. Alternatively levels below the detection limit can grow, given the right conditions to hazardous levels. Fixing reference values for various product types would provide targets for product designers and the supply chain and allow the integrated effect of process steps, relative to a limit to be expressed.

At present, finding accepted reference values for products, process conditions, chances of recontamination, levels of microbial survival or reduction in numbers after a process step is problematic; because of the range of consumer sensitivities and the unpredictable nature of their response to a level of hazard.

At the regulatory, or government level, the problem of reference values is beginning to be addressed through Microbiological Food Safety Objectives (MFSOs) that give a target level considered necessary to protect the health of consumers. Usually this means (maximum) levels of a pathogen or toxin in a food, and therefore leads to end-product criteria, supply chain performance indicators or target prevalence rates/levels for pathogens. To be useful, MFSOs must be feasible and practical and should identify the food, the hazard and the level of protection required. At present very few quantitative values such as acceptable rates of illness or death, are published. In principle, Governments should be able to use them to communicate expected levels of food safety to consumers and the food industry, and industry may in turn use them to show that their products meet acceptable levels of risk. MFSOs do not prescribe how levels of food safety can be achieved, and therefore they allow processors to select appropriate, or equivalent, technologies and performance criteria that will provide food complying with the reference value. At an international level they could provide the basis for determining equivalence by showing that different control measures (e.g. hygiene practices or critical control points) give the similar levels of protection.

Because there are significant differences in the occurrence of pathogens in different foods, countries and regions, MFSOs (or, more specifically, sampling plans, criteria, etc.) cannot be global, but must take into account national and regional situations at both ends of the supply chain. MFSOs are important tools in the implementation of risk management decisions, because they communicate the level of safety that should be achieved and focus process monitoring and limited regulatory resources. Much of the future acceptance and use of risk-based systems relies heavily on finding MFSOs.

Generally the application of existing food hygiene principles and, in particular, HACCP and prerequisites in food production chains will form the basis for any control of food-poisoning micro-organisms. Decisions on control measures should give priority to preventing risks, not just controlling them. But even where risk-based control systems are functioning, production units still need guidance on acceptable levels of public health protection and specific guidance on targets (MFSOs) for any control method. This guidance could be provided by extending the coverage of MFSOs to take account of the level of risk or health protection accepted by consumers and risk managers and enforceable within a country's legal and regulatory structure.

13.2.7 Microbiological knowledge gaps and requirements

Biological hazards in food include pathogenic strains of bacteria, viruses, helminths, protozoa, algae and their toxic products (see Fig. 13.2). Pathogenic

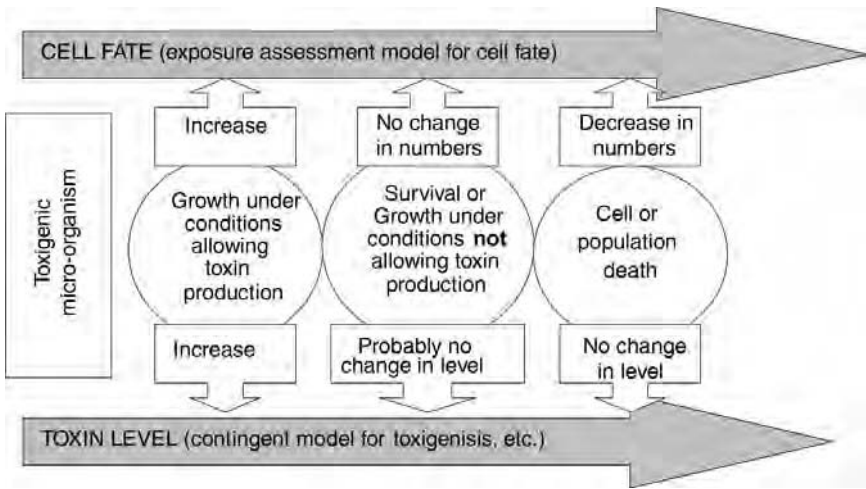


Fig. 13.2 Toxigenesis and cell fate.

bacteria are currently the most significant public health challenge internationally. In many cases quantitative assessment of the risks they pose cannot be done, because of knowledge gaps concerning their behaviour and resistance in food. These gaps are widened by cultural (e.g. cooking and storage), geographical (e.g. pathogen prevalence and ambient temperature) and practical differences (e.g. agriculture, processing and storage) that affect the chances of pathogens being in a food at consumption. These differences will mainly be reflected in the exposure assessment, but should also be examined by hazard characterisation, as process and other factors may also affect virulence or pathogenicity. If there are knowledge gaps on pathogen numbers or incidence or uncertainties about pathogenicity, a quantitative assessment is not possible and a qualitative assessment may be the only realistic alternative. To bring about recognition of risk analysis as the underpinning tool for regulation of food safety control, microbiologists must move on from qualitative risk assessment by generating the data needed for quantitative assessments.

Certain food commodities and pathogens represent special risks in relation to foodborne disease, related to their potential for growth and infectivity or toxigenesis in food (e.g. *L. monocytogenes* and listeriosis or *Staphylococcus aureus* and toxin production). Knowledge of the boundaries for survival and multiplication or synthesis of toxins can be used to group food commodities and supply chains relative to conditions for growth and activity.

While scientific studies increase information on hazards in food, uncertainty and knowledge gaps continue to cause concern to decision-makers and consumers. Only continued research can provide the necessary answers. Until answers are available, much of what is known about hazards and used for controlling risks is based only on partial information, with uncertainties and

assumptions factored in. Although in future, risk managers will need to take greater account of consumer perception of risk and cost v. benefit, it is essential that data and scientific analysis continue to play the major role in risk management; even though consumers may not be convinced by a purely scientific, or technical, approach, or accept the authority of scientific opinion.

13.2.8 Risk acceptance: identifying an acceptable or tolerable level of risk

The *perception* and *acceptance* of risk by consumers differs from issue to issue. Whereas *experts* consider risk in terms of estimates arrived at through scientific methods, consumers are more value driven and manufacturers may be market driven. In order to decide on product, hazard or technology, consumers and manufacturers need information on:

- the nature of the hazard;
- the likely scale of the risk;
- the urgency of the situation;
- who is at risk;
- any uncertainty surrounding the information;
- possible risk management options and likely costs.

This information should form the risk profile and MFSOs, or a consensus on the tolerable level of risk may suggest priorities for actions.

There is currently limited (and unsuccessful) experience of decision-making predicting value judgements concerning the 'acceptance' of risk. This is because inappropriate weighting has been given to different factors such as the certainty and severity of the risk; its health effect; consumers' technical knowledge, the implications of any control measures; and whether the risk is seen as voluntarily accepted or imposed. Consumers do not accept or reject risks in isolation. Usually they make choices between various courses of action. How this is done is very poorly understood. It is obvious that low-risk technologies and products whose risks are generally regarded by consumers as acceptable can be sold without worrying further about consumer response to the inherent risks. On the other hand riskier technologies may need regulation, or public discussion, to gain acceptance. For designers and producers to have well-defined ideas of the boundaries of acceptable risk would provide them with clear targets and courses of action for managing technology and market development. For regulators, reliable identification of acceptable levels of risk would mean they could propose valid levels of protection, and allow technical staff to concentrate on monitoring performance routinely, without having to make case-specific decisions. For consumers, the availability of trusted, acceptable levels of risk would provide them with a means for evaluating how well food safety is being protected, and remove the need for them to understand technical details.

To accept and communicate on tolerable risk levels and express risk reduction preferences, consumers need understandable information on hazards.

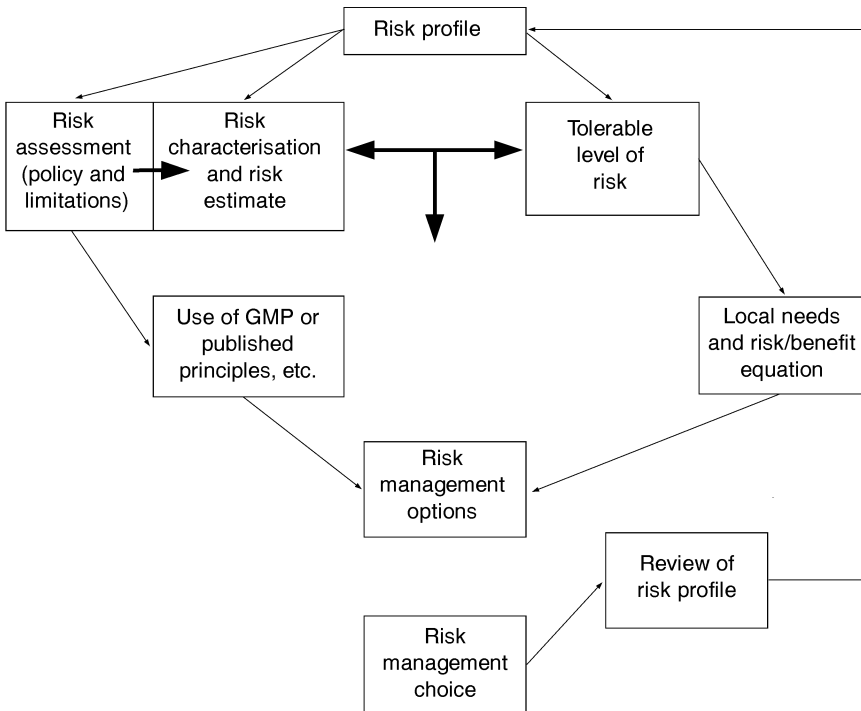


Fig. 13.3 Overall scheme for risk-based food safety control.

They need to know the extent, severity and time course of any health effects, attendant uncertainties in information and their potential exposure to the hazard. These should be contained in a summary of the distribution of risks and benefits of a product or process. Specified risks should include the direct risks, any others that may arise from controls and the cost of prevention and control versus the effectiveness and feasibility of the proposed prevention or control options. Such information is not published by current risk analysis studies and is essential to their acceptance. An overall scheme for risk-based food safety control is shown above (Fig. 13.3).

13.3 How should risk assessment processes develop?

The importance of the risk assessment process lies not only in its capacity to estimate risks to human health, but also in its ability to organize and communicate data on food safety and allocate responsibilities for data analysis and control or preventative actions. At present processes are limited to the technical appraisal of risks.

Topics for risk assessment, or problems, may be identified by consumers or industry, single stakeholders or by collaboration between different stakeholders and should form the major input to the risk profile (see pages 280–1). Formal

procedures for problem identification and management may not be necessary if food hygiene problems and control measures are well known. This usually means they can be dealt with on a routine basis, or managed directly, by applying hygiene and other guidelines or codes already developed for specific food hazards. The strength of risk assessment lies in the systematic collection and evaluation of information on new hazards, and in dealing with altered conditions or supply chain changes. On the down side, risk assessment is likely to be ineffective or misleading where there is absent or variable data, uncertainties or knowledge gaps are recognized or alternative interpretations of the data are scientifically plausible. If models or analogies are used, there will be doubts about the origin and applicability of their information, and these must be balanced by discussion of their value as an aid to decision making, when directly relevant data is not available.

In scope, a risk-based approach to safety should address the supply chain from farm to table. Its output should be directly useable as control measures, in combination with prerequisite/good manufacturing practice programmes and HACCP. Controls based on risk analysis progressively place responsibility for safe foods with the supply chain and retailer. And as a consequence, if the approach is effectively used, the role of regulators progressively becomes limited to providing the necessary criteria (e.g. MFSOs), monitoring, support and direction. A key part of their role will be review and guiding revision of the existing good manufacturing practices and criteria (e.g. specifications) used to control risk. Non-risk-based control systems place greater responsibility for ensuring compliance on the regulatory authorities as they are based on generic criteria, that may or may not offer the best protection of public health whilst promoting trade. Properly validated, targeted control measures can cause significant reductions in pathogen contamination levels in foods, but they limit innovation and improvement and may increase the regulatory cost burden. Because of their inflexibility (e.g. based on prescriptive requirements), locally-enforced regulatory systems cannot always respond to changes in risk levels, new hazards or provide remedies for individual situations in a cost-effective manner. Their future usefulness in international trade is likely to be limited, because they do not take account of the needs of a global economy or developing economies trying to export to countries with fully developed food safety control systems. Therefore there is a major economic and regulatory need to develop risk-based safety management systems that contain risk to tolerable levels, are able to handle equivalence and maintain consumer confidence.

Any regulatory policy using a risk-based approach to determining product safety needs, must have consumer protection as its focus and be based on 'formal' procedures, open to review during their development and application. Such a consumer focus may challenge existing global or national standards, or identify regulatory criteria that are seen as underweight or alternatively too restrictive by consumers. Hence a process for balancing risks and benefits in their local context is urgently needed, to promote general acceptance of risk-based management of microbiological risks. Industry (or regulatory agencies, if

they are responsible for the control of technology), would benefit from a generally credible procedure that promotes acceptance of a balance of risks and benefits, prevents unpleasant surprises and reduces the costs of regulatory intervention. Consumers need to be involved in building such a process and its development should leave producers with design freedom; so that trade is not limited and innovation is promoted. This means that technical resources and information to support exposure assessment have to be better directed, to stop narrow or conservative approaches being used to speed decision making. On a routine basis application of studies to particular lines, technologies or products with recurrent problems may provide solutions and build consumer confidence.

Use of risk analysis processes in industry and by regulators is likely to be limited by availability of data and competent personnel. At the outset of any microbiological risk analysis activity, competent risk assessors, risk managers and experts need to be identified as early as possible, although the correct choice may not be evident until knowledge gaps or risk management options have been identified. Correct preparation of the risk profile should minimise the chances of making incorrect choices. Depending on circumstances, risk management and communication responsibilities may pass to different stakeholders and the messages and outputs should be tailored to meet their needs. Public authorities and research institutes need to take on a pivotal role in ensuring scientific integrity, especially by ensuring (e.g. by training) that the roles of assessment and management are separated but interactive. Where assessors and managers have dual roles in a study, they need to be alert to conflicts of interest, as they need to maintain frequent and transparent interactions to arrive at effective and practical risk management decisions.

13.4 Key steps in risk assessment

Risk assessment involves four sequential and interrelated steps and in the foreseeable future will have many limitations. Ways of recognizing and managing these need to become better defined, to prevent the technique becoming discredited or misused. Risk assessment needs to have a formal preparatory step, the risk profile, to ensure it has the required outputs.

13.4.1 Risk profile

The risk profile forms the essential starting and reference point for risk analysis. It provides a situation analysis of the microbiological food safety problem and its context. It covers what is known and what is not known, and what is relevant to risk management decisions. It is a checklist of the areas of risk relevant to prioritising and setting the limits for risk analysis. Preparation of a risk profile may be triggered by information on the presence, or an unusual level, of hazards in food or the environment, by disease surveillance or monitoring information, clinical or laboratory studies. In industry, alerts may come from knowledge of

Table 13.1 Risk profile: scope and content

<ul style="list-style-type: none"> • A brief description of the situation, product or commodity involved; including the source of problem or topic (e.g. from the entire food chain, a specific food-stuff or animal or person to person transmission) • Identification and description of the hazard and supply chain involved, including concern levels of the hazard • Who (e.g. consumer sensitivity based on disease incidence data and the type and severity of the adverse effects, indicating any consumers particularly at risk (e.g. the elderly, children or those whose exposure may be increased by dietary intake; socio-economic status, or other characteristics) and what (economic concerns) is at risk and potential consequences 	<ul style="list-style-type: none"> • The proposed risk analysis team and stakeholder involvement • Relevant regulatory or GMP tools and any microbiological food safety objectives • Information on tolerable level of risk. Possible: <ul style="list-style-type: none"> • control options • need for precaution • Likely responsibility for implementation of microbiological risk management decisions • Monitoring and review requirements • Consumer perception of the risk and local considerations or restrictions • Anticipated channels of risk communication • The expected or acceptable distribution of risks and benefits
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production practices including process innovation, a failure to comply with specifications, expert opinion or consumer complaints.

After identification of a problem, the risk profile needs to identify the hazard and define the scope of the problem. It needs to outline any potential consequences associated with courses of action and the likely consumer perception of the problem and any solutions. It should indicate whether or not a risk assessment can or should be carried out and whether it will improve control of the hazard (Table 13.1). Because of its importance, risk profiling needs to be developed into a more 'formal' activity within risk assessment. It needs tools to indicate before a study is undertaken, whether there is insufficient information and resources, or whether control can better be established by defaulting to established controls. Possible controls may include planned inspection, end-product testing, or existing regulatory measures. The risk profile should therefore outline a range of control actions that are likely to be acceptable to all the stakeholders and should indicate whether likely concerns are interim (*acute*) or long-term (*chronic*). Increased globalisation of the trade in foodstuffs, and the regional prevalence of food borne pathogens, increases the challenge of providing accurate risk profiles for hazards that require the use of technically complex controls in parts of the world that are remote from both control agencies and customers.

13.4.2 Risk assessment

If the risk profile suggests that risk assessment can improve decision making, the team must then collect and structure scientifically derived information on hazards, food vehicles, the supply chain and usage habits. This basic information must allow them to determine, through hazard identification and exposure

assessment, if they are dealing with a recognized, new or latent microbiological public health problem or one linked to changes in technology or the food or supply chain. Information should fully describe the hazard (e.g. growth, survival or toxigenesis characteristics), its fate during processing and distribution (e.g. kinetics of killing), routes of contamination (e.g. levels and incidence) and the effects on consumers.

Better information in this area is needed if the risk assessment is to allow the exposure assessment to outline risk determining steps in the food chain, in the context of the food and its use. All risk assessments will include uncertain and variable data, its importance should be communicated to all the interested, affected and expert parties and decision-makers, so that they can take effective and sustainable decisions and explain the basis to consumers at risk. Confronted with variability and uncertainty in information, assessors need to recognize when there is insufficient sound, scientific data, or resources, to produce a valid risk estimate or allow risk managers to decide between risk-based options with confidence. Under these conditions, either the risk profile or assessment should indicate whether existing measures or practices could provide better management of a risk than one derived from a risk analysis.

Technically satisfactory solutions may not be able to maintain or restore consumer trust in a product. Therefore as a second stage risk assessment, Impact Assessment (see pages 287–9) needs to consider the perception of risk by consumers, so that any limitations (e.g. on controls) can be presented to risk managers and communicators, improving their chances of providing effective and acceptable control measures and ensuring risk acceptance.

Hazard identification

Correct identification and understanding of hazards needs to be based on their association with food and consumer illness. Research to provide targeted experimental data and support predictive models for growth/survival/elimination and toxin production is essential and at a practical level needs to provide knowledge for control of 'house strains' in factories. The availability of better data will lead to the use of wider hazard descriptions and improve the identification of key input parameters (risk determining steps) such as potentially hazardous properties in raw materials, and changes in risk associated with formulation, processing and product usage. Better detail will lead to better estimates of inputs, fate of pathogens during processing and factors affecting their eventual presence in the product, such wider descriptions are already used in the USA for MRAs that take account of, for example, the effects of environmental stress on microbial resistance or virulence.

Hazard characterisation

This stage should produce a qualitative and/or quantitative evaluation of the impact of the hazard on human health. Its quality and relevance need to be improved, so that the hazard and its effects can be more realistically described, and prevent unnecessary caution or risk acceptance by sensitive sub-populations.

At present the focus of microbiological risk assessment is on acute disease, chronic diseases receive little attention. With greater interest in long-term health and a wider range of susceptibilities among consumers this must change. Similarly current knowledge of virulence and pathogenicity is limited to a few food vehicles and incidents. Because of food vehicle effects on harmful dose and illness response, progress in technology should be used to improve knowledge on the links between cell physiology and pathogenicity. The first step is to identify critical gaps in our knowledge about hazard inputs and invasion/transmission pathways. Dose-response models have been used in many studies and are likely to form the future basis for risk characterisation. Buchanan *et al.* (1997) have already used an exponential model combining epidemiological data with survey data on *L. monocytogenes* in foods.

Exposure assessment

Reliable exposure assessment is at the heart of risk analysis. Improved qualitative and/or quantitative evaluation of the impact of the supply chain on likely pathogen or toxin levels at consumption will come from data on:

- supply chain and especially process conditions (e.g. times, temperatures and hygiene in manufacturing premises and equipment);
- the microbiological environment (e.g. pH, A_w) within raw materials, food and packaging;
- knowledge of the kinetics and limits of pathogen behaviour;
- likely pathogen distribution and levels.

Integrating this data will show levels and likely intakes of pathogens from different processes or foods or groups of foods. If direct data is not available or there are requirements from process design, estimates may draw on predictions from modelling programs or use assumptions or expert opinion. To ensure maximum accuracy, a strategy for measurement and rules for populating and using predictive models, are needed, with clear explanations of any default values, criteria or assumptions used for particular foods or hazards. The reliability of models must always be considered in the context of the requirements of the study and rules to do this need to be developed.

The use of groups of processes or unit operations (such as pasteurization or acidification) as reference points or short cuts in a study can be illustrated by reference to the management of continuous heat exchangers, where design principles are used to set control parameters for product heating during sterilization. Sterilization process conditions are related to the inactivation kinetics of target micro-organisms (e.g. *Clostridium botulinum*) using product residence time and temperature, based on (validated) assumptions concerning heat transfer and heat penetration into the product. Products may be grouped depending on their heating or flow characteristics or the microbial load of raw materials, to use models and reduce the need for repetition of experimental work. There are limitations to grouping products and using generic exposure assessments. For example, if food products containing particles are made, the

composition or particle size may vary from batch to batch making it difficult to predict the exact heat treatment of each portion of the product during passage through a heat exchanger. Mathematical models exist to predict the distribution of residence times, heat transfer and heat penetration and allow processes to be based on the residence time of the fastest moving particle. The weakness is that models are least accurate at their tails, where the extremes (i.e. fastest or slowest moving product) are found and these include the most critical area for safety. Risk assessments have been used (Brand *et al.*, 2000) to provide insight into this problem based on assumptions (e.g. liquid carrier rheology, minimal temperature loss from equipment and predictable solids shape and concentration) derived from thermophysical characterisation of the food material. Probabilistic, rather than deterministic, risk assessments can be used to take account of this type of uncertainty and improve to process design and management.

Risk characterisation

Integration of information from the first three assessment steps into an estimate of adverse effects in target consumers is the aim. Risk characterisation may address a current situation and suggest a range of reasonable options or alternatives. To improve consumer understanding, risk characterisation may present a comparison of the current microbiological risk with other health risks. Scenarios may improve the reliability and understanding of uncertain information, e.g. a span of sensitivities derived from health statistics or process treatments derived from models, including for example temperature changes associated with retail practices.

An extended framework for risk analysis is needed for many reasons. The current Codex version was developed for regulatory purposes, not for day-to-day supply chain use. Current activities need to be undertaken in a more practical manner and with an aim of widening use and accessibility and improving interaction between the sub-activities.

13.5 Risk acceptance

An additional activity, risk acceptance, is needed to improve the ability of risk analysis to provide messages that maintain consumer choice and provide working information for risk managers, so that they can meet consumer needs based on scientific data. 'Risk acceptance' would structure and take account of the factors valued by stakeholders for identified hazards and try to outline the boundary between acceptance and rejection of a risk within the terms of reference of the risk profile (Fig. 13.4). A balancing stage in risk acceptance should identify acceptable trade-off and ensure that this information is incorporated into a credible control process. This is beyond what can be captured by current technical summaries of risks and benefits and should form the new discipline of risk acceptance. Currently, risk assessment only indirectly provides information leading to risk acceptance. In future the credibility of information providers may

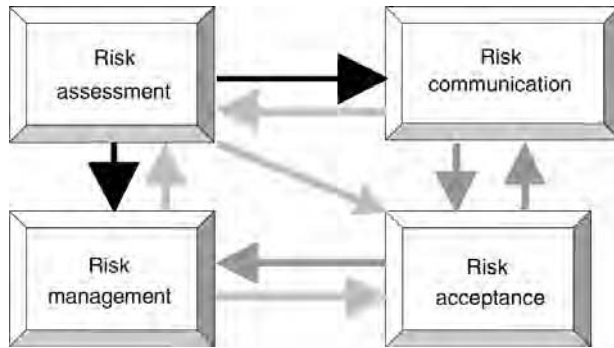


Fig. 13.4 Risk analysis outcomes: messages to consumers and actions for providers.

need to be established and the information needs of consumers better understood within risk analysis. The activity is implied by current schemes, but because of its sensitivity is not made explicit and hence not really managed.

At the beginning of the study, the risk management has to provide the risk assessor with a clear and unbiased brief for collection of data, set out in the risk profile. Risk assessment is currently limited to an analysis of technical data and scientific uncertainty. In future, its output must meet the information needs of risk managers more closely and this must be usable by risk communicators to retain consumer confidence. Effective interaction is needed between risk assessors and risk managers and this should be contained in the risk profile. Risk communication needs a strong 2-way interaction with risk acceptance to ensure that the latter receives the necessary or desired information from the risk assessment, and in turn allows the risk communicator to profile responses to meet consumer demands. This information flow should re-focus, re-direct or extend information gathering by risk assessment (Fig. 13.5).

To derive operational principles for risk acceptance, it is important that the general rules and information sources used by consumers for screening products and technologies are identified and used to provide guidance for producers and regulators on risk acceptance for any topic. The core of any safety determination by consumers is their value judgement of the 'acceptance' of a risk. Expression of 'technical' risk in terms of a performance standard, outlining the cost-benefit trade-offs of a technology may give more informed consumer judgement than use of a technical standard specifying only product and operational details. Properly prepared, a performance standard would allow product and process risks to be evaluated by individual consumers and eventually produce a set of general rules for screening innovations or hazards, so that producers and innovators could eliminate from the risk assessment process technologies that are seen to pose a negligible risk. In the remaining cases, an inventory of costs and benefits would be prepared, thereby characterizing acceptable trade-offs. Such a system needs to contain a means for adjusting the balance statement to accommodate additional factors, for example those pertinent to special groups of consumers.

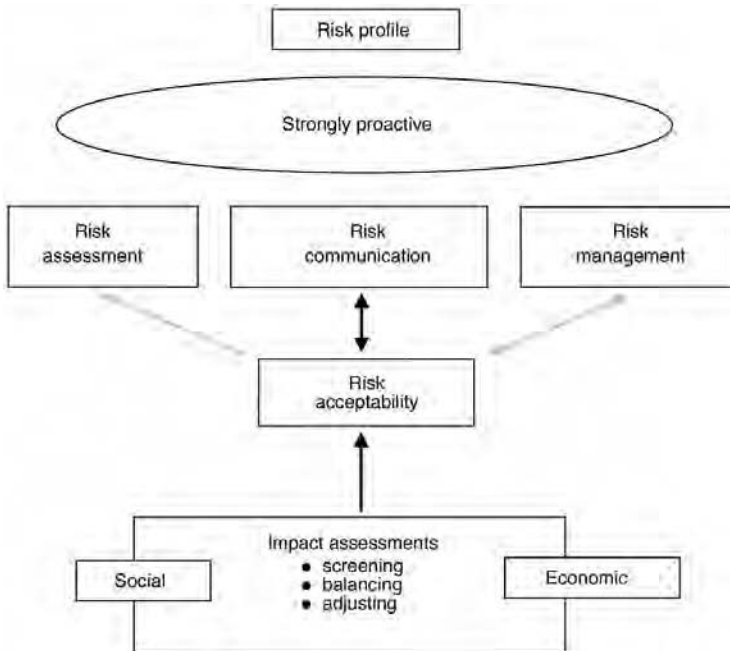


Fig. 13.5 Information flows in risk acceptance.

13.5.1 Finding acceptable risk standards and trade-offs – screening, balancing and adjusting

Many different approaches to understanding consumer perception of risks and hazards have been tried. These include gathering data from those likely to be affected; participatory research with interested parties and consumers to plan, analyse, and react to risk profiles or the findings of a risk assessment. To support decision making, interested parties, such as the media have been involved in creating adapted or alternative plans to assess the potential impact of different courses of action.

To encourage consumers to define acceptable trade-offs, they need to understand how risks are managed and tolerable levels of risk, meeting their needs, are fixed. To do this, they need a credible and orderly procedure for evaluating risk management options (cost/benefit) against individual topics. Availability of such a capability would affect industry, regulatory agencies, consumers and public interest organisations. But consumer trust can only be improved by giving them greater insight into safety systems and better involvement in regulatory processes. This approach may improve acceptance of novel technologies, because consumers would perceive that they have a strong role in determination of safety criteria. Therefore regulators and industry should move from only offering ‘technical’ solutions to risk management and communication, within a strict risk/benefit context, towards factoring in risk perception.

A methodology for finding acceptable levels of risk is needed and within it, procedures for three activities are required: screening, balancing and adjustment. Screening would establish whether a consumer is aware of, or may be exposed to, a new hazard or altered level of risk by a supply chain problem or change or new technology. Balancing would identify acceptable trade-offs based on perception of the change and adjustment would incorporate additional factors needed to ensure perception of a safe control or regulatory process, within the framework of the risk benefit equation. These stages would normally provide levels of protection in excess of that needed for strictly public health purposes. With suitable information and trust, consumers will readily accept products where they accept that they pose a negligible risk, in the remaining cases, they balance risks and benefits to reach acceptable trade-offs or rejections. In some circumstances they may accept a given risk once they are aware of it (e.g. cheese from unpasteurized milk). But they may not accept a similar risk if it challenges their values (e.g. beef or beef on the bone) or acceptance may be adjusted to accommodate personal factors (e.g. consuming raw or undercooked meat). To understand how this is done and make use of it in developing products and technologies with a high chance of consumer acceptance is the function of the impact assessment part of risk acceptance, quantifies consumers' willingness to trade costs and benefits.

If scientific knowledge of the hazard is insufficient or there is uncertainty over interpretation of data, risk managers may apply tighter requirements (a precautionary approach) until better information is available. This is an essential element of risk analysis. It is important at all steps that provide an input to the precautionary measures, especially screening, balancing and adjustment, and their use may lead to a formal requirement for pre-market approval or enhanced QA procedures. Requirements may be relaxed as safety data on new ingredients or technologies become available. Where data is insufficient, additional information should be sought before precautions are relaxed; principles for making decisions are not available at the moment.

13.5.2 Impact assessments

Assessments are analytical techniques to provide risk managers with information to identify and anticipate potential hazards and maximise the effectiveness of risk management actions. To help risk managers decide effectively between alternative means of risk reduction, information from other types of assessment (e.g. social and economic) in addition to the strictly microbiological may be needed, each one being focused on particular aspects of the topic and included under risk acceptance. For example changes in sourcing, preservation or technology may have additional economic and social effects that affect acceptability to consumers. A general analytical methodology (similar to microbiological risk assessment) is not likely to be suitable for examining all these impacts of a decision.

Conflicts arising from different value systems or interpretations of scientific data are inherent in assessments and may require trade-offs or compromises to

reach an action plan, contributory factors need to be given priorities. Tools are needed to provide these priorities and balance risks, costs and benefits in the short and long-term. For example in food safety matters, some consumers may have a technically unjustifiable preference for decentralized, simple, technology versus centralized, complex corporate technology, although from a technical perspective simple technology may be riskier. An impact assessment tool should expose such counter pressures; to show where choices cannot be based only on technical inputs, but have to account for consumer and producer values. Inputs to impact assessments should not be made by experts alone, but should include consumer views and a process for doing this does not currently exist as part of the risk analysis framework. Although some manufacturing and other technical staff may not be directly engaged in conducting either impact or risk assessments, they need to know what sound assessments look like; so that they can make use of the outputs or contribute to impact assessments when needed.

Social impact assessments

A procedure to analyse social impact is needed to determine the social acceptability of products and technologies and produce solutions that are consistent with consumer values. This is necessary because many consumers recognize that although the negative effects of technological change cannot always be prevented, they need to be balanced against benefits. Impact assessment could provide a tool for doing this. Social impact assessments need to assemble information on the likely effects of new products or technologies, including showing options (e.g. alternative approaches or technologies) for preventing or minimizing adverse effects and demonstrating how well consumers are protected. Those having an interest in a particular product may be unclear about the potential problems, thus descriptions of it may require different techniques (e.g. cost-benefit analysis) or reworking information (e.g. as trends, historical surveys or analogy) to meet their needs. Extension to the assessment process would provide a basis for solutions that provide the optimum balance between protection and acceptance. Involvement of consumers leads to the practical problem of expressing risks and benefits. Accessibility may be improved by presenting analyses of the risk/cost/benefit distribution as scenarios. These analyses should be illustrated by various groups including those at greatest risk (to show their benefits), those with the least benefit (to estimate their risks) and a group with an intermediate level of both. In this way individuals, or sub-groups, may be identified whose sensitivity requires more detailed analysis to propose an optimal solution. Accepted changes or risks should be acceptable to every consumer based on best estimates of technological effects and the values used by reasonable individuals.

Some current methods of impact assessment are based on what people say about their values, but outcomes (e.g. product or technology acceptance) rely on what people actually do. No methodology is likely to be perfect, the most they can do is provide insight based on strengths, weaknesses and drivers. Better understanding of the framework of consumer response to hazards; the fewer issues will have to be addressed on an *ad hoc* basis.

Economic impact assessments

To date major users of economic impact assessments have been businesses and governments, who typically ask whether any proposal is workable or feasible, who is affected by it and what is the cost/benefit ratio. These considerations should lead to selection from alternatives. Currently assessment processes to take account of economic considerations do not exist for MRA, although they are a key part of risk acceptance. The process is likely to be based on supply chain cost data collection and analysis, followed by screening, balancing and adjusting to provide optimal, least cost solutions.

13.6 The outputs of risk assessment: risk management and communication

The outputs of impact assessments should accompany risk characterisations and allow relevant information to be fully communicated and/or explained to users and consumers before risk management actions are undertaken.

13.6.1 Risk management and risk/benefit information

Risk management weighs alternative courses of action currently based on the results of a risk assessment and then selects and implements suitable preventative or control options, whilst contending with the uncertainties left by risk and benefit assessments. The future development and use of a process to determine risk acceptance would improve the reliability of these decisions. Because from an industry view, the current three tools are biased towards regulatory and policy use, to be usable at a more practical level, risk management needs to be reinforced with a group of tools to ensure that risks are managed at tolerable cost whilst satisfying the expectations of customers.

This optimisation would be helped by the development of explicit regulatory criteria for acceptable safety performance of specific or novel technologies, for use after impact assessments have determined their fate. To do this effectively questions raised by impact assessments should be resolved early on in any study, so that risk management only focuses on application of the outcome and technical requirements to meet the criteria. Benefits and costs of reducing risk need to be compared, from both operational and consumer perspectives, so that a choice can be made and risk reduction measures implemented – right first time. Quantification of risk and benefit, without balancing and adjusting may in some circumstances be enough to demonstrate acceptance or provide practical guidance. Consumers may eventually accept replacing case-by-case assessments with generic assessments, especially if the science is more convincing at an aggregated level and the value of the approach has been validated by everyday examples.

Involvement of consumers in the risk assessment and risk management process through the development of open transparent procedures for risk acceptance may make the overall process of risk analysis more complex.

Decision-making within this extended framework would take greater account of the needs of all stakeholders (e.g. consumer perception of the problem, the distribution of risks and benefits, expressed preferences for risk reduction and the cost of prevention and control versus effectiveness of risk reduction measures). But progress would provide certainty for risk managers and decision-makers struggling over recommendations.

13.6.2 Selection of options

When risk management options are presented, irrespective of perception, the primary driver for decision-making should be the protection of human health (level of protection), based on scientific knowledge of the microbiological hazards. Technical and economic information on the hazard will have been assessed to show the effects of primary production and processing technology, inspection, and sampling methods on risk level. Any course of action will have technical and economic implications for the operations involved and these will determine its feasibility in a particular situation. The best solutions will provide cost-effective means of limiting risk, with benefits and costs reasonably related, based on the tolerable level of risk and preferences expressed by consumers.

End-product testing alone cannot ensure effective control of food safety, because it cannot assure the absence of pathogens. Increased levels of testing should not be a recognized risk management outcome, because the low levels and the non-uniform distribution of pathogens in most foods make it statistically impossible for end-product testing to ensure low levels of risk. These are only obtainable from correct product/process design and process control. However microbiological testing can be used to validate control measures (e.g. HACCP) and to verify, on a day to day basis, their consistent implementation and effectiveness. Where HACCP has not been employed, or there are production problems or limited access to verification information (e.g. from suppliers), testing has a useful role in risk management. The development of protocols and 'generic' schemes for the validation and verification of risk-based systems would increase their accessibility to small businesses and improve their acceptability to consumers, if part of the validation process involved showing their relation to an impact assessment (see below).

13.6.3 Monitoring and review

Risk management decisions will lead to control or preventative measures. Their implementation, effectiveness and relevance should be monitored in relation to the incidence and level of linked food-borne diseases and should be reviewed, as new information becomes available. In addition to regular verification, new information should trigger the review of scientific (e.g. epidemiological studies, knowledge of the virulence of the organism or its prevalence and level in foods), supply chain (e.g. changes in food technology or the supply chain) or consumer information (e.g. changes in intake patterns, product use or the extent of

sensitive populations). This may be compared with and used to update the risk profile and would be a valuable addition to any web-based system containing hazard and risk data along with generic studies.

Producers and consumers should contribute to the development of guidelines for review, who will conduct them, what will be evaluated and the techniques to be used. The review should be based on performance criteria to judge success in implementing risk reduction plans and reducing risk, for example by reference to the incidence and nature of product recalls and consumer complaints, or information on the effectiveness of HACCP or pre-requisite programs. Government may also carry out reviews to support their responsibilities for setting objectives, including the availability of information relating to the food borne pathogen(s) targeted for control measures and the effectiveness of the regulatory control programmes. Such reviews need to ensure that additional information from disease surveillance and research programmes, is fed through to existing studies to ensure that uncertainties and knowledge gaps are progressively reduced. Both producers and governments should review costs and benefits and promote discussion with consumers and producers; results may warrant changing parts of the risk assessment or risk management activities to ensure that on-going measures remain effective and are perceived as such.

13.6.4 Risk communication

Risk communication is the final element of the risk analysis process and an integral part of the other elements. Risk communication should provide consumers with an effective representation of risks and controls, including the probability of realization and the consequences (hazard). Communicating the results of a risk assessment and interaction with risk management may be done to as part of risk acceptance, to answer questions from decision-makers. The questions will often be context dependent e.g. probability of harm in different markets, sensitivity of incidence to the level of hazard in raw materials, risks per typical product portion and effects of product use. Providing clear answers is a function of the impact assessments and the process of screening, balancing and adjustment.

Clearly risk communication has dual roles. Firstly, to provide consumers with information from the expert scientific review of the hazard and assessment of risks, including information relevant for specific target groups, such as infants or the elderly. For any hazard, this information should allow consumers at risk to exercise their own options to achieve preferred levels of protection. Secondly, it needs to provide producers and regulators with the information specific for risk management. The outputs needed by consumers and users, especially decision-makers need to be identified from the risk profile onwards. However risk assessment is structured, dealing with uncertainty and variability results from lack of information or the availability of controls remains a knotty problem.

The Codex Alimentarius position on communication in risk analysis is too narrow for practical use, it needs to develop from being 'an interactive process of exchange of information and opinion on risk among risk assessors, risk

managers and other interested parties' (Codex Alimentarius, 1997), towards the broader definition from The United States Research Council 'an interactive process of exchange of information and opinion among individuals, groups and institutions which involves multiple messages about the nature of risk and other messages, not strictly about risk, that express concerns, opinions or reactions to risk messages or to legal and institutional arrangements for risk management' (US National Research Council, 1996).

13.7 Conclusion

Orderly safety management and regulation against accepted criteria requires well-specified, logically defensible procedures that are perceived as acceptable by all the parties involved. Without them, control is inconsistent and unpredictable, failing to provide either the level of protection that consumers expect and the stable environment needed by producers. The aim of microbiological risk analysis in an extended form should be to provide a global standard for identification of hazards and management of the acceptance of risks associated with foods for different groups of consumers. Risk assessment is an essential part of risk analysis because it specifies technical risks for pathogenic micro-organisms and foods, on the basis of sound science, combining process and scientific data. Its further development should deal with perceived risks to increase its acceptance as a risk management tool among consumers. This concept is still in its infancy, but needs to be developed globally.

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Index

- acceptable daily intakes (ADIs) 24
- acceptable level of risk *see* appropriate level of protection (ALOP)
- acceptance of risk *see* risk acceptance
- acidity 80–1
- adjustment 287
- Adulteration of Food Act 1860 218
- adverse health effects 55–6
- alar 190
- ALARA principle (as low as reasonably achievable) 27, 176
- algebra 146–7
- animals 117
 - small animal studies 84, 85–6
 - extrapolation to humans 93
- Appert, Nicholas 7
- apples 190
- appropriate level of protection (ALOP) (TLR) 27, 30–1, 177, 178, 179–80, 239–40, 263, 277–8
- @RISK 203–5
- attributes sampling plans 222, 238–9
- audience 163–4
- Australia 195, 236
 - E. coli* process criteria 217, 233
- Bacillus cereus* 5, 31–3
- bacteria 70, 275–6
 - see also* pathogens
- 'bad bug book' 69, 195, 196
- balancing 287
- Bayesian statistics 147
- benchmarking 176
- Beta-binomial function 89
- Beta-Poisson function 89
- bio-informatics 271
- biomarkers 84, 86
- blood products 9
- bongkrek 10
- botulinum cook (bot cook) 189, 216–17, 234
- Campden and Chorleywood Food Research Association (CCFRA) 250, 251, 258–61
- Campylobacter* 33–4, 160
- canned foods 11–13, 118–21, 189
- case-control studies 270–1
- Center for Disease Control and Prevention (CDC) 69, 195, 196
- Center for Food Safety and Applied Nutrition 195, 196
- cheese 182
- chemicals 27–8
- Chicago Department of Public Health (CDPH) 96
- chicken products 150
 - see also* poultry meat
- clearing houses 195–6
- clinical trials 83–4, 92–3, 270–1
- Clostridium botulinum* 11–13, 30–1
 - botulinum cook 189, 216–17, 234

- Clostridium perfringens* 5
- Codex Alimentarius Commission (CAC)
2, 17, 20, 24, 25, 78, 215
- Codex Committee on Food Hygiene 2
- Codex Committees 24, 25, 26
- General Principles of Food Hygiene
184
- HACCP 250, 251
- microbiological criteria 185–6, 215–16,
219–20
- Principles and Guidelines for the
Conduct of MRA* 22, 49–50
- qualitative risk assessment 143
- risk 157
- risk communication 155, 166
- risk management 177–8
- cold smoked fish 234–6, 247
- Communicable Diseases Centre 195
- communication
concept 163–6
- risk communication *see* risk
communication
- comparative MRAs 143
- computing skills 134
- confidence intervals 140, 141, 201
- consumers
information on consumption and 59,
68, 110–11, 117
- risk perception 158–63, 190, 286
- contagious flesh, selling of 9
- contamination levels 73, 238–9
- content sites 195, 196
- continuous heat exchangers 283–4
- control measures 181, 267–8
see also food safety management
strategies
- control points 232–3
see also critical control points
- cooked ham 118–21
- corrective action plan 250, 255, 261
- Coxiella burnetii* 13–14
- criteria *see* microbiological criteria;
performance criteria; process
criteria
- critical control points (CCPs) 17, 18, 70,
183, 250, 254, 260
- critical limits 184, 250, 254, 260
- D*-value 74, 116–17
- data *see* information
- databases, linked system of 194, 209–10
- death of pathogens 73–4, 272
- decision support 203, 204
- decision support systems 207–9, 210
- decision trees 203, 204, 254
- default hazard characterization 237
- Department of Health 167–9
- design weakness 256–7
- deterministic (mechanistic) models 60,
87–8, 145, 201–3
- Disability Adjusted Life Years (DALY)
55, 229–31
- disease triangle 54, 54–5, 79–81
- distribution functions 88–9
- distribution of microbiological hazards
72–3
- DMFit 205
- documentation 250, 255–6, 261
- dose–response relationship 2, 14, 36, 50,
54–7, 77–99, 283
- characters of pathogen, host and
environment 54–5
- disease triangle 54, 54–5, 79–81
- dose–response analysis 56–7
- evaluation of adverse health effects
55–6
- extrapolation from high doses to low
doses 93
- hazard characterization v. 78–9
and microbiological criteria 228–9, 237
- modelling dose–response relationships
56–7, 86–90, 91
- theories of infection 81–2
- types of dose–response data 83–6
see also hazard characterization
- dying, risk of 137, 158
- dynamic models 197
- economic impact assessments 289
- egalitarians 164
- eggs and egg products 150, 189
- empirical models 87–8, 197–201
- end-product testing 14–16, 270–1, 290
- Enterobacteriaceae 189
- epidemiological studies 84, 84–5, 270–1
- equivalence 261
- Escherichia coli* (*E. coli*) 91, 110, 150–1,
217, 232–3, 233
- European Union (EU) 215–16, 249
- Eurosurveillance system 196
- experimental design 198
- expert consultations 21–3, 24, 26, 155–6,
167, 169
- expert opinion 84, 114, 152
- expert systems 147
- experts 117
- risk perception 161–3
- exponential function 89

- exposure assessment 2, 14, 35–6, 50,
 57–60, 100–26, 283–4
 building up supply chain data for
 109–11
 characterization of sources, routes of
 exposure and pathogen occurrence
 58–9
 compared with hazard identification
 65
 and HACCP 103–5, 109–10
 hazard characterization, risk
 characterization and 135–6
 integration with other MRA stages in
 risk characterization 128, 130, 133
 output 117–22
 role in MRA 101–5
 scope 114–15
 sources of information 111–14
 stages in 105–8
 team for 109
 types of data 114–17
 use of models 35–6, 59–60
 extrapolation 93
- factor analysis 160–1, 162, 162–3
 Failure, Mode and Effect Analysis
 (FMEA) 248
 fatalists 164
 first order exponential growth model 197
 fish
 cold smoked fish 234–6, 247
 pufferfish 9–10
 unsold 9
 flow diagrams 253, 260
 Food and Agriculture Organisation (FAO)
 20, 24, 25, 78, 175, 195, 196
 joint expert consultations 21–3, 24, 26,
 155–6, 167, 169
 Food Design Support System 207
 Food and Drug Administration (FDA) 96,
 147, 148–50, 249
 ‘bad bug book’ 69, 195, 196
 food matrix effects 54–5, 80–1
 Food MicroModel 206
 Food and Nutrition Alliance 163–4
 food processing skills 135
 food safety 183, 268–9
 historical background 6–7
 trends in food safety control 29–34
 food safety control scheme 278
 Food Safety Information Center 69
 food safety management strategies
 181–90
 definitions and equation 181–2
 microbiological criteria 185–90
 performance criteria 181, 183–4
 performance standards 181–2, 182–3
 process criteria 181, 184
 product criteria 181, 184–5
 food safety objectives (FSOs) 3, 37, 177,
 181, 261–3, 275
 establishing 177–80
 and microbiological criteria 185, 186,
 189–90, 226–7
 performance standards 182–3
 food safety risk assessment tool 208–9
 food safety standards 23–9, 29–30
 setting 23–6
 trends in 27–9
 food safety systems 7–23
 establishing process criteria 11–14
 GMP 8, 16, 29
 HACCP *see* HACCP
 microbiological testing 14–16
 ‘precautionary’ principle 10–11
 predictive modelling 18–20
 ‘prohibition’ principle 9–10
 QRA 8, 20–3
 Food Standards Agency (FSA) 159,
 257–8
 FORECAST system 206–7
 frozen products 118–21
 fugu 9–10
 future of MRA 266–92
 development of risk assessment
 processes 278–80
 information for risk assessment 269–78
 key steps in risk assessment 280–4
 risk acceptance 284–9
 risk management and communication
 289–92
- gastrin 81
 General Agreement on Tariffs and Trade
 (GATT) 1, 20, 214, 226
 see also World Trade Organisation
 generic studies 273–4
 genomics 271
 Gompertz model 116, 196–7
 good hygienic practice (GHP) 176, 179,
 180, 227
 good manufacturing practice (GMP) 8,
 16, 29
 governmental MRA 148–50, 151–2, 176–7
 ground beef hamburgers 150–1, 232–3
 growth of pathogens 71–2, 73
 growth curves 116, 198–200
 guidelines, microbiological 216

- HACCP (Hazard Analysis and Critical Control Point) system 3, 248–65
 common failures 257
 exposure assessment and 103–5, 109–10
 food safety control 29, 33–4
 future relationship with MRA 261–3
 implementation problems 256–8
 interaction between HACCP systems and MRA 258–61
 international guidance on
 implementation 250–6
 introduction of 8, 17–18
 legal requirements 249–50
 and microbiological criteria 215, 218, 226, 227, 231
 principles 18, 250
 risk management 176, 179, 180
 team 252, 259
- ham, cooked 118–21
- hamburgers 150–1, 232–3
- hazard analysis
 HACCP system 250, 253–4, 260, 267
 industrial 176
- hazard characterization 2, 5, 50, 54–7, 65, 77–99, 282–3
 default 237
 disease triangle 54, 54–5, 79–81
 v. dose–response 78–9
 evaluation of adverse health effects 55–6
 exposure assessment, risk
 characterization and 135–6
 future trends 94–6
 integration with other stages of MRA in
 risk characterization 128, 130, 133
 key issues 77–82
 modelling dose–response relationships 56–7, 86–90, 91
 multidimensional 139
 problems in 90–4
 research needs 95
 theories of infection 81–2
 types of dose–response data 83–6
see also dose–response relationship
- hazard identification 2, 5, 13, 49, 53–4, 64–76, 282
 changes in microbial hazards 73–5
 conducting 66–7
 coverage 65–6
 decision support in 203, 204
 defining 64–5
 integrating with other stages of MRA
 in risk characterization 128, 130, 133
 key information 67–9
 microbial hazards 70–2
 origin and distribution of microbial
 hazards 72–3
 other biological hazards 75
 scope 66
 tools 69–70
- hazards 70–2, 266
 defining for HACCP 17–18
 severity 71, 187–8
 dose and 228–9
 sampling plans 188, 225
- health effects, adverse 55–6
- heat exchangers 283–4
- heat treatment 7, 74, 232, 272
 botulinum cook 189, 216–17, 234
D and *z* 74, 116–17
 process criteria 11–14
see also temperature
- heuristic knowledge 194
- hierarchists 164
- host factors 54, 54–5, 79–80
- human volunteer feeding studies 83–4, 92–3, 270–1
- humans *see* people
- illustrative studies 273–4
- ILSI Risk Science Institute 50–1
- impact assessments 282, 287–9
- in vitro* studies 84, 86
- incompatibility 133
- indicator organisms 15
- individualists 164
- industrial MRA 151–2, 176–7
- industry records 180
- infection, theories of 81–2, 179, 227–8
- infectious disease triangle 54, 54–5, 79–81
- infectious dose 79
- infectious microorganisms 79
- inference engine 210
- influence diagram 234, 235
- information
 for exposure assessment 111–17
 sources 111–14
 types of data 114–17
 flows in risk acceptance 285, 286
 for hazard identification 67–9
 internet sites 69, 195–6
 linked system of databases 194, 209–10
 microbiological information 67–8, 103, 106, 116–17
 quality 69, 112–14
 for risk assessment 269–78

- data needs 269–70
 - knowledge gaps 275–7
 - risk characterization 152
 - sources for MRA 193–4
- inputs, appropriate 133
- intensive outbreak investigations protocol 96
- interactive food safety risk assessment tool 208–9
- International Commission on Microbiological Specifications for Foods (ICMSF) 15, 17, 35, 261
- sampling plans 186–8, 221, 222, 225
- international food safety standards *see* food safety standards
- internet information sites 69, 195–6
- iso-risks 229–31

- Japan 9–10, 85
- joint expert consultations 21–3, 24, 26, 155–6, 167, 169
- Joint FAO/WHO Expert Committee on Food Additives (JECFA) 20, 25–7
- Joint FAO/WHO Expert Meeting on Microbial Risk Assessment (JEMRA) 78
- Joint FAO/WHO Meeting on Pesticide Residues (JMPR) 24, 25, 26

- kinetic models 116
- knowledge gaps 275–7
- Koch, Robert 7, 14

- Level of Protection (LOP) 262–3
 - see also* appropriate level of protection (ALOP)
- linked system of databases 194, 209–10
- Listeria monocytogenes* 5, 110, 182, 185, 208, 226, 274
 - dose and hazard severity 228–9
 - dose–response models 90, 91
 - exposure assessment 118–21
 - FSO 179, 189, 234
 - process criteria 234–6
 - risk assessment for RTE foods 148, 191
- listeriosis 148, 224, 229
- low-acid canned foods 11–13, 118–21, 189

- management neglect 257
- mandatory criteria 215
- mandatory guidelines 216
- mathematical models *see* modelling/
 - models
- mathematical skills 134
- matrix effects, food 54–5, 80–1
- maximal residue levels (MRLs) 26
- mechanistic (deterministic) models 60, 87–8, 145, 201–3
- media 165–6
- medical skills 134
- message 164–5
- microbiological criteria 3, 15, 16, 185–90, 214–47
 - dose and hazard severity 228–9
 - early use of 218–19
 - ‘equivalent’ food safety risk 229–31
 - and food safety assurance 226–7
 - and FSOs 185, 186, 189–90, 226–7
 - future trends 239–40
 - key issues in use of 217–20
 - principles for establishing 219–20
 - prioritising risk management actions 236
 - sampling plans 185–8, 221–5
 - specification of 220
 - types of 215–16
 - using MRA to set 227–31
 - using MRA to develop performance and process criteria 231–6
 - using in risk assessments 236–9
- microbiological guidelines 216
- microbiological information 67–8, 103, 106, 116–17
- microbiological models *see* modelling/
 - models
- microbiological reference values 274–5
- microbiological risk assessment (MRA) 2, 3, 13–14, 47–63
 - current activities 22–3
 - current issues 34–8
 - exposure assessment *see* exposure assessment
 - future of *see* future of MRA
 - hazard characterization *see* hazard characterization; dose–response relationship
 - hazard identification *see* hazard identification
 - interaction between HACCP systems and 258–61
 - key steps 49–53, 280–4
 - limitations 49
 - principles 51–2
 - risk characterization *see* risk characterization
 - safety 268–9

- microbiological risk assessment (*cont.*)
 - tools for *see* tools for MRA
 - trends in food safety control 29–34
 - usefulness 48
- microbiological skills 134
- microbiological specifications 216
- microbiological standards 215–16
- microbiological testing 14–16, 270–1, 290
- Microfit 205
- MIDAS system 207
- milk 13–14, 31–3
- minimum infective dose (MID) (threshold model) 81–2, 179, 227–8
- modelling/models 52, 73
 - deterministic (mechanistic) models 60, 87–8, 145, 201–3
 - dose–response relationships 56–7, 86–90, 91
 - empirical models 87–8, 197–201
 - exposure assessment 35–6, 59–60
 - Monte Carlo 35–6, 60, 113, 145–6, 205
 - off-the-shelf models 205–7
 - predictive *see* predictive modelling
 - process and performance criteria 234–6, 246–7
 - risk characterization 144–51
 - selection of models 88
- moderate hazards 187
- molecular biological techniques 69–70
- monitoring 290–1
 - HACCP 250, 254, 260
- Monte Carlo modelling 35–6, 60, 113, 145–6, 205
- Mortimore, S. 250, 251
- most probable number (MPN) 238
- multiple infection sites 82
- multiple outbreak investigations 85

- National Advisory Committee on Microbiological Criteria for Foods (NACMCF) 250
- neural networks 147
- non-compliance 235–6, 237
- non-threshold model (single–cell) 81–2, 179, 228

- objectives 130
- off-the-shelf models 205–7
- Office International des Epizooties (OIE) 51
- older people 10–11
- operating characteristic curve (OC curve) 223–4
- options, selection of 290
- outbreak investigations 96, 117
- outline MRA 132, 144
- outputs
 - exposure assessment 117–22
 - risk assessment 289–92
 - risk characterization 131–2, 142–7
- outrage factors 158–61
- oysters 149

- parasites 75
- Pasteur, Louis 7
- pasteurisation 7, 13–14, 232
- pasteurised milk 31–3
- paté 191
- Pathogen Modelling Program 69, 205–6
- pathogen risk management *see* risk management
- pathogenicity, mechanisms of 79
- pathogens 35
 - death of 73–4, 272
 - disease triangle 54, 54–5, 79, 80
 - growth *see* growth of pathogens
 - identifying origin and distribution 72–3
 - information about 67–8, 103, 106, 116–17
 - knowledge gaps 275–7
 - source(s), route(s) and occurrence 58–9
 - survival of 74
 - virulence 36, 68, 80
- people
 - consumers *see* consumers
 - extrapolation of animal data to 93
 - host factors 54, 54–5, 79–80
 - lack of quantitative human data 92–3
 - susceptibility 68, 79–80, 229
 - types 164
 - vulnerable groups 10–11, 12, 160
- performance criteria 179, 181, 183–4, 216–17, 262, 291
 - development using MRA 231–6
 - heat pasteurization of milk 13–14
- performance standards 181–2, 182–3, 285
- Pillsbury Company 248, 249
- portal sites 195, 196
- portion size 110
- poultry meat 33–4, 118–21, 150
- ‘precautionary’ principle 10–11, 191, 287
- predictive modelling 18–20, 29, 59–60, 108, 196–203, 271–3
 - empirical modelling 197–201
 - mechanistic models 201–3
- pregnant women 11, 12

- preliminary MRA 132, 144
- prioritisation 236
- proactive risk communication 167, 167–9
- probabilistic modelling 60, 209
- probability 157
- process criteria 7–8, 11–14, 181, 184, 216–17, 262
 - low-acid canned foods 11–13
 - pasteurization of milk 13–14
 - using MRA to develop 231–6
- Process Hygiene Index 217
- process-related information 68–9
- process risk model (PRM) 150–1, 232–3
- product 252–3
 - description 259
 - diversity 34–5
 - identification of intended use 259
- product criteria 181, 184–5
- ‘prohibition’ principle 9–10
- psychometric techniques 160–1, 162, 162–3
- Public Health Laboratory Service 195
- pufferfish 9–10
- purpose 128
 - clear statement of 130–2
- Q fever 13
- qualitative information (narratives) 62
- qualitative risk assessment 52, 59, 117–22, 276
 - risk characterization 142–4
 - tools for MRA 194, 195–6
- quality of life indicators 55, 229–31
- quantitative risk assessment (QRA) 8, 20–3, 52, 59–60, 122, 276
 - examples of 102, 147–51
 - risk characterization 144–7
 - tools for MRA 194, 196–209
- quasi-mechanistic models 202
- quorum sensing 80
- reactive risk communication 167
- ready-to-eat (RTE) foods 148, 189, 191
- record keeping 250, 255–6, 261
- reference values, microbiological 274–5
- regulators 279
- review 261, 290–1
- risk 156–8, 267
 - meanings 156–7
 - technical expression of 157–8
- risk acceptance 277–8, 284–9
 - acceptable standards and trade-offs 286–7
 - impact assessments 287–9
- risk analysis 3, 95–6
 - expert consultation 21
- risk assessment 3
 - expert consultations 21–2
 - food safety standards 24–6
 - key steps 280–4
 - microbiological *see* microbiological risk assessment
 - in a risk analysis framework 95–6
 - tools for 267–8
- risk assessors 280
- risk-based food safety control scheme 278
- risk/benefit information 289–90
- risk characterization 2, 14, 36–7, 50, 60–2, 127–54, 284
 - current problems and future trends 151–2
 - examples 147–51
 - key issues 127–9
 - methods 135–42
 - qualitative outputs 142–4
 - quantitative outputs 144–7
 - requirements 129–35
 - appropriate inputs 133
 - clear statement of purpose 130–2
 - skills and tools 133–5
 - risk characterization curve 179–80
 - semi-quantitative outputs 143, 144
 - stages 128–9
- risk communication 3, 155–71, 190, 285, 291–2
 - benefits and uses 166–7
 - concept of communication 163–6
 - concept of risk 156–8
 - expert consultation 21–2
 - future of 169–70
 - proactive and reactive 167
 - risk perception 158–63
 - strategy 167–9, 169
- risk comparisons 157, 158, 165
- risk determining factors 139–40
- risk estimate 60–1, 137
- risk factor analysis 160–1, 162, 162–3
- risk management 3, 29–30, 103, 175–92, 285, 289–91
 - Codex Committees 26
 - developing food safety management strategies 181–5
 - establishing FSOs 177–80
 - establishing microbiological criteria 185–90
 - expert consultations 21, 22
 - future trends 191

- risk management (*cont.*)
 - implementation problems 190
 - monitoring and review 290–1
 - prioritization using MRA 236
 - and risk/benefit information 289–90
 - selection of options 290
- risk managers 101–2, 280
- risk perception 158–63, 190, 286
 - expert perception vs public perception 161–3
 - outrage factors 158–61
- risk profile 143–4, 280–1
- route(s) of exposure 58–9

- safety *see* food safety
- Salmonella* 15, 16, 150, 160, 189, 256–7
 - dose–response relationships 90, 91
 - exposure assessments 118–21
 - targets 33–4
- Salmonella enteritidis* 85, 91, 150
- salt 6
- sampling plans 185–8, 221–5
 - reliability of 223–5
 - and risk 225
 - stringency 188, 225
 - variability and 221–2
- SAS 203
- Sanitary and Phytosanitary (SPS)
 - Agreement 1–2, 20–1, 177, 226, 239–40, 261
- Sanitation Standard Operating Procedures (SSOPs) 249
- scope
 - exposure assessment 114–15
 - governmental and industrial MRAs 151–2
 - hazard identification 66
 - risk characterization 130–1
- screening 287
- second-order modelling 87, 146
- semi-quantitative MRA 143, 144, 225
- sensitivity analysis 61, 232–3
 - risk characterization 129, 136–7, 139–40, 140
- sensitivity coefficient 137
- sequelae 93–4
- serious hazards 187
- severe hazards 187
- severity
 - disease 55, 229–31
 - hazard 71, 187–8, 225, 228–9
- severity assessments 92
- shelf-life model 234–6, 246–7
- shellfish 149

- SIEFE model (Stepwise and Interactive Evaluation of Food safety by an Expert system) 207–8
- sigmoid growth curves 116, 198–200
- single-cell (non-threshold) model 81–2, 179, 228
- Single-Hit function 89
- social impact assessments 288–9
- source(s) of pathogen 58–9
- specifications, microbiological 216
- spreadsheet-based food safety risk assessment tool 208–9
- SPSS 203
- standards
 - international food safety standards 23–9, 29–30
 - microbiological 215–16
 - performance 181–2, 182–3, 285
- Staphylococcus aureus* 15, 16, 75, 118–21
- static models 196–7
- statistics 134, 146–7
- Steering Group on HACCP Standards 252
- sterilization 11–13, 189, 283–4
- storage criteria 31–3
- supply chain 279
 - core information 115–16
 - data for exposure assessment 109–11
 - generic model 103, 104
 - model 105–8, 111
- surveys 270–1
- survival of microorganisms 74
- susceptibility 68, 79–80, 229

- taboos 6
- targets 33–4, 37
- tempe bongkrek 10
- temperature 32–3, 116–17
 - see also* heat treatment
- terms of reference 250–2, 259
- testing, microbiological 14–16, 270–1, 290
- tetrodotoxin poisoning 9–10
- threshold (minimum infective dose)
 - model 81–2, 179, 227–8
- tolerable level of risk (TLR) (ALOP) 27, 30–1, 177, 178, 179–80, 239–40, 263, 277–8
- tools for MRA 193–213
 - decision support in hazard identification 203, 204
 - decision support systems 207–9
 - future trends 209–10
 - model development and validation 203–5

- off-the-shelf models 205–7
- predictive modelling 196–203
- qualitative tools 195–6
- toxico-infectious microorganisms 79
- toxins 71, 72, 79, 110
 - toxigenesis 74–5, 275–6
- trade-offs 285, 286–7
- trust 159
- uncertainty 87
 - distinguishing variability and 138
 - exposure assessment 112–14
 - risk characterization 61–2, 129, 132, 138, 140–1
- United Kingdom (UK) 218, 252
 - FSA 159, 257–8
 - risk communication 167–9
- United States (USA) 236, 250
 - CDPH 96
 - Department of Agriculture (USDA) 147, 148–50, 195, 196
 - FDA 69, 96, 147, 148–50, 195, 196, 249
 - HACCP regulations 249
 - internet information sites 69, 195–6
 - listeriosis outbreak 1998/9 224
- unsold fish 9
- Uruguay Round 1, 20, 226
- validation 62, 129, 142
 - dose–response models 94
 - HACCP 255
 - performance criteria 183–4
 - predictive models 200, 201, 202, 203–5
- variability 87
 - distinguishing uncertainty and 138
 - exposure assessment 112–14
 - risk characterization 61–2, 128, 132, 138–9
 - and sampling plans 221–2
- variables sampling plans 221–2
- verification
 - HACCP 250, 255, 261
 - MRA 37–8, 62
- Vibrio cholerae* 7
- Vibrio parahaemolyticus* 91, 149
- virulence 36, 68, 80
- viruses 75
- vulnerable groups 10–11, 12, 160
- Wallace, C. 250, 251
- Weibull-gamma function 89
- World Health Organisation (WHO) 20, 25, 78, 175, 195, 196
 - joint expert consultations 21–3, 24, 26, 155–6, 167, 169
- World Trade Organisation (WTO) 8
 - SPS Agreement 1–2, 20–1, 177, 226, 239–40, 261
 - see also* General Agreement on Tariffs and Trade
- z-value 74, 116–17

