2. How to perform risk assessments

To carry out risk assessments you need resources – people, information and data handling. Even modest assessments will cost in the tens of thousands of dollars and some of the very large QRAs probably exceed the million dollar mark. So before you make an investment in risk assessment you should have at least one good reason for doing it. Of course, the need may already have been specified for you, for example, by regulators in a country to which you export. Suppose all the major seafood importing blocs (European Union, United States, Japan) decide that they require risk estimates for all products they import – then every exporting country would have to respond to that requirement.

2.1 PROCESS INITIATION

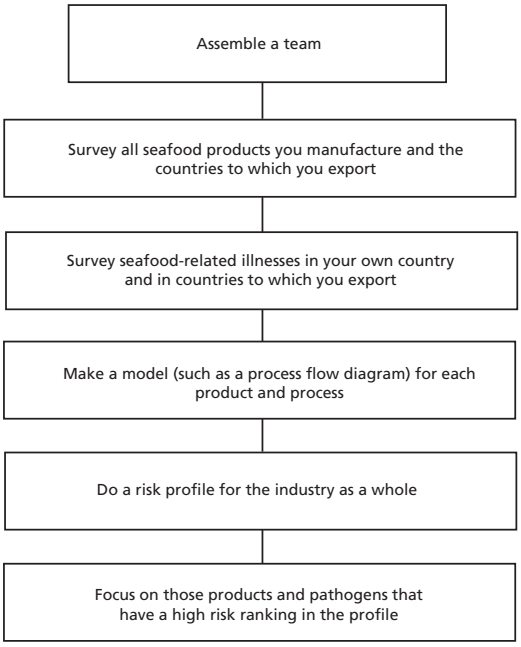
The first task is called process initiation – getting started on responding to your customers' requirements. One strategy is to proceed in the following manner.

Stage 1: Assemble a team

As for HACCP planning, you need a team that covers a range of disciplines:

- a seafood technologist with knowledge of processes and products;
- a food microbiologist who knows about microbial ecology;
- a statistician to assemble and handle data;
- a manager to direct the work

As the manager, it is your task to find the specialists needed to undertake the risk assessment work on behalf of your country. In larger countries with a history of seafood exports, this will not be a great problem. In smaller countries, however, you may need help. Together with WHO, FAO has prepared a number of texts that take you to advanced levels in risk assessment, and these are included in the Resources Bank.



Stage 2: Survey the industry

Make a survey of all the seafood products you manufacture and the countries to which you export. This is a straightforward task since every nation keeps a record of its seafood production volumes and species.

Stage 3: Survey seafood-related illness

Do a preliminary study of seafood-related illnesses in your own country as well as in countries to which you export. This will set the scene for doing a risk profiling exercise.

If your Health Department keeps records of food poisoning incidents, that is a good place to start your survey. You can make a list of seafood incidents, linking products with hazards (micro-organisms and toxins) and include these hazard:product pairs in the risk profile. In many countries, however, resources are so scarce that keeping statistics is not a high priority so you should spend some time searching and talking to people who would be likely to know of any illnesses caused by seafood consumption. This is purely anecdotal evidence but has some value – therefore make notes of your conversations.

The next stage is to look for statistics from customer countries. If you have Internet access, there are a number of Web sites, some of which are listed below, where information on food poisonings are included (Table 2).

TABLE 2
Sources of information on seafood illness and recalls of seafoods

Country	Organization	Web site
European Union	Eurosurveillance Weekly	http://www.eurosurv.org
USA	Centre for Science in the Public Interest	http://www.cspinet.org
USA	Morbidity and Mortality Weekly	http://www.cdc.gov/mmwr
UK	Public Health Laboratory Service (PHLS)	http://www.phls.nhs.uk
Australia	Communicable Diseases Intelligence	http://www.health.gov.au
Australia	Food Standards Australia and NZ	http://www.anzfa.gov.au
International	Food Safety Network	http://www.foodsafetynetwork.ca

Once you have gathered data, assemble them into a summary table. A collection of outbreaks of seafood-related illness in the United States and Australia over the period 1990–2000 is an example of the hazards and products involved in those countries (Table 3).

The data in Table 3 are valuable because they:

- identify the main seafood hazards;
- provide background on what has caused problems in importing countries.

If you look a little more carefully at the data, you can make a list of hazards and products that will shape your risk profiling exercise (Table 4).

You now have a list that can form the basis of your risk profile. There may be other perceived issues that need to be added to the list, for example mercury in species such as swordfish, and sulphite or chloramphenicol in shrimp. Some countries perceive these as food safety issues and they also become trade issues, so they are important, and you may wish to assemble some information on them.

TABLE 3
Seafood related illnesses in the United States and Australia (1990–2000)

	USA		Australia	
Category	**Cases**	**Outbreaks**	**Cases**	**Outbreaks**
Ciguatera	328	75	616	10
Histamine	680	103	28	10
Viruses	1 573	13	1 737	3
Bacterial pathogens	1 246	35	159	6
Biotoxins	125	9	102	3
Total	3 952	235	2 642	32

TABLE 4
Hazards and products that should be included in the risk profile

Hazard	Product
Chemical hazards	
Ciguatera	Reef fish
Mercury	Predaceous fish
Sulphite	Shrimp
Biotoxins	Bivalve molluscs
Biological hazards	
Viruses	Bivalve molluscs
Listeria monocytogenes	Smoked seafoods
Salmonella	Cooked shrimp
Vibrio parahaemolyticus	Shellfish eaten raw
Staphylococcus aureus	Cooked seafoods
Clostridium botulinum	Canned, vacuum-packed seafoods
Histamine	Scombroid fish
Parasites	Raw fish

Further reading on seafood statistics
If you want to read in more depth about statistics on seafood-borne diseases there is a section in *Assessment and management of seafood safety and other quality aspects,* which you will find in the Resources Bank.

Stage 4: Do a risk profile

If you do a risk profile of the industry as a whole this will give you a focus on products and pathogens of most concern. For the purpose of this document, risk profiling is defined as "*a description of a food safety problem and its context developed for the purpose of identifying those elements of a hazard or risk that are relevant to risk management decisions*".

This phase of the work entails gathering data in three areas:

- hazard identification
- hazard characterization
- exposure assessment

Once this is done you will know which pathogen:product pairings should be investigated as a matter of priority.

2.2 HAZARD IDENTIFICATION

For each of the hazard:product pairings you identified in Table 3 you now look for:

- links with confirmed food-borne illnesses both in your country and in importing countries; search the published literature and any national health statistics;
- international food-borne disease outbreaks;
- recalls monitored by food authorities in importing countries.

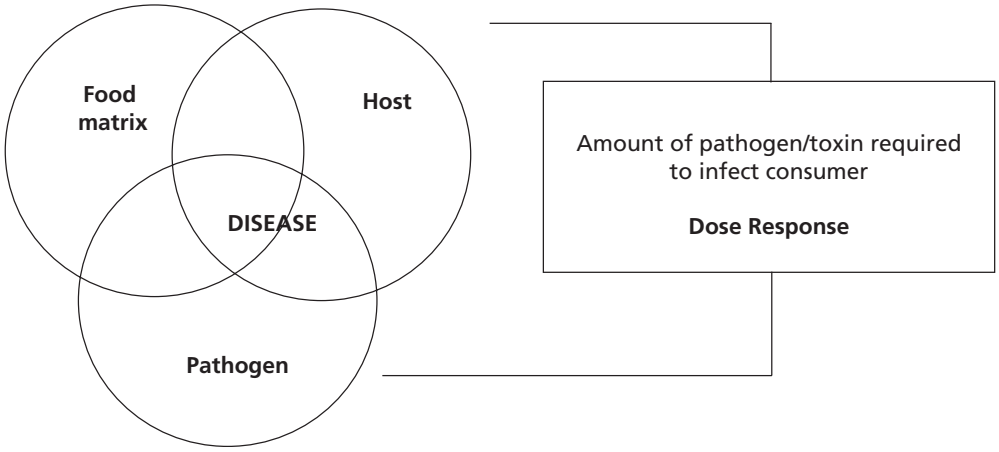
When you put all this information together you will have some idea of the food safety relevance of the hazard:product pairing.

At this stage you will be in a position to verify whether a particular hazard: product pairing is sufficiently important to remain in the risk profile. If it has not caused any problems, then you can use your resources more accurately on other pairings. For example, you may decide not to include parasitic worms in your risk profile because all finfish you export are frozen fillets and freezing kills the parasites. In other words, there are critical control points (freezing and frozen storage) that eliminate the hazard and, with it, the risk.

The Resources Bank includes hazard identifications of all the hazard:product pairings included in Table 3. This will get you started on your risk profiles but you should update the information by searching the sources recommended above (Table 2).

2.3 HAZARD CHARACTERIZATION

Hazard characterization is composed of inter-relationships, which are summarized in this simple diagram.



The three main areas for consideration – the pathogen/toxin, the host and the food matrix – all combine to make hazard characterization a very complex part of risk assessment. The simplest way of thinking about hazard characterization is to consider what happens whenever there is large-scale food poisoning. In general, only a proportion of consumers become ill, of whom a much smaller proportion may die. Why does not everyone become ill and why do not all those affected die? The reasons are many and complex but let us identify some of them by looking at a large outbreak of listeriosis from Mexican cheese. The main factors are summarized below.

Case history: Listeriosis in California in 1985 from consumption of Mexican cheese

Total of 142 cases of human listeriosis in California
Pregnant women: 93 cases (65.5 percent)
Death occurred in 30/93 cases (32.2 percent) – all were foetuses or newly-born babies
Non-pregnant adults were 49 cases (34.5 percent)
Immunocompromized: 38 cases (3 had cancer, 12 were taking steroids and 23 had chronic illness such as diabetes, renal disease, heart failure or cirrhosis)
Elderly: 5 cases (>65 years)
AIDS: 3 cases
Post-partum (just given birth): 2 cases
Full details are available in Linnan et al. *(1988).*

(i) The host

The illnesses occurred over the first eight months of 1985, during which time it is fair to assume that there were many thousands, if not millions, of servings of Mexican cheese eaten from the implicated factory. Because we do not know how many servings there were, we have no idea of the attack rate. We do know that 142 women were admitted to hospital with listeriosis, and these may have been a very small proportion of those who ate contaminated cheese. All of the 142 individuals were vulnerable:

- pregnant
- foetuses
- Newly-born
- immunocompromised
- elderly

In addition to the 142 cases of listeriosis, there may have been cases of gastro-enteritis due to the contaminated cheese, which did not show up in the health statistics

for California because the symptoms were not severe enough to warrant a visit to the doctor.

(ii) The pathogen

The pathogen, *Listeria monocytogenes*, has several properties that allow it to infect particular groups:

- It can cross the placenta and infect the foetus.
- The number of cells needed to cause listeriosis is probably much lower for vulnerable groups.

(iii) The food matrix

There are several aspects of the microbial ecology of *L. monocytogenes* in Mexican cheese that give it a competitive advantage:

- tolerance to the salt levels in cheese while competing bacteria are inhibited by salt;
- ability to grow in the refrigerator;
- possible protection within curd particles or fat through the stomach of the consumer.

The above case history defines the three broad areas of information you need when you think about hazard characterization. Let us consider them in enough detail so you will be able to do your own hazard characterization.

2.3.1 Consumers (hosts)

When we think about consumers (hosts) we need some background on why some people become infected more readily than others. Then it is necessary to know how many consumers fall into at-risk groups. The Resources Bank contains a background publication, *Natural defences to illness*, which gives information on how people cope with the invasion of pathogens.

For various reasons, all individuals lose immunity either progressively as they age, or catastrophically if they undergo chemo- or radiotherapy or if they acquire diseases that impair the immune system. But how many are there in society who are likely to be more vulnerable to infection? To calculate this proportion you need access to national statistics but, if these do not exist, you can use 20 percent as a reasonable indication. Table 6 shows that 20–25 percent of Australians fall into the vulnerable category, and this level seems similar for other western countries. The relevant subcategories are given below.

- ***Ageing***

You can look at national statistics to estimate the number of elderly and aged people in the community. Sort your data into a summary similar to that shown in Table 5; data from Australian statistics are given as an example of how age categories break down across a society.

Antibody levels are highest in childhood. By age 55, levels are reduced on average by 50 percent, and by 90 years of age only 25 percent of the original antibody level remains. The aged also have a reduced neutrophil function, which reduces intracellular antimicrobial activity. The loss of immunity and antimicrobial activity in the "very old" segment is of particular concern because it is a segment that is increasing in developed countries, which incidentally also represents the major importers of seafood products.

TABLE 5
Estimated numbers of elderly and aged people in the population

Age group	No, of males (%)	No. of females (%)
55–64	4.2	4.2
65–74	2.3	2.6
75–84	1.6	2.3
85 and over	0.3	0.8
Total	8.4	9.9

• *Acquired immune deficiency syndrome*
Those infected with human immunodeficiency virus (HIV) are at increased risk of gastro-enteric infections, in general, and of *Salmonella* infection, in particular.

• *Cancer*
Each year new cases of cancer are diagnosed that require therapy. Cancers most likely to increase an individual's susceptibility to food-borne disease are lung, bowel, breast, lymphoma, leukemia and renal. It is difficult to estimate those undergoing cancer treatments but, if the median treatment time is five years, it is likely that large numbers within the population are affected.

• *Diabetes*
Consumption and lifestyle patterns in developed countries have seen a rise in the number of sufferers of this disease, of whom around 10 percent are insulin-dependent. Non-insulin-dependent diabetes is more common in those older individuals who are overweight and sedentary. It is estimated that a similar number are undiagnosed, asymptomatic diabetics. Diabetes is particularly common among indigenous and Pacific island groups, with prevalence rates for the former approaching 100 cases/1 000 people.

• *Pregnancy*
There are two phases of pregnancy during which mother or foetus are at greater risk. In the first trimester, foetuses are at risk from the effects of heavy metals. In the third trimester both mother and foetus are susceptible to *Listeria monocytogenes*.

• *Very young*
Children younger than five years are considered to have a greater risk of food-borne illnesses. The prevalence of salmonellosis among children less than six months old is probably due to low gastric acidity, immature immune response and low protective effect from residential gut microflora (D'Aoust, 1994).

• *Hypochlorhydria*
In many western countries people use preparations to reduce stomach acidity. It is difficult to determine the proportion of individuals who take an acid-lowering agent but it is likely to be significant, perhaps as high as 1–5 percent.

As an example, Table 6 summarizes the at-risk segments in the Australian population. It is likely that 20–25 percent of Australians have impaired defence to microbial pathogens with some, the very old, having multiple impairment factors.

The linkage between a predisposing condition and infection from food-borne micro-organisms has been well-documented. In an outbreak of *Vibrio vulnificus* in Los Angeles in 1996, three people died after consuming oysters; a 38-year old man was a heavy consumer of alcohol and also an insulin-dependent diabetic; a 46-year old man was an alcoholic and had contracted jaundice; a 51-year old woman had had breast cancer and chronic Hepatitis C (Mascola *et al.*, 1996).

In Australia, four cases of septicaemia from *V. vulnificus* related to oyster consumption involved people aged between 53 and 74, all with chronic liver disease; two people died (McAnulty, 1990).

In summary, when considering the risk of infection, both the general population and those predisposed to the hazard must be considered.

TABLE 6
Susceptible populations and proportions in Australian society in 2000

Population	Percentage
Pregnancies	1.25
Neonates	1.35
Children 1–5	7.02
Elderly >60	16.01
Elderly >55	20.50
Diabetes (insulin-dependent)	0.36
Diabetes (non-insulin-dependent)	2.50
Cancer patients	2.10
AIDS patients	0.1

2.3.2 Dose-response

Dose-response is a measure of how much disease agent is required to cause illness. For example, how many salmonella cells in a meal of cooked shrimp are needed to give you salmonellosis? How many Hepatitis A virus (HAV) particles could you eat in a meal of raw oysters without contracting hepatitis? How much ciguatoxin must there be in a reef fish before you get ciguatera poisoning? In the first place, it all begins with you. If you are in a susceptible group, the number of micro-organisms needed to make you ill will be much lower than if you are not susceptible.

Then, the ability of the specific micro-organism becomes important – its virulence or pathogenicity. We have been able to gain some information on how many micro-organisms are required to cause illness by conducting a range of studies:

- ***Volunteer feeding studies***

This is a straightforward way of finding out how many micro-organisms are required to cause illness. In early studies, men serving prison sentences were fed meals containing different levels of *Salmonella,* and at least 100 000 living cells were needed before illness occurred (Bryan, 1979). It is doubtful whether volunteer feeding studies will ever be done in future because of changes in the way society feels about such a study. So alternate methods need to be found.

- ***Epidemic data***

Whenever an outbreak of food poisoning occurs, leftover food is tested, if possible, to find out the causative organism and its population. The results of such tests sometimes cause a re-think on how many organisms are needed to produce illness. For example, early findings that a person needs to eat >100 000 cells of *Salmonella* to become ill have been shown to be not always true because, in a number of outbreaks, only a few caused infection (Table 7).

TABLE 7
Examples of salmonelloses produced by serovars at low dosage

Vehicle	Serovar	Infectious dose
Chocolate	*S. eastbourne*	100
Chocolate	*S. napoli*	10–100
Chocolate	*S. typhimurium*	<10
Cheese	*S. heidelberg*	100
Cheese	*S. typhimurium*	1–10
Hamburger	*S. newport*	10–100

Source: after D'Aoust, 1994.

The food matrix, especially its fat content, is important and all the foods in Table 7 have high fat contents, which may protect the salmonellas from gastric juices.

In other outbreaks, the numbers needed for illness have appeared much higher than previously thought. For example, in Australia, three people became ill after eating smoked mussels. The level of *L. monocytogenes* in the mussels was >10 million/g, suggesting that more than 100 million listerias were consumed in each meal. Although all three people were ill (and one was 83 years old) the illness was confined to gastro-enteritis and did not progress to listeriosis.

- ***Surveillance statistics***

Many countries keep statistics to link types of pathogens with numbers of illnesses. In many western countries these statistics show that *Campylobacter* and *Salmonella* cause the vast majority of illnesses reported to doctors. But not all campylobacters and salmonellas are equally capable of causing illness. For example, in Australia, the major *Salmonella* on poultry is *S. Sophia* but, although it is present on the majority of chicken carcases, it causes only a small proportion of illnesses, suggesting its dose-response is different from that of other salmonellas.

- ***Animal studies***

Laboratory animals have long been used instead of humans to try and determine how much disease-causing agent is needed to cause symptoms. These animals range from

mice, which are cheap to raise and feed, to primates and pigs, which are obviously more expensive. There are disadvantages in using laboratory animals, both because their response may be different from that of humans, and also because, in many countries, there is ethical opposition to making animals suffer. Nonetheless, mouse injection is important in studying the toxin of *Clostridium botulinum*, one of the most dangerous organisms in seafoods.

- **In-vitro *studies***

It is now possible to maintain cell lines in culture and to test toxins and micro-organisms under controlled conditions. The major limitation is that it is difficult to relate the findings to human dose-response.

So what is known about the dose-response of different disease-causing agents associated with seafoods? Table 8 summarizes the levels required to cause illness and are an indication of the relative toxicity of seafood toxins ranging from the very high toxicity of botulinum toxin to the relatively low toxicity of histamine. For micro-organisms, there is great disparity between levels required to infect susceptible versus non-susceptible individuals.

TABLE 8
Ranges of agents associated with seafoods needed to cause disease

Agent	Susceptible groups	Non-susceptible groups
Toxins	Based on 50-kg person	
Ciguatera	approx 50/ng	approx 1 ng/kg body weight
Histamine	approx 50/mg	approx 1 mg/kg body weight
Paralytic shellfish poison	150–1 500 µg	150–1 500 µg
C. botulinum toxin	0.1–1.0 µg	0.1–1.0 µg
Micro-organisms		
Salmonella	10–100 cells	100 000 cells
Vibrio parahaemolyticus	>10 000 cells	>10 000 cells
Listeria monocytogenes	1 000–10 000 cells	>1 000 000 cells
Hepatitis A virus	1–10 particles	10–100 particles

The Resources Bank includes information on hazard characterization for each of the above agents, including:

- virulence and infectivity for various consumer groups (vulnerable and non-vulnerable);
- illness caused (time of onset, duration, symptoms);
- sequelae (ability to cause further conditions such as arthritis);
- effect of food matrix (composition, processing, meal preparation, etc.) on the agent.

Dose-response models

"Modelling" is an important part of risk assessment studies, and risk modellers have become an integral part of risk assessment work. Risk modellers think differently from microbiologists and food technologists. The latter worry if they do not have reliable data. Modellers, on the other hand, say "*No problem – we will model it*", which ends up worrying the microbiologists even more! However, modellers are indispensable if you are going to do quantitative risk assessments.

There are several models surrounding dose-response described in *FAO/WHO guidelines on hazard characterization for pathogens in food and water,* which is supplied in the Resources Bank.

2.4 EXPOSURE ASSESSMENT

For any component in our diet, exposure to a disease-causing agent (toxin or micro-organism) in that component depends on three factors:

- the level of the agent in the meal;
- the amount we eat (serving size);
- the frequency with which people consume that component.

Let us take an example – ciguatera in reef fish. Suppose you live on a Pacific atoll. Seafood plays a large part in your diet. You probably eat it every day, including species such as Spanish mackerel, which are caught off the reef, and you may consume up to 250 g of finfish at one sitting. Compare that exposure with a consumer in a European city, where seafood is eaten once a week, serving size around 100 g, with reef fish eaten once a year. Obviously the exposure to ciguatera in the two communities is very different. A consumer on an atoll may consume 50 kg of reef fish each year, compared with 100 g for the European city dweller.

The above comparison shows a 500-times difference in potential exposure, based only on mass consumed. In fact, assessing exposure is rather more complicated because there are usually a large number of other factors to consider such as:

- frequency of contamination (prevalence) with toxin or pathogen;
- changes in level of contamination through the marketing chain;
- seasonal effects;
- consumption patterns;
- susceptibility of consumer;
- preparation effects.

In Section 5, Examples of risk assessments, there are examples of how to do the work needed under exposure assessment. This is the part of a risk assessment where you need to do much investigative work. The better the exposure assessment, the more valid will be your risk estimate. Availability of local data is very important for exposure assessment.

2.5 RISK CHARACTERIZATION

In risk characterization, all previous information from hazard identification, exposure assessment and hazard characterization are brought together to give a picture of the risk. The picture is an estimate of how many people become ill, and how seriously ill they become, if a specific pathogen is in the product. This is called the risk estimate. If a qualitative risk assessment has been done, the risk estimate will be a simple statement that the risk is high or low or medium. If it is a quantitative risk assessment, the risk estimate will be a number, such as predicted illnesses per annum in the population, or the probability of becoming ill from eating a serving of the product.

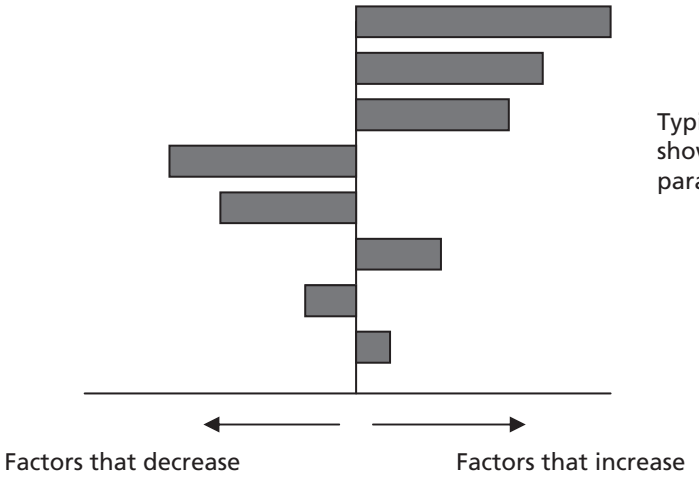
Do not forget that the main reason for doing risk assessments is so that risk managers can use the output – the risk estimates in the characterization. Therefore, the managers need to know whether there is uncertainty and variability in your estimate. A good example of the effect these two properties have is shown by the Lindqvist and Westöö (2000) study on smoked and gravad trout in Sweden. They estimated the number of annual cases by two dose response models. Method one predicted a mean of 168 cases and a range of 47–2 800 cases. Method two predicted a mean of 95 000 cases with a range of 34 000–1 600 000. The ranges reflect the uncertainty built into the predictions, and the authors list the data that should be collected to make more accurate predictions.

Another output in the risk characterization that is invaluable for risk managers is a sensitivity analysis. This analysis ranks the influence that each parameter has on the risk. Some factors increase the likelihood of illness while others decrease it. Lindqvist and Westöö found that the probability of becoming ill after eating smoked or gravad fish was most affected by:

- level of contamination (number of *L. monocytogenes* on the product);
- prevalence of contamination (percentage of servings contaminated);
- serving size (the more you eat the more likely you are to become ill);
- proportion of virulent strains of *L. monocytogenes*.

These findings help the risk manager to focus on areas that should receive priority action. If the assessors identify uncertainty within these areas, the managers may decide to invest in studies to obtain better data and reduce the uncertainty.

Some risk assessments present the sensitivity analysis as a chart with bars representing the extent of the impact each parameter has on risk. A typical chart is shown below, and because of its shape it is usually called a "Tornado chart"; each bar refers to a particular property that is correlated either with increased or decreased risk.



Typical Tornado chart showing the effect each parameter has on risk

Reality check

Whether you do a qualitative or quantitative risk assessment you must do a reality check and compare your predictions of annual illness with statistics kept by your country's Health Department. Referring to the risk assessment of Lindqvist and Westöö (2000) of listeriosis from smoked fish in Sweden, the predictions are wide-ranging. The authors state that there are around 37 cases of listeriosis each year in Sweden, from all sources, and method one (mean 168 cases) is in reasonable agreement.