SCIENTIFIC OPINION

Scientific Opinion on the development of a risk ranking framework on biological hazards[1]

EFSA Panel on Biological Hazards (BIOHAZ)[2 3]

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ABSTRACT

The risk ranking exercises related to biological hazards undertaken in fourteen risk assessments of the EFSA/BIOHAZ Panel were reviewed. The aim was to suggest risk ranking tools to be used in future risk assessments and to analyse strengths and weaknesses of different approaches to risk ranking. It was concluded that there is no universal methodology for risk ranking. A conceptual risk ranking framework with nine separate stages is proposed to allow the adoption of the appropriate risk ranking methodology at each stage. Further, nine risk ranking tools developed by other institutions worldwide were described, although none of these could be recommended as the single risk ranking tool for the BIOHAZ Panel. It is recommended that the risk ranking exercise should take a structured approach and be transparently and consistently documented so to be reproducible. The importance of the proper correspondence between the time frame and the requirements of the risk ranking exercise was stressed as well as the interaction between the risk managers and the risk assessors in the definition of the risk ranking purpose and the presentation of the results. Furthermore the development of a risk ranking toolbox based on the proposed framework should be investigated, since such a toolbox would support the construction of consistent and transparent risk ranking models.

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KEY WORDS

Risk ranking, biological hazards, risk modelling

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SUMMARY

The European Food Safety Authority (EFSA) asked the Panel on Biological Hazards i) to reflect on the lessons and experiences from risk ranking exercises undertaken by the BIOHAZ Panel, in particular describing successful approaches and challenges; ii) to suggest risk ranking tools related to biological hazards to be used in risk assessments; iii) to analyse strengths and weaknesses of different approaches to risk ranking on biological hazards.

A comparative study of fourteen previous opinions adopted by the BIOHAZ Panel presented different types of risk ranking. These opinions differ widely in methodology reflecting that models are fit for purpose. The availability of data and the time frame can affect the selection of the methodology. Therefore there is no universal methodology for risk ranking. The harmonization in model structure and presentation of the results will increase consistency and transparency of the risk ranking models.

Therefore the BIOHAZ Panel proposed a conceptual risk ranking framework comprising nine separate stages. The proposed framework allows the adoption of the appropriate risk ranking methodology by selecting different options at each stage. At the same time it provides the basis for a consistent presentation of model structure where all the components are clearly defined and the reasons for the selection of each component are described.

Nine risk ranking tools developed by other institutions worldwide were described. They differ in their purpose, the degree of complexity, level of quantification, and approach to model construction. None of the available tools could be recommended to be used as universal use risk ranking tool for biological hazards. However for future mandates, some of the presented available tools with proper adjustments to answer specific questions could be used.

The Panel recommended that the risk ranking exercise should take a structured approach and be transparently and consistently documented so to be reproducible. A correspondence between the time frame and the requirements of the risk ranking exercise is needed.

The Panel also stressed the importance of interaction between the risk managers and the risk assessors in the definition of the risk ranking purpose and the presentation of the risk ranking results.

In the future this conceptual framework might be translated into a guidance document with more details on the risk ranking methodology. Furthermore the development of a risk ranking toolbox based on the proposed framework should be investigated, since such a toolbox would support the construction of consistent and transparent risk ranking models.

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BACKGROUND AS PROVIDED BY THE EUROPEAN COMMISSION

The European Commission requested EFSA assistance in providing the scientific basis for the modernisation of meat inspection in the EU. The terms of reference of this mandate also require the identification and ranking of the main risks for public health that should be addressed by meat inspection at EU level. The BIOHAZ Panel has adopted the first opinion on public health hazards to be covered by the inspection of meat (swine)[4]. The next opinion (poultry)[5] is foreseen for adoption in June 2012 and four more opinions (bovines, small ruminants, solipeds, farmed game)[6] are planned for adoption in June 2013. To answer the terms of reference, the BIOHAZ Panel decided to apply a consistent and transparent approach of ranking hazards.

Risk-ranking techniques may be valuable, for instance in prioritisation when comparing relative risks from multiple hazards or from different intervention strategies. Risk ranking can be based on expert elicitations, qualitative measures or, more recently, developed on the basis of quantitative risk models.

Risk ranking, using tools that rely on knowledge of risk factors to rank risks and prioritize regulatory controls, is often commissioned by risk managers. Such rankings may or may not be based on risk assessments. Some tools categorize a food business against specified risk factors, e.g. by type of food, type of food preparation, type of business, compliance record, food user population. Other tools are used to rank hazard-food combinations in a national context by deriving a "comparative risk" scoring system (FAO, 2006[7]).

The BIOHAZ Panel has already adopted scientific opinions where risk ranking was requested in the terms of reference, e.g. the scientific opinion on food-borne antimicrobial resistance as a biological hazard, adopted in July 2008[8].

The BIOHAZ Panel foresees that the number of mandates that require a risk ranking exercise in the context or risk assessment will increase in the future. Gathering experience from previous and ongoing applications of risk ranking into a single document that provides a framework for risk ranking in the area of biological hazards would be very useful for the BIOHAZ Panel since it will improve consistency and transparency of the opinions.

The proposal is that the BIOHAZ Panel develops a risk ranking framework for the risk assessors, such as the BIOHAZ Panel, to ensure a consistent approach in different opinions where the risk managers ask to rank the risks. The risk ranking framework can be based on a stepwise approach including the identification of the objectives and expected needs for risk ranking. It will be built upon previous experiences, such as the BIOHAZ opinions on public health hazards to be covered by the inspection of meat, the evaluation of the available tools against the identified objectives and the design and development of a toolkit.

The output will be a draft opinion that will be presented for adoption by the BIOHAZ Panel in May 2012.

[4] www.efsa.europa.eu/en/efsajournal/pub/2351.htm
[5] EFSA-Q-2010-01469
[6] EFSA-Q-2011-00364, EFSA-Q-2011-00365, EFSA-Q-2011-00366, EFSA-Q-2011-00367
[7] ftp://ftp.fao.org/docrep/fao/009/a0822e/a0822e.pdf
[8] www.efsa.europa.eu/en/efsajournal/pub/765.htm

TERMS OF REFERENCE

EFSA requests the BIOHAZ Panel:

- To reflect on the lessons and experiences from risk ranking exercises undertaken by the BIOHAZ Panel, in particular describing successful approaches and challenges
- To suggest risk ranking tools related to biological hazards to be used in risk assessments
- To analyse strengths and weaknesses of different approaches to risk ranking on biological hazards

APPROACH TAKEN TO ANSWER THE TERMS OF REFERENCE

Under the time frame of this mandate it is not possible to develop a full risk ranking tool. The present opinion will focus on the development of a standardised risk ranking framework, in order to ensure consistency and transparency in the opinions where it is requested to rank risks. The framework will be built upon previous exercises carried out by EFSA. In addition available risk ranking tools will be investigated.

ASSESSMENT

1. Introduction

Food safety is a complex and dynamic issue. Policy makers and food safety authorities must deal with numerous food safety issues, often simultaneously and resources inevitably are insufficient to manage all issues at any given time (FAO, 2006). Thus, the adoption of a more science- and risk-based approach for setting priorities and allocating resources is needed.

The setting of priorities plays a crucial role in the decision-making process. The term 'priority' can be defined in a number of ways, including 'precedence, rank, urgency, consequence, primacy, and importance'. This implies that a 'priority' issue is essentially one that is considered to be a matter of greater importance, and which should thus be addressed with more urgency and in precedence to other issues. In the face of finite resources, and an almost infinite number of conflicting demands upon those resources, the establishment of priorities is a necessity.

In most cases risk ranking in food safety could be defined as the analysis and ranking of the combined probability of food contamination, consumer exposure and the public health impact of certain foodborne hazards. Risk ranking has been recognized as the proper starting point for risk-based priority setting and resource allocation, because it would permit policymakers to focus attention on the most significant public health problems and develop strategies for addressing them. In a science- and risk-based system, resources for food safety should be deployed in a manner that maximizes the public health benefit achieved through risk reduction.

1.1. Role of risk ranking in risk management

Due to its significance in priority setting risk ranking has been established as an important component of risk management frameworks. In 2006, FAO and WHO developed a generic framework for Risk Management (Figure 1) to improve food safety regulators' understanding and use of risk management in national food safety frameworks. In this framework risk ranking is included as the last step in the preliminary risk management activities. The objective of the risk ranking in the general framework is the evaluation of the perceived relative level of risk each issue presents to consumers, so that risk management resources can be optimally applied to reduce overall food-borne public health risks. Applied as part of risk management, other factors are also often considered in the prioritisation, including serious restrictions in international trade resulting from different food safety control measures; the relative ease or difficulty of resolving the issues; and, sometimes, pressing public or political demand that attention be paid to a particular problem or issue.

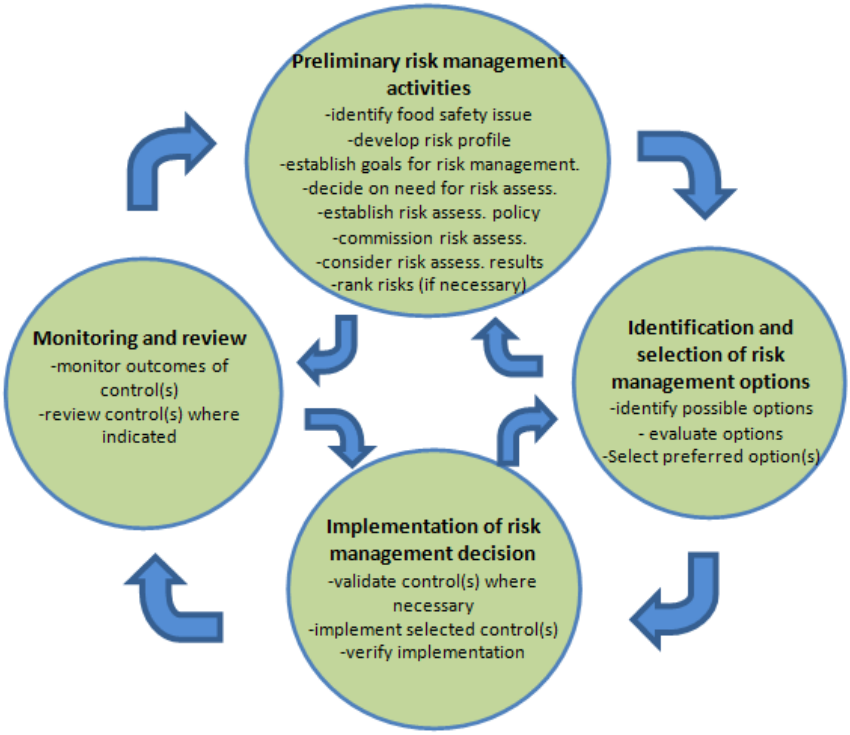


Figure 1: WHO Generic framework for Risk Management (WHO, 2006)

The New Zealand Food Safety Authority (NZFSA) has adopted a structured approach to food safety risk management similar to the WHO generic framework where risk ranking is included in the risk evaluation activities, as shown in the box below:

NZFSA Generic framework for Risk Management (Ministry of Health/Ministry of Agriculture and Forestry, 2000)

1. **Risk evaluation**
   - •identification of the food safety issue
   - •establishment of a risk profile
   - •ranking of the food safety issue for risk management
   - •establishment of risk assessment policy
   - •commissioning of a risk assessment
   - •consideration of the results of risk assessment
2. **Risk management option assessment**
   - •identification of available risk management options
   - •selection of preferred risk management option
   - •final risk management decision
3. **Implementation of the risk management decision**
4. **Monitoring and review**.

In 2010, the Institute of Medicine/National Research Council published a report in response to a congressional request that the U.S. Food and Drug Administration (FDA) contract with the National Academies for a comprehensive study of gaps in public health protection provided by the food safety system in the United States. The latter report recommends a risk-based safety system (Figure 2) with

risk ranking as the first step in support of the strategic planning in order to identify which risks constitute the greatest threat to public health and hence should be a priority for future analysis. The risk ranking step includes 1) the development or selection of tools (models, measures, or other) for public health risk ranking in consultation with stakeholders; 2) the risk ranking based on public health outcomes and 3) the reporting of results to stakeholders and soliciting feedback. At this risk-ranking step, the emphasis is on identifying and comparing hazards and foods with the greatest impact on public health, without consideration of other factors that might also play a role in decision making.

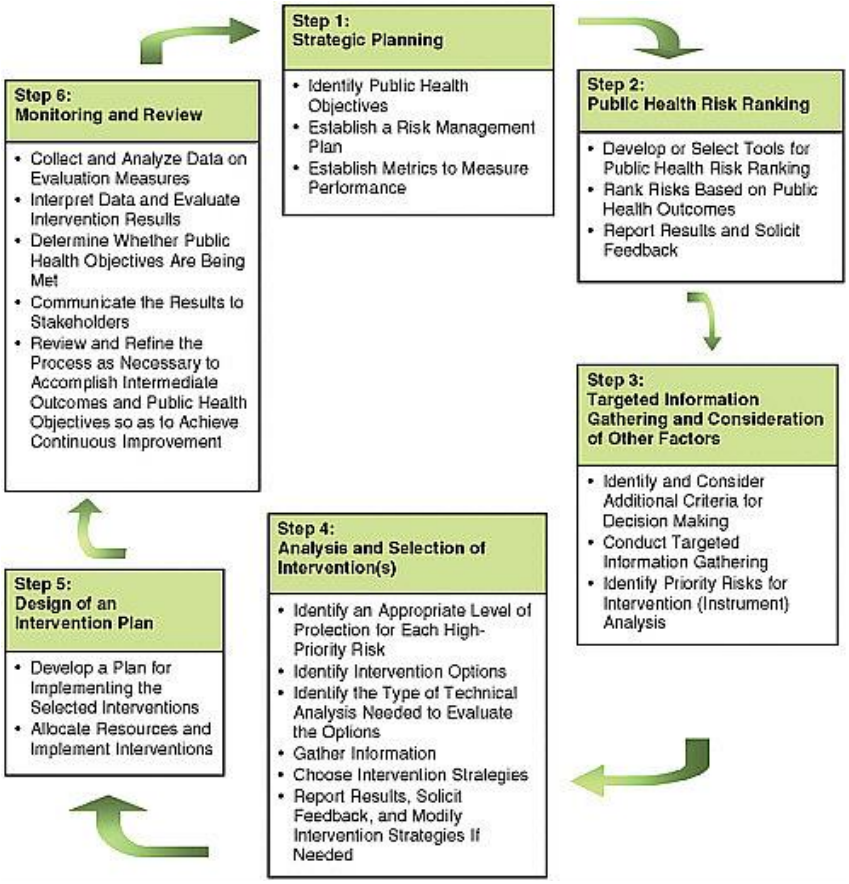


Figure 2: The risk-based food safety system proposed by the Medicine/National Research Council after request of U.S. Food and Drug Administration (FDA)

At European level, risk analysis forms the foundation of the European food safety system as foreseen by the EFSA founding regulation (Reg. 178/2002): in order to achieve the general objective of a high level of protection of human health, EU policies on food and feed safety shall be based on EFSA scientific advice. Risk assessment shall be based on the available scientific evidence and undertaken in an independent, objective and transparent manner, and risk management shall take into account the results of risk assessment. The risk assessment framework and definitions of a number of risk-related terms described in the EFSA's founding regulation are similar to those provided by the Codex Alimentarius Committee (CAC, 1999, 2011). In this context, particular importance is given to the precautionary principle, namely the provisional risk management measures that may be taken when following an assessment of available information, the possibility of harmful effects on health is identified but scientific ambiguity persists (Stirling and Scoones, 2009). One further aspect to be considered by risk assessors and of great importance for risk managers is that the models developed should be transparent, the steps followed in the implementation and the reasons for choices should be clear and understandable.

In this context of risk analysis as a pillar of EU food safety policy, national food safety authorities have recently begun to look to risk ranking as a mean of informing broad priority setting.

Using a structured risk ranking framework, the variables which are considered in the decision process and the weights assigned to those variables can be clearly defined and the basis for their justification can be examined. The explicit nature of such frameworks can result in decisions that are both transparent and more defensible. The use of structured risk ranking models can also provide decision-makers with a logical framework for making comprehensive assessments in a way which deals consistently with the matrix of factors considered to be relevant to a given issue. The adoption of a standardised framework which structures judgements according to clear and explicit variables, therefore, is likely to improve consistency in the decision making process.

1.2. Scope of the opinion

The scope of the present opinion is to develop a standardised risk ranking conceptual framework, in order to ensure consistency and transparency in the future opinions where it is requested to rank risks. The tool will be built upon experiences done by EFSA, such as the previous scientific opinions containing risk ranking approaches which are reviewed in this document, as well as the risk ranking tools developed by food safety agencies worldwide. The risk ranking framework developed in this opinion focuses on public health outcomes and does not considered other factors that may be relevant for decision makers such as public risk perception and/or economic and practical feasibility of ensuring a risk reduction, as these factors are considered to be a part of the risk management framework as described by WHO (2006).

The risk ranking conceptual framework developed by the BIOHAZ Panel is also in line with EFSA Science Strategy 2012-2016 which outlines the key challenges and demands the organisation will be facing in the forth coming years. In order to address all areas of EFSA remit adequately, the Scientific Committee of EFSA has outsourced a project[9] to critically review suitable methodology, tools and appropriate proposals for ranking risks and benefits for diet and health, food and feed, in support of the implementation of a structured and transparent framework for the prioritisation of requests for scientific work of EFSA.

[9] Call for proposals - CFP/EFSA/SCOM/2012/01: Critical review of methodology, and applications for risk ranking and benefit ranking for prioritisation of food and feed related issues, on the basis of the size of anticipated health impact. www.efsa.europa.eu/en/art36grants/article36/cfpefsascom201201.htm

2. BIOHAZ outputs presenting risk ranking – a review

In the present section a selection of scientific opinions adopted so far by the BIOHAZ Panel and containing risk ranking are presented. These opinions have been selected by BIOHAZ Panel members according to their relevance to risk ranking and to give examples covering different subjects of BIOHAZ remit (e.g. foodborne disease, Transmissible Spongiform Encephalopathy, food hygiene, etc.).

2.1. Scientific Opinion on Public health risks represented by certain composite products containing food of animal origin

The objective of this opinion (EFSA Panel on Biological Hazards (BIOHAZ), 2012b) based on the ToRs were to:

- Recommend/identify physico-chemical parameters for composite products containing no meat and/or less than 50% of products of animal origin that could be relevant for the growth/survival of pathogenic microorganisms of public health importance, taking into account the importance of other factors such as processing conditions, transport and/or storage conditions, and therefore assisting the risk manager on deciding to carry out risk based controls.

- Identify and profile the microbiological hazards for public health related to import of certain composite products (list provided by the European Commission) containing no meat and/or less than 50% of products of animal origin.

Two approaches, a top-down and a bottom-up approach, were used to rank the microbiological hazards for public health related to composite products:

In the top-down approach the model variables used were 1) outbreak data 2) EU prevalence data and 3) EU RASFF alerts notifications. Experts of the EFSA BIOHAZ Working Group on "Public health risks represented by certain composite products" were asked to independently provide a scoring scale for the different model variables. The total scores resulting from the assessment of the individual experts for each combination hazard-composite product were normalised in a 1-100 scale and a global average score was calculated. The experts were then asked to provide thresholds to define the importance of the combination hazard-composite product. The results of the top-down approach are presented in Table 1.

In the bottom-up approach a qualitative risk ranking was performed using decision trees. The model variables (questions in the decision trees) are based on the treatments applied to the composite products that could inactivate pathogens, on the physico-chemical conditions of the composite foods that could permit pathogens growth, and on some of the characteristics of the pathogens considered (e.g. infectivity, ability to sporulate, production of toxins). Three decision tree models were developed based on the infectivity of the hazards and on their need to grow in food in order to cause illness, directly or through toxins, (Figure 3, 4, 5) The trees do not give a full assessment of the risk but propose a categorization of the composite foods into "low risk", "moderate risk" and "qualified presumption of risk" (QPR), for the hazards considered by each tree, based on information on the foods and their impact on the pathogens. "Qualified presumption of risk" means that the pathogens considered by this tree have the potential to cause disease via consumption of the composite product, if present in the food or its ingredients. The "qualified presumption of risk" must also be interpreted in light of the results of the top-down approach (knowledge on the prevalence of the pathogen in the food concerned and its involvement in past outbreaks). It indicates that further information and actions are needed for this type of products. These can be: more accurately defining food composition and shelf-life, better defining the potential of the pathogen to survive or grow (e.g. challenge test), or having more information on the level of hygiene during production and processing. "Low risk" means that the composition and processing of the food should cause inactivation of the pathogen or prevent the

pathogen to reach hazardous levels at consumption. “Moderate risk” concerns foods cooked before consumption. It is not low risk, since the hazard may be still present at the moment of its preparation by the consumer. The possibility of cross contamination in consumer’s kitchen of other foods consumed raw, or that the food is eaten without prior cooking, must be considered. In addition, the way of cooking will influence the level of inactivation of the pathogens.

Table 1: Summary of the data available on the association between biological hazards and composite products according to EU prevalence and food-borne outbreak data (2004-2009), RASFF data (2001-2011) and scientific literature.

Hazards		Biscuits, bread and bakery products	Cakes (no raw eggs)*	Cakes (raw eggs)§	Chocolate	Confectio-nery and sweets	Pasta and noodles	Food supplements	Soup stocks and flavourings	Unfilled gelatine capsules	Olives with fish	Meat extracts and meat concentrates
Illness may occur without growth of hazards in food	viruses											
	Salmonella	some food types within these categories are not at high risk (see Chapter 6)				some food types within these categories are not at high risk (see Chapter 6)						
	Campylobacter											
	Escherichia coli											
	Yersinia enterocolitica											
Growth of hazards in food is usually required to cause illness	*Listeria monocytogenes*											
Growth of hazards in food is required for production of toxins or toxic metabolites that cause illness	*Clostridium*										olives stuffed with other product involved in outbreaks	
	Bacillus cereus											
	Staphylococcus aureus		no real higher risk than "*cakes (no raw eggs)*"									
	histamine											

No evidence of association | Evidence of medium importance of association | Evidence of high importance of association | Evidence of very high importance of association

* Cakes (no raw eggs): includes several types of cakes in which the presence among ingredients of raw eggs associated with absence of subsequent processing was not explicitly indicated.

§ Cakes (raw eggs): includes cakes and desserts for which raw eggs were explicitly indicated among ingredients and that were not subsequently processed, and cakes and desserts for which this can be assumed. Cakes and desserts containing raw eggs among their ingredients and that are not subsequently processed are not composite products since they contain unprocessed products of animal origin.

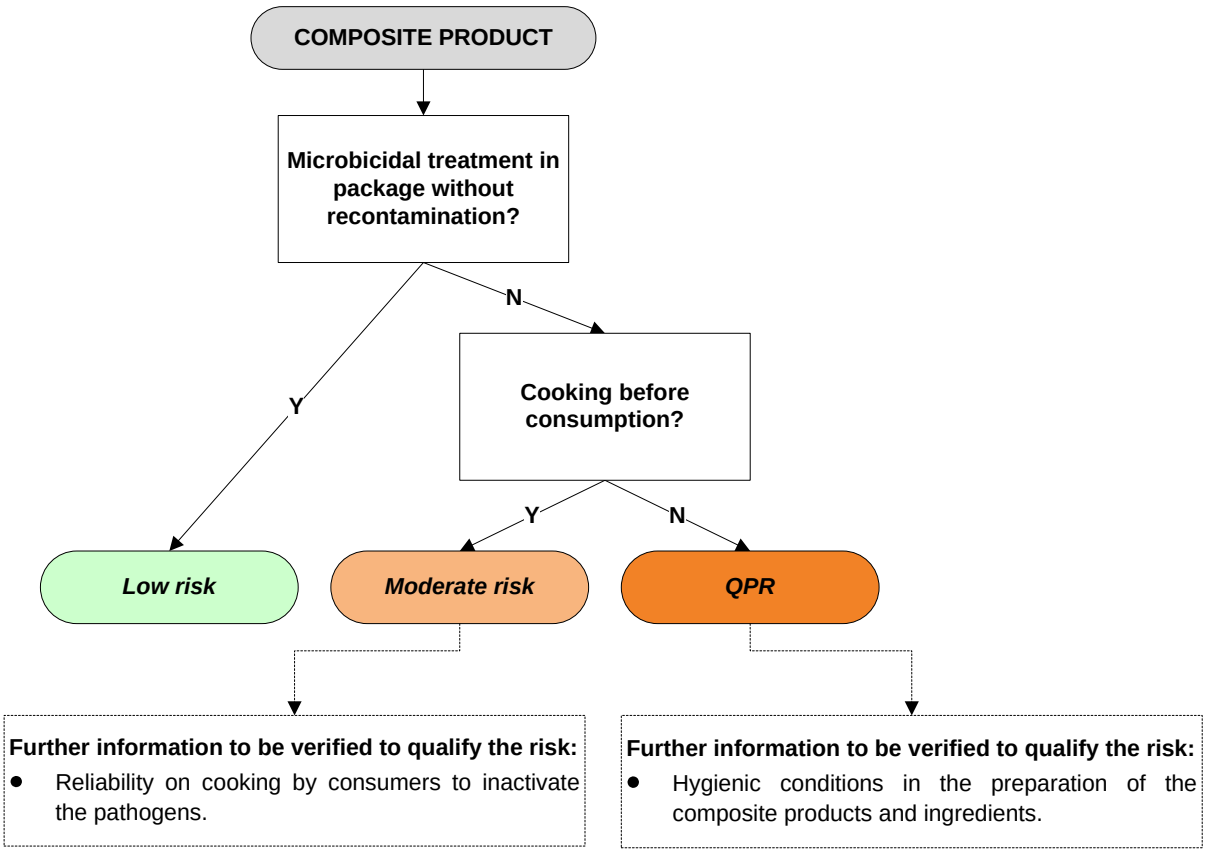


Figure 3: Decision tree for categorisation of risk in composite products due to pathogens whose growth may not be needed in the food in order to cause illness.

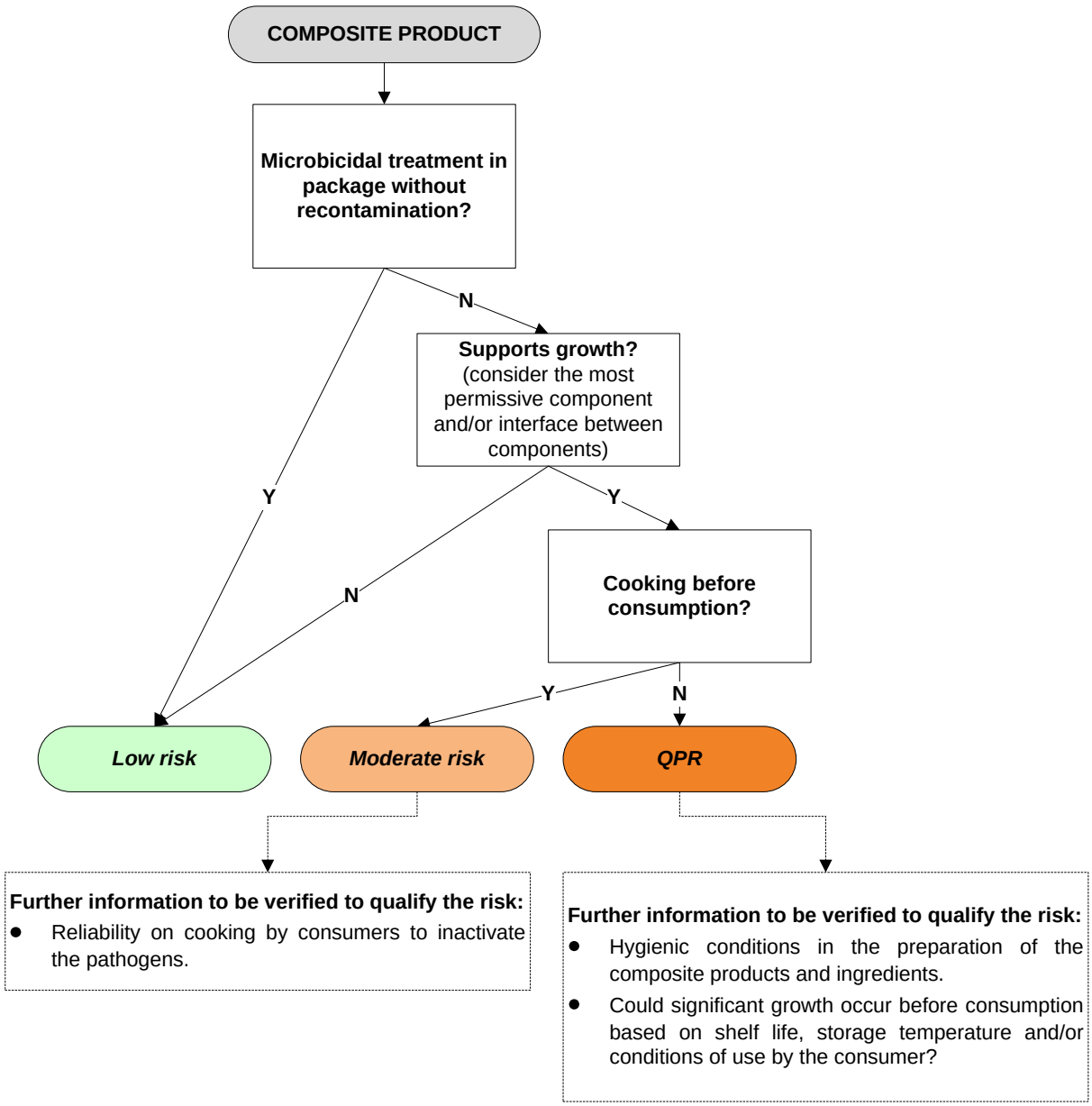


Figure 4: Decision tree for categorisation of risk in composite products due to pathogens whose growth is usually required in the food in order to cause illness.

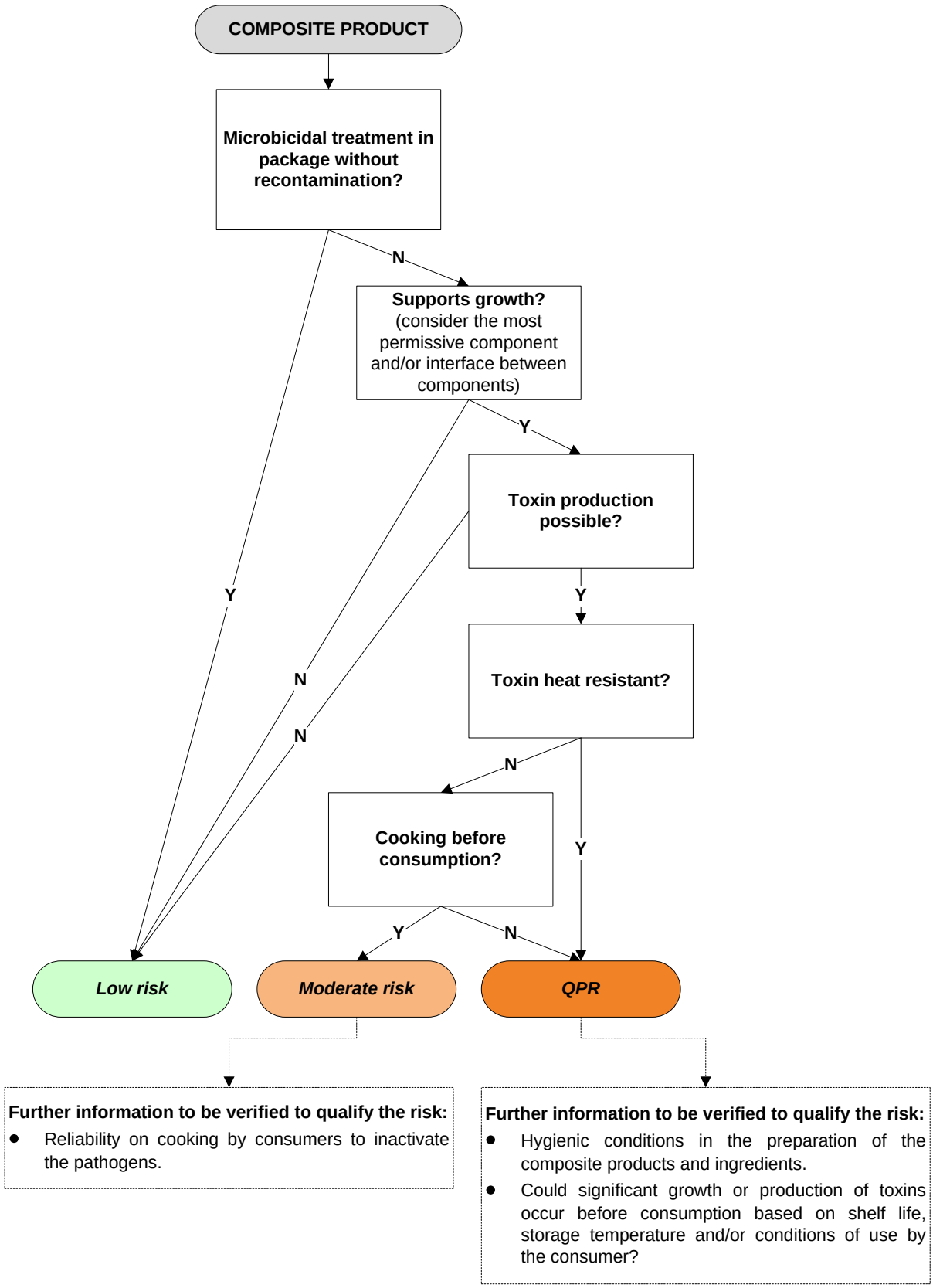
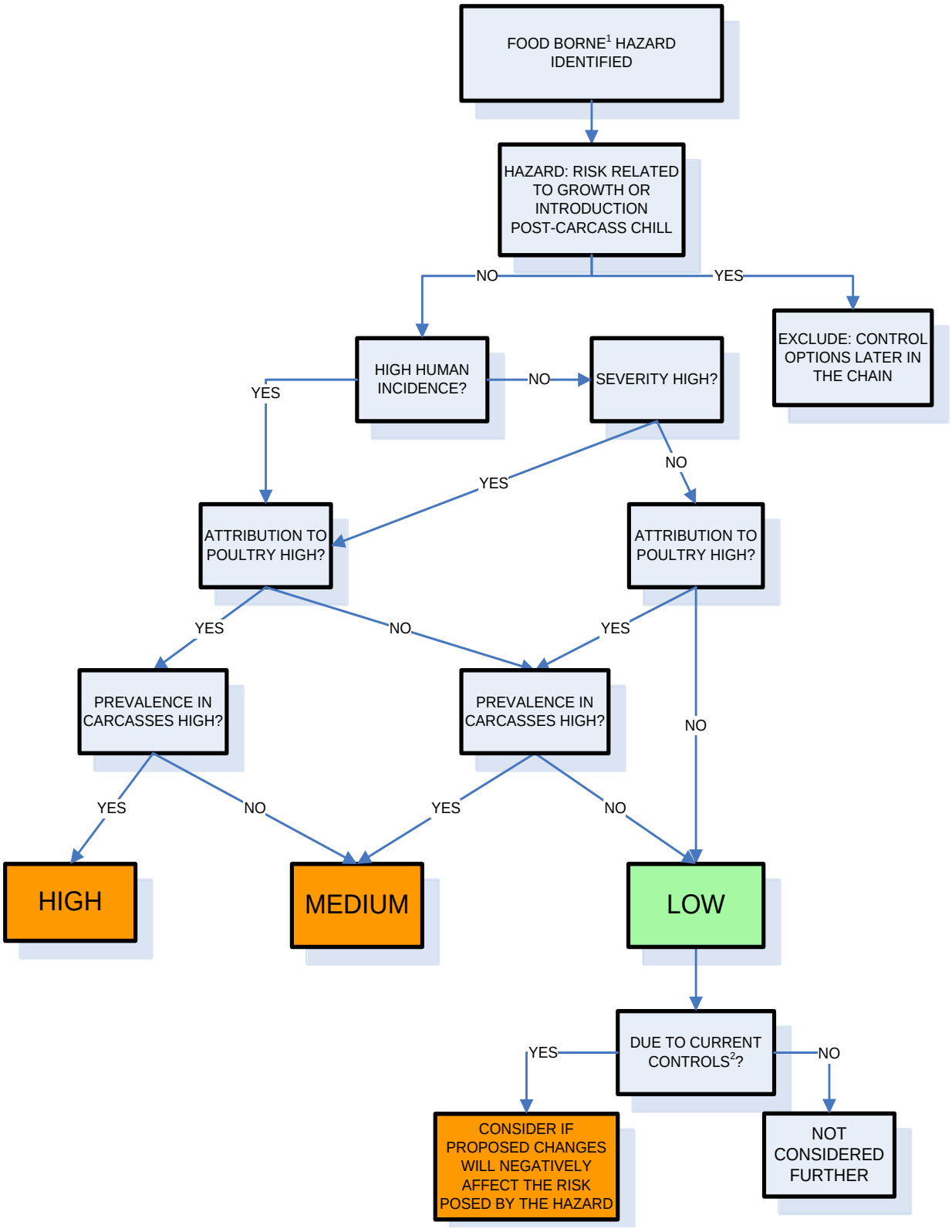


Figure 5: Decision tree for categorisation of risk in composite products due to pathogens whose growth is needed in the food for production of toxins or toxic metabolites that cause illness.

2.2. Scientific Opinion on the public health hazards to be covered by inspection of meat from poultry

The scope of this opinion was to evaluate and propose changes to the current meat inspection in poultry in order to optimize the identification and monitoring of poultry meat-borne hazards of public health relevance without jeopardizing neither the detection of certain animal diseases nor the verification of compliance with rules on animal welfare at slaughter (EFSA Panel on Biological Hazards (BIOHAZ), 2012c).

The BIOHAZ Panel developed a decision tree that was used for risk ranking of the poultry-meat borne hazards (Figure 6). The first step in the decision tree aimed at identifying and excluding those hazards that are introduced and/or for which the risk for public health risk relates exclusively to growth that occurs during processing steps after carcass chilling. The reasons for excluding such hazards for further assessment were that: 1) the scope and target of meat inspection are focused on the food-safety risks of the final poultry carcass at the end of slaughter when the carcasses are chilled, but before they are further processed; and 2) hazards introduced and/or for which the risk relates to growth during post-chill processes are better controlled later on in the food-production chain through for instance HACCP programs.



[1] Risk of infection through handling, preparation or consumption of poultry meat.
[2] Current controls: any hazard-specific control measures implemented at farm and/or slaughterhouse level before chilling of the carcasses.

Figure 6: Flowchart providing risk ranking of different hazards

The identified hazards are ranked as shown in Table 2.

Table 2: Risk ranking of hazards according to the categorisation in Figure 6.

Hazard	Notification rate in humans	Severity (% deaths)	Severity (DALYs)	Source attribution	Prevalence in carcasses	Risk category
Criteria	*(High ≥ 10/100,000)*	*High in more than one year ≥ 0.1%*	*High ≥ 100 DALYs per 1,000 cases*	*Expert opinion**	*High ≥ 5%*	
Campylobacter spp. (including *C. jejuni*, *C. coli* and *C. lari*)	High	Low	Low	High	High	High
Clostridium difficile	Not available	(Expert opinion) High	Not available	Unknown	Not available	Unknown, expected to be low - not considered further
E.coli (toxicoinfectious strains including VTEC)	Low	High	High	Low	Low	Low – not considered further
ESBL/AmpC (*E. coli*)	N/A	(Expert opinion) High	N/A	High	Not available at EU level	Medium to high
ESBL/AmpC (*Salmonella*)	N/A	(Expert opinion) Low	N/A	High	Not available at EU level (Low proportions resistant isolates using flock data)	Low to medium
Salmonella spp. (non-typhoidal)	High	Low	Low	High**	High	High
Yersinia enterocolitica	Low	Low	Low	Low	N/A	Low – not considered further
Toxoplasma gondii	Low	High	High	Low	N/A	Low – not considered further

* The criterion for source attribution was not based on a specific value but on an assessment made by experts which is explained elsewhere in EFSA, (2012).

**The attribution estimates vary greatly between MSs, which is considered to be a reflection of the effectiveness of implemented control programmes including for how long the control efforts have been in place.

2.3. Scientific Opinion on the public health hazards to be covered by inspection of meat from pigs

The term of reference of this opinion was to identify and rank the main risks for public health that should be addressed by meat inspection at EU level. General (e.g. sepsis, abscesses) and specific biological risks as well as chemical risks (e.g. residues of veterinary drugs and contaminants) should be considered (EFSA Panel on Biological Hazards (BIOHAZ), 2011c).

The following hazards are covered by the Community Summary Report according to Directive 2003/99/EC, can occur in pigs and were therefore considered in a first instance: *Campylobacter* spp.,

Brucella suis, *Clostridium botulinum* and *Clostridium perfringens*, *Taenia solium* (cysticercosis), *Echinococcus* spp., *Listeria monocytogenes*, *Mycobacterium* spp., *Toxoplasma gondii*, verotoxigenic *Escherichia coli* (VTEC), *Yersinia enterocolitica.* In this Opinion *Yersinia enterocolitica* is defined as human enteropathogenic *Y. enterocolitica* with biotype/serotype combinations that have their main reservoirs in pigs, in particular biotype 4/serotype O:3, biotype 2/serotype 9, but also biotype 2/serotype O:5,27.

An important inclusion criterion for the public health hazards were that the hazards should be meat borne, all others were excluded from the risk ranking.

A classification tree to systematically identify relevant foodborne hazards to be considered in a public health risk assessment related to meat inspection for pigs and pig carcasses. Using this approach the hazards were ranked (Table 3 and Figure 7).

The risk ranking was a top down approach and the variables used were:

- Human incidence (in the EU EFSA/ECDC zoonoses report)
- Case fatality rate (lethality, from ECDC)
- Prevalence on pig carcases (EU baseline studies for *Salmonella*, EFSA zoonoses reports for *Toxoplasma*, *Yersinia*, *Trichinella*)
- Source attribution estimates from pork (findings in literature, expert opinions and previous EFSA opinions).

A qualitative risk assessment of foodborne hazards was conducted using data on prevalence in/on chilled carcases, incidence and severity of disease in humans, and source attribution of hazards to pork, with the chilled carcasses as the target. Based on this assessment presently in the EU, *Salmonella* spp. were considered of high relevance, *Yersinia enterocolitica*, *Toxoplasma gondii* and *Trichinella* spp. as of medium relevance.

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Table 3: Preliminary qualitative hazard prioritization

Preliminary qualitative evaluation of the risk level: probability of occurrence against severity of consequences		**Severity of consequences**			
		High severity of consequences: human cases >10/100000, and case-fatality <0.1%	Medium severity of consequences: human cases 1-10/100000, and case-fatality <0.1%	Low severity of consequences: human cases <1/100000, and case-fatality >0.1%	Low severity of consequences: human cases <1/100000, and case-fatality <0.1%
Probability of occurrence	High probability: Prevalence on chilled carcass >5%	HIGH RISK *Salmonella*			
	Medium probability: Prevalence on chilled carcass 0.1-5%	MEDIUM RISK *Campylobacter*[3]	MEDIUM RISK *Yersinia enterocolitica*	MEDIUM RISK *L. monocytogenes*[5] VTEC[4]	LOW RISK *Toxoplasma*
	Low probability Prevalence on chilled carcass <0.1%			LOW RISK *Cl. botulinum*[1,5]	LOW RISK *Sarcocystis suihominis*[1,2] *T. solium cysticercus* *Trichinella* *Cl. difficile*[1,5] *Cl. perfringens*[1,5] *Mycobacterium* *Staph. aureus* (MRSA)[5] HEV[1,2]

The final risk ranking diagram is shown in Figure 7 below.

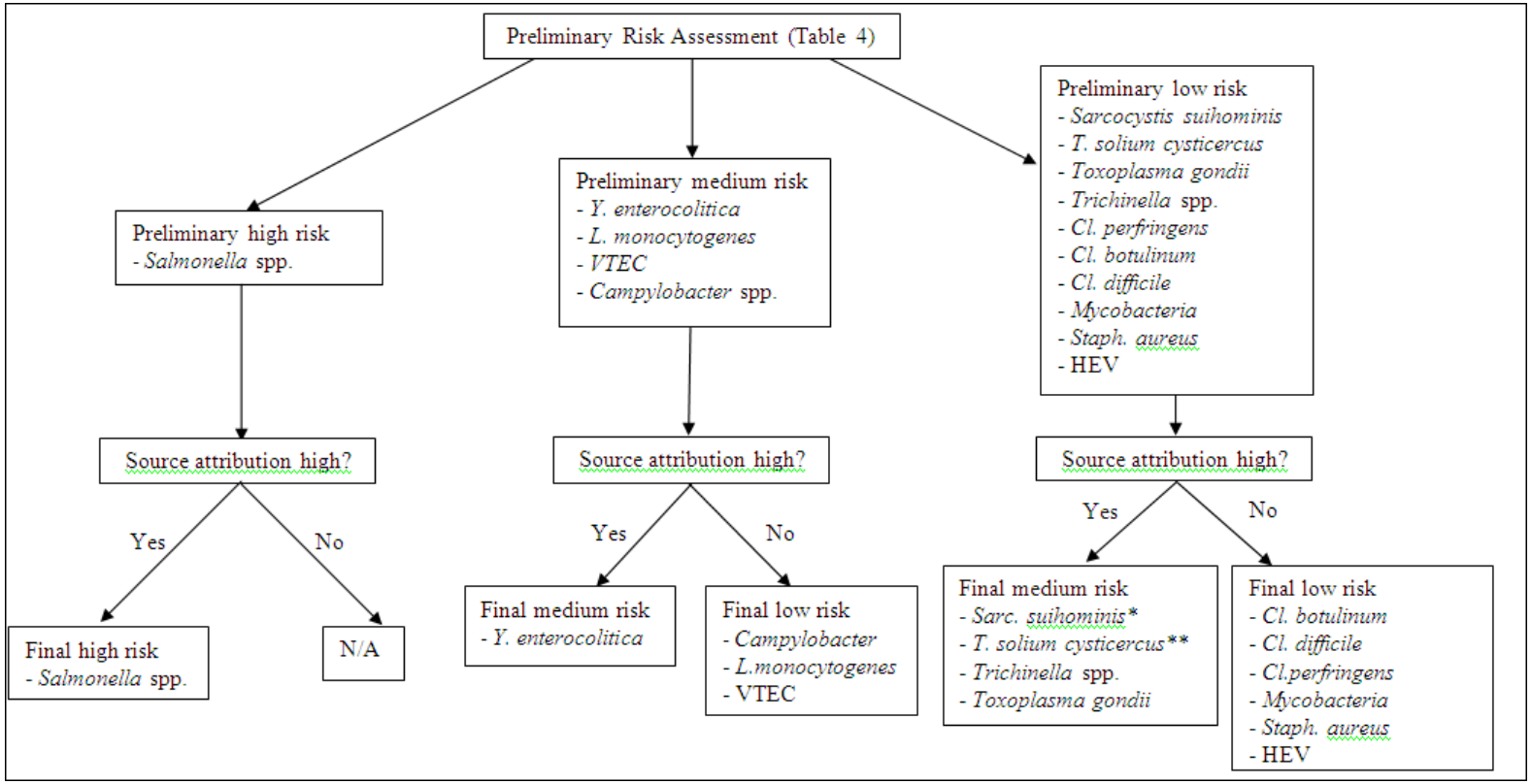


Figure 7: Final ranking of the main risks associated with chilled pork carcasses in the EU.

The final risk ranking included the source attribution:

- High risk: *Salmonella*
- Medium risk *Yersinia enterocolitica*, *Trichinella*, *Toxoplasma* (the last two due to their high source attribution)
- Low risk (VTEC, *Campylobacter*, *Listeria*, HEV, *Cl. botulinum*,….)

From the medium risk *Sarcocystis* and *Taenia solium* was excluded due to the absence of evidence of these agents being presenting a disease problem in EU.

Campylobacter was downgraded to low risk due to the chilling and drying of carcases was foreseen to kill the bacteria and apparent in the low source attribution. *Listeria* was not considered a problem attributable to pork carcases.

A group of hazards not classified but thought to be low was *Sarcocystis suihominis*, *Staph. aureus* (MRSA), *Cl. difficile*, *Cl. botulinum*.

An important caveat was that the present ranking is only valid under current husbandry, slaughter and inspection practices.

2.4. Scientific opinions on the assessment of the impact of setting new targets for the reduction of *Salmonella* in different poultry populations

Since 2009 EFSA has issued four scientific opinions on the impact of setting new targets for the reduction of *Salmonella* in certain poultry populations, including chickens (*Gallus gallus*), and turkeys (EFSA Panel on Biological Hazards (BIOHAZ), 2009, 2010b, 2010a, 2011a, 2012b).In those opinions, the relative importance of serovars originating from the poultry reservoir was assessed based on specific criteria defined by Regulation (EC) No. 21060/2003. This led to ranking of the different serovars according to their public health relevance in the context of the individual poultry production types (EFSA Panel on Biological Hazards (BIOHAZ), 2011a).

The criteria to be taken into account are as follows:

- the most frequent *Salmonella* serovars in human salmonellosis on the basis of data collected through the EC monitoring systems;
- the route of infection (that is, the presence of the serovar in relevant animal populations and feed);
- whether any serovar shows a rapid and recent ability to spread and to cause disease in humans and animals;
- whether any serovars show increased virulence, for instance as regards invasiveness, or resistance to relevant therapies for human infections.

In the opinions of breeding hens (EFSA Panel on Biological Hazards (BIOHAZ), 2009) and layers (EFSA Panel on Biological Hazards (BIOHAZ), 2010b), only a qualitative indication of the ranking is presented. This qualifies those serovars as of being of public health importance based on a simple assessment of epidemiological data and biological evidence of transmission of the serovars. Key was the evidence available on the vertical vs. horizontal transmission of the serovars.

In the opinion related to broilers (EFSA Panel on Biological Hazards (BIOHAZ), 2011a), and turkeys (EFSA Panel on Biological Hazards (BIOHAZ), 2012b), a *Salmonella* source attribution model was

used to estimate the quantitative contribution of four major animal-food sources (turkeys, broilers, laying hens (eggs) and pigs) to the burden of human salmonellosis in the European Union. This source attribution model estimated the number of human salmonellosis cases by the serovars included in the model and originating from the broiler and turkey reservoir, respectively. It led to a quantitative ranking of serovars involved in human disease.

2.5. Joint Scientific Opinion on any possible epidemiological or molecular association between TSEs in animals and humans

The Panel on Biological Hazards (BIOHAZ) and the European Centre for Disease Prevention and Control (ECDC) were asked to deliver a scientific opinion on any possible epidemiological or molecular association between Transmissible Spongiform Encephalopathies (TSEs) in animals and humans. The opinion reviews and discusses the existing scientific evidence that links animal and human TSEs currently known.

The objective of this document is to assess the potential associations between animal and human TSEs. An assessment of the potential causal links between animal and human TSEs according to the Bradford Hill's guidelines (Bradford Hill, 1965) is shown in Table 4 below. One conclusion is that only the BSE/vCJD link is established. It is important to stress that future scientific information might result in changes to the assessment of one or more of the other animal TSEs.

Table 4: Assessment of putative links between animal and human TSEs according to the criteria of the Bradford Hill guidelines.

Criteria	Cattle BSE	Small ruminant BSE[(a)]	Atypical BSE (L-BSE)	Atypical BSE (H-BSE)	CWD	Classical scrapie[(b)]	Atypical scrapie
1. Strength	+						
2. Consistency	+						
3. Specificity	+						
4. Temporality	+						
5. Biological gradient	+						
6. Plausibility	+	+	+	+	+	+	+
7. Coherence	+	+/-					
8. Experiment	+	+	+		+/-	+/-[(c)]	
9. Analogy	+	+	+	+	+	+	+

+: some scientific evidence is available for a positive interpretation
+/-: debatable or conflicting evidence is available
[(a)]: Classical BSE has not been identified in sheep, but two cases of BSE in goat have been reported in France and UK
[(b)]: there are multiple strains of the Classical scrapie agent
[(c)]: a single study has reported transmission of a natural sheep Classical scrapie isolate to primates

2.6. Scientific Opinion on quantification of the risk posed by broiler meat to human campylobacteriosis in the EU

This scientific opinion assesses the extent to which meat derived from broilers contributes to human campylobacteriosis at EU level (EFSA Panel on Biological Hazards (BIOHAZ), 2010c). Handling, preparation and consumption of broiler meat may account for 20% to 30% of human cases of campylobacteriosis, while 50% to 80% may be attributed to the chicken reservoir as a whole. Strains from the chicken reservoir may reach humans by pathways other than food (e.g. by the environment or by direct contact). Results may be biased by inaccurate exposure assessments, confounding by immunity and incomplete data on reservoirs.

There are five main mathematical modelling approaches that have been developed for attributing disease on a population level using microbial subtyping (MLST). Table 5 summarises the results from published studies using modelling attribution approaches based on MLST subtyping.

Table 5: Summary of published studies using MLST subtyping for source attribution

Attribution Model	Source Animal Dataset	Clinical Dataset	Species	% Attribution to chicken	% Attribution to Other Sources	Comments	Reference
Asymmetric Island	1145 isolates from 10 previous studies	1255 from NW England; Jan 2000 till Dec 2002	*C. jejuni*	56.5	35.0 (cattle) 4.3 (sheep) 2.3 (wild animals) 1.1 (environment)		(Wilson et al., 2008)
Population structure	5247 from Scotland July05 to Sept06 (9.6% *C. coli*)	999 From Scotland and 3419 from PubMLST	*C. jejuni*	58	38 (ruminants) 4 (wild bird & environment)		(Sheppard et al., 2009)
Asymmetric Island	As above	As above	*C. jejuni*	78	38 (ruminants) 4 (wild bird & environment)		(Sheppard et al., 2009)
Population structure	As above	As above	*C. coli*	40	40 (sheep) 14 (cattle) 6 (pigs) 1 (turkey)		(Sheppard et al., 2009)
Asymmetric Island	As above	As above	*C. coli*	56	40 (sheep) 2 (cattle) <1 (pigs) <1 (turkey)		(Sheppard et al., 2009)
Population structure	680 contemporaneous isolates from Scotland	225 from rural children in Grampian 2000-06	*C. jejuni* and *C. coli*	19	42 (cattle) 24 (wild birds) 12 (sheep) 3 (pigs)	Rural children <5 years	(Strachan et al., 2009)
Population structure	As above	85 from urban children in Grampian 2000-06	*C. jejuni* and *C. coli*	43	35 (cattle) 6 (wild birds) 15 (sheep) 1 (pigs)	Urban children <5 years	(Strachan et al., 2009)
Modified Hald	793 isolates	481 from Manawatu, New Zealand	*C. jejuni*	80	10 (cattle) 9 (sheep) 4 (environment)		(Mullner et al., 2009b)

Attribution Model	Source Animal Dataset	Clinical Dataset	Species	% Attribution to chicken	% Attribution to Other Sources	Comments	Reference
Dutch Model	521 isolates	As above	*C. jejuni*	52	17 (cattle) 10 (sheep) 5 (wild bird) 11 (water)		(French and the Molecular Epidemiology and Veterinary Public Health Group, 2008)
Modified Hald Model	521 isolates	As above	*C. jejuni*	67	23 (cattle) 8 (sheep) 1 (wild bird) <1 (water)		(French and the Molecular Epidemiology and Veterinary Public Health Group, 2008)
Island Model	521 isolates	As above	*C. jejuni*	75	17 (cattle) 4 (sheep) 2 (wild bird) <1 (water)		(French and the Molecular Epidemiology and Veterinary Public Health Group, 2008)

2.7. Scientific Opinion on risk assessment of parasites in fishery products

The aim of this opinion was to assess the food safety risks related to parasites in fishery products, in particular the food safety concerns due to possible allergic reactions in consumers to parasites that may be present in fishery products; to evaluate alternative treatments for killing viable parasites in fishery products; set criteria for when products are eaten raw almost raw or cold smoked do not present a health hazard with regard to the presence of parasites (EFSA Panel on Biological Hazards (BIOHAZ), 2010d).

In the EFSA opinion about fish parasites a table was presented about the risk profile of aquaculture practices in farmed fish species with potential for infection by parasites of public health importance. The table about the risk profile is an example of qualitative risk ranking.

The criteria considered were susceptibility of certain fish species to parasites of public health importance coupled with the production system, feeding practices (for larvae and adult fish), processing methods and grow-out time span.

The aquaculture practices at risk for transmission of parasites are shown in Table 6, and these are linked to the different farmed species (yes/no).

Table 6: Risk profile for aquaculture practices in farmed fish species with potential for infection by parasites of public health importance.

	Fish species	Production system				Larval feeding	Adult feeding		Larval/juvenile stages		Grow-out time span	Processing		Monitoring data available	Susceptible for parasitic infection in wild	Overall risk of parasite infection
		Open			Closed	Live food	Fresh food[10]	pellet	Wild	Farmed	months					
		Cages	Ponds	Flow-through tanks	Recirculation tanks	Rotifers, *Artemia*	Fish (anchovies, sardines)					Gutted	Ungutted			
Seawater	**Atlantic salmon**	X						X		X	>24	X		Y	*A. simplex; P. decipiens; Metagonimus spp.;*	*Negligible*
	Pacific salmon and rainbow trout	X						X		X	12	X		N	*A. simplex; P. decipiens, Diphyllobothrium* spp.	*Not known*
	Sea bass	X		X		X		X		X[11]	14-18	X		N	*A. simplex; P. decipiens*	*Not known*
	Sea bream	X				X	X	X		X	12-16	X		N	*A. simplex; P. decipiens*	*Not known*
	Tuna	X							X		12	X		N	*A. simplex; P. decipiens*	*Not known*
	Turbot	X				X		X		X	>24	X		N	*A. simplex; P. decipiens*	*Not known*
	Cod	X				X	X	X	X	X	>24	X		N	*A. simplex; P. decipiens; Cryptocotile spp.*	*Not known*
Freshwater	**Trout**	X	X	X	X			X		X	12	X		N	*Diphyllobothrium* spp	*Not known*
	Eel		X		X			X	X		>24	X	X	N	-	*Not known*
	Common carp		X			X	X				>24		X	N	*C.sinensis; O.felineus; Metagonimus takahashii; Haplorchis taichui; Echinochasmus fujianensis*	*Not known*
	Grass carp and bighead carp		X			X	X				>24		X	N	*C. sinensis; Haplorchis taichui*	*Not known*

Practice with increased potential for parasite infection of fish	Y	N

[10] Negligible risk if frozen for more than 24 hours
[11] In some extensive systems (valliculture), larvae/juvenile stages could be wild

2.8. Scientific Opinion on foodborne antimicrobial resistance as a biological hazard

The objective of this opinion was to identify, from a public health perspective, the extent to which food serves as a source for the acquisition, by humans, of antimicrobial-resistant (AMR) bacteria or bacteria-borne antimicrobial resistance genes, to rank the identified risks and to identify potential control options for reducing exposure (EFSA, 2008a).

This EFSA scientific opinion includes an example of exposure assessment template about food as a source of antimicrobial resistant bacteria. The risk pathway presented starts at the point of retail sale, thus there is no need to include the earlier production stages of farm, transport and lairage, abattoir and further processing.

The criteria considered were probability of bacteria being present in food at retail and the probability that bacteria present in food at retail are resistant to an antimicrobial class of interest are combined, multiplicatively, to provide an overall probability of the food at retail being contaminated with antimicrobial-resistant bacteria. This is combined with the probability that the food is purchased and consumed. The end-point of the risk pathway is the probability of a human being exposed to the antimicrobial -resistant bacteria of interest due to the consumption of the food of interest. Data are estimated either using available data or expert opinion. A diagram is reported in Figure 8.

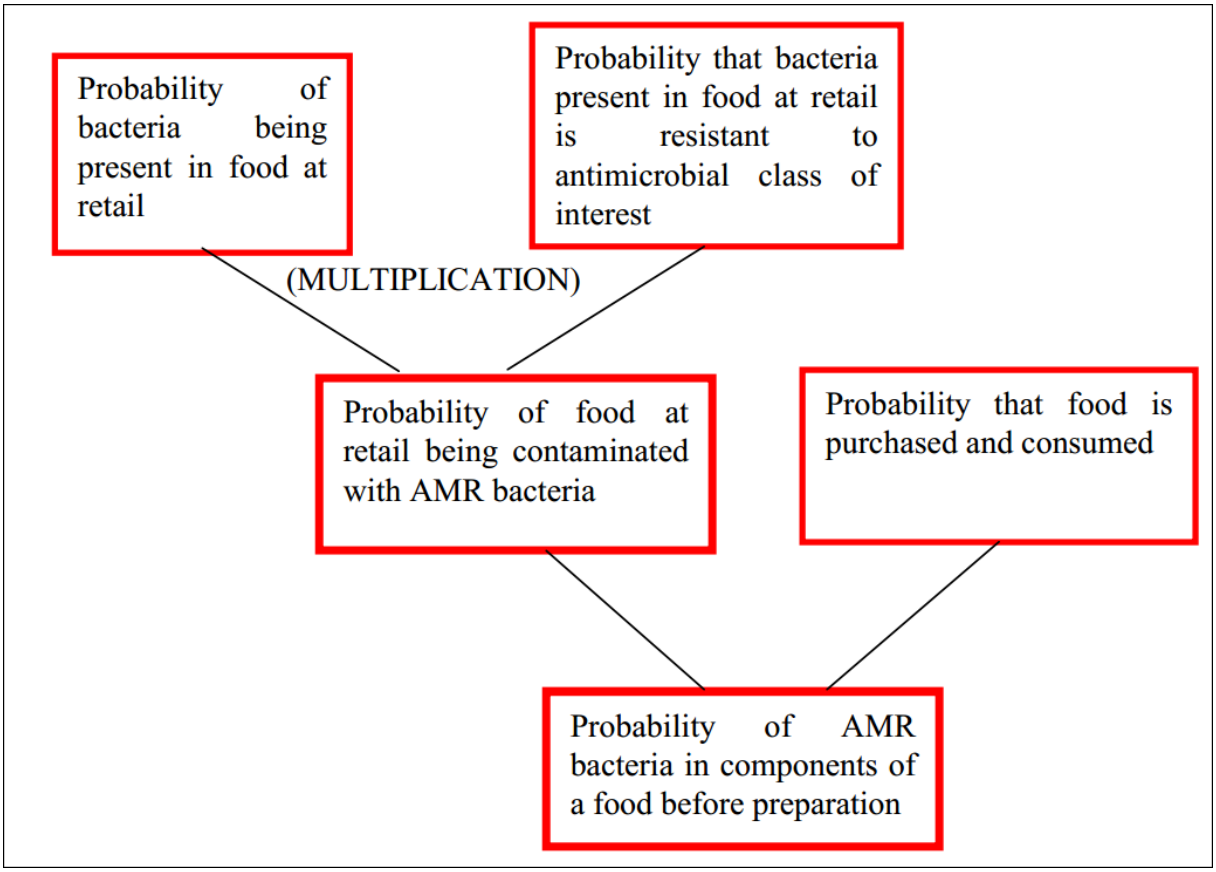


Figure 8: Example of a risk pathway for assessing the contribution of different foods to the occurrence of AMR bacteria in meal components.

In this preliminary risk ranking, the risk of preparing a meal with food components that are contaminated with AMR bacteria is simply presented by cross-tabulation. This eliminates the need to apply seemingly simple, but arbitrary combinatorial rules. An example of case studies about chasing food contaminated with fluoroquinolones-resistant *Campylobacter* is reported in Table 7.

Table 7: Examples of the risk of purchasing food contaminated with fluoroquinolone-resistant *Campylobacter*.

Prevalence of FQ-resistant *Campylobacter*	**Frequency of consumption of purchased food items**			
	Daily (>50%)	**Weekly (5-50%)**	**Monthly (0.5-5%)**	**Rarely (<0.5%)**
High (>1%)	Raw broiler meat			
Medium (0.01-1%)	Raw beef Raw pork	Raw sheep Raw turkey	Offal Private water supplies	Raw milk Raw dairy
Low (<0.01%)	Processed milk Processed dairy Processed cheese Eggs Fish Vegetables Soft fruit Juices Cereals Community water supplies	Processed beef Processed pork Processed sheep Processed poultry Raw shellfish	Game	Raw cheese

2.9. Opinion of the Scientific Panel on Biological Hazards on the revision of the Geographical BSE risk assessment (GBR) methodology

The aim of this opinion was to review and update the GBR method, an indicator of the likelihood of the presence of one or more bovines being infected with Bovine Spongiform Encephalopathy (BSE), pre-clinically as well as clinically, at a given point in time, in a country (EFSA, 2007). This was performed by taking into account the World Organisation for Animal Health (OIE) Terrestrial Animal Health Code and quantitative surveillance data and models. In this opinion the risk assessment method was updated taking into account quantitative surveillance data and models (e.g. BSurvE).

Essentially, any GBR exercise attempts to point out the likelihood that the BSE-agent was imported into the country under consideration (external challenge) and, if the BSE-agent was introduced into a country, whether it is likely that it would have been recycled and amplified or was the BSE/cattle system of that country able to eliminate the agent (i.e. internal stability). In addressing these issues a number of factors are taken into account including: the structure and dynamics of the cattle population, trade of cattle and meat and bone meal (MBM), the use of MBM and bans, the use of specified risk materials (SRM) and bans, the surveillance of BSE, the rendering and feed processing and use of feed. Under the SSC GBR method the country was assigned a GBR category between I to IV.

A schematic overview of the methodology for evaluating the stability is given in Figure 9.

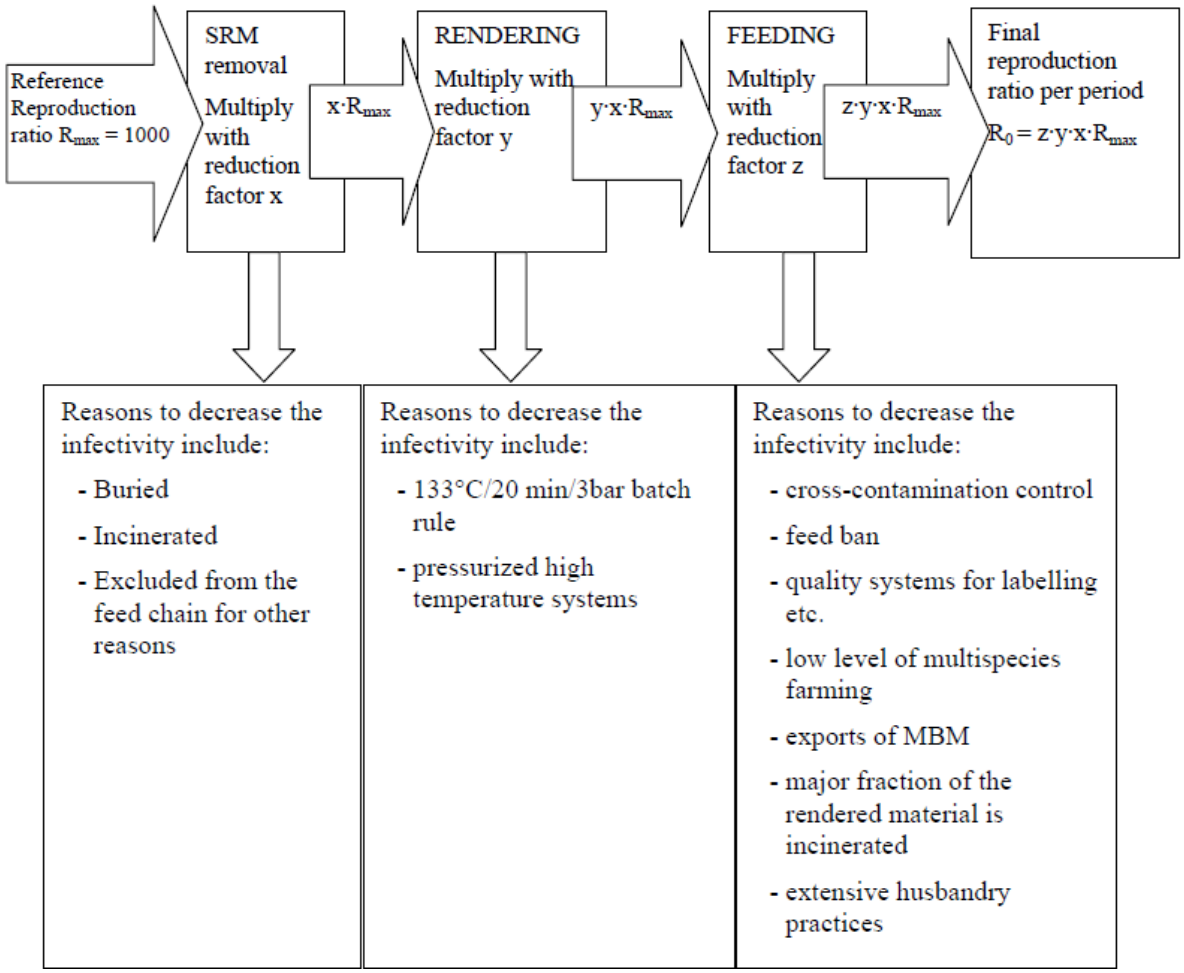


Figure 9: Schematic overview of the method to analyse stability.

2.10. Opinion of the Scientific Committee on Veterinary Measures relating to Public Health On *Salmonella* in Foodstuffs

The objective of this opinion was to identify categories of foodstuffs where *Salmonella* spp. represents a hazard to public health. The Committee interprets ”hazard to public health” as representing a high risk to human health (SCVMPH, 2003a).

Considering the possibility of hazards to public health posed by food categories, the Committee took account of :

- the reported prevalence of salmonellae,
- the incidence of human salmonellosis including the serotypes implicated, and
- the food technologies and/or preparation and handling applied.

Food categories possibly posing a greater hazard to public health include raw meat and some products intended to be eaten raw, raw or undercooked products of poultry meat, eggs and products containing raw eggs, unpasteurised milk and some products thereof. Sprouted seeds, unpasteurised fruit juices as well as home-made mayonnaise are also of major concern.

Although there have been occasional outbreaks linked to other food commodities, these are considered accidental and not a persistent risk to human health.

2.11. Opinion of the Scientific Committee on Veterinary Measures relating to Public Health on verotoxigenic *E. coli* (VTEC) in foodstuffs

The objective of this opinion was to identify categories of foodstuffs where verotoxigenic *E. coli* (VTEC) represents a hazard to public health. The Committee interprets "hazard to public health" as representing a high risk to human health (SCVMPH, 2003b).

Based on assessment of the food chain and epidemiological studies, it appears that risk factors for human exposure to HP-VTEC are linked to either direct or indirect exposure to ruminants and ingestion of food commodities contaminated by faecal contents from ruminants or humans. This exposure could be minuscule given that the infectious dose could be as low as ten bacteria.

The identified foodborne pathways for exposure were raw or undercooked beef, unpasteurised milk and products thereof, fresh fruits and vegetables or products thereof that have been contaminated by manure or exposed to contaminated irrigation or processing water and contaminated drinking water.

Moreover, further exposure could result from cross-contamination at the primary and secondary production stages by faecal contents from wild or domestic ruminants or humans, or cross-contamination from raw meat products.

It appears that sprouts might be a particular risk vegetable since the bacteria might multiply during sprouting.

The following categories of foodstuffs where (VTEC) represents a hazard to public health were identified:

- raw or undercooked beef and possibly meat from other ruminants;
- minced and/or fermented beef, and products thereof;
- raw milk and raw milk products;
- fresh produce, in particular sprouted seeds, and unpasteurised fruit and vegetable juices;
- and water.

2.12. EFSA Comprehensive European Food Consumption Database in Exposure Assessment

The EFSA Comprehensive European Food Consumption Database (Comprehensive Database) has been built from existing national information on food consumption at a detailed level. Competent organisations in the European Union's Member States provided EFSA with data from those most recent national dietary survey in their country, at the level of consumption by the individual consumer (EFSA (European Food Safety Authority), 2011b).

By the end of 2008, competent organisations in EU Member States were approached to provide EFSA with data from the most recent national dietary survey in their country, including at least the adult population, at the level of consumption by the individual consumer. In addition, food consumption data for children, obtained through the EFSA Article 36 project "Individual food consumption data and exposure assessment studies for children" (acronym EXPOCHI), have been included in the Comprehensive Database.

EFSA has the right to use the raw individual food consumption data for carrying out risk assessments and other scientific analyses within the activities related to EFSA mandate and a formal authorisation

from the data provider must be requested for any other use of the data. Currently, the EFSA Comprehensive Database is the best available source of food consumption information providing data on a EU-wide basis and will be very useful in the risk assessment work conducted by EFSA.

The collection of accurate and detailed food consumption data derived from a harmonised methodology across Europe is therefore still a primary long term objective for EFSA and has been recognised as a top priority for collaboration with the EU Member States.

2.13. Conclusions from the comparative study of the BIOHAZ opinions on risk ranking

Fourteen opinions of the BIOHAZ Panel related to risk ranking were selected as examples and reviewed. An overview of the selected opinions is presented in Table 8.

The selected opinions cover a wide variety of purposes and include ranking of single hazard in multiple food products (e.g. the opinions on *Salmonella* and VTEC in foodstuffs), multiple hazards in a single food product (e.g. the opinion on meat inspection in swine and poultry) and multiple hazards in multiple food products (e.g. the opinion on composite products, and the one on fish parasites). In one opinion, the purpose was to rank different countries in relation to a single hazard (the opinion on association between TSEs in animals and humans). The review showed that in each opinion a different risk ranking methodology was developed. Risk ranking models were based on different risk metrics, ranking approaches, model types, variables and data integration methods. The risk was expressed using a variety of risk metrics mainly related to probability of an adverse effect. However, none of the opinions used summary measures of public health like QALYs or DALYs or metrics for monetary valuation of public health. The risk ranking approaches included top-down in most cases (seven outputs), bottom-up (the opinions on fish parasites, on foodborne AMR and TSE) and combinations (the opinions on *Salmonella* and VTEC in foodstuffs and the one on composite products). Most of the risk ranking models were qualitative using decision trees for data integration. Three opinions have a semi-quantitative approach (the one on composite products, on foodborne AMR and TSE). In one opinion (*Salmonella* serotypes) a fully quantitative model was developed. The model variables used included epidemiological, disease severity, hazard characterization and dose response variables. Data were collected from various sources including national and international databases, literature reviews, predictive microbiology tools and expert opinion.

The risk ranking exercises of the reviewed opinions differ widely in methodology emphasising the fact that models are tailored to fit the purpose for which they are developed. In addition, the availability of data largely determines the variables in the model development while the given time frame for risk ranking exercises can affect significantly the decision on the selection of the methodology. As each model has to be specifically tailored to each specific purpose, data availability and time frame there is no universal methodology for risk ranking. The identification of successful risk ranking approaches and tools among those examined in this opinion requires a comprehensive review of each model taking into account its purpose, the available data and the time frame of each mandate. This is a very time consuming process which was not feasible under the timeline of this mandate.

The structure of the risk ranking models was different in each opinion. The harmonization in model structure and presentation of the results is an important challenge for the BIOHAZ Panel since this will increase consistency and transparency of the risk ranking models. The development of the risk ranking conceptual framework would contribute to this harmonization. This framework should allow the development of different methodologies but at the same time provide the basis for a consistent presentation of model structure where all the components of the models are clearly defined, the reasons for the selection of each component and how the final conclusions were reached should be described.

Table 8: Table about comparison of risk rankings developed in EFSA opinions

Ref. in the text	Opinion	What was ranked	Metrics	Approach	Model structure	Model variables	Data collection	Data integration
2.1	PH risks linked to composite products containing food of animal origin (1st approach)	Multiple hazards in multiple foods	Probability of illness per annum	Top down	Semi-quantitative-Tabulation	1) outbreak data 2) prevalence data 3) EU RASFF alerts notifications	EU reports, Literature review	Reasoned opinion
2.1	PH risks linked to composite products containing food of animal origin (2nd approach)	Multiple hazards in multiple foods	Probability of illness per serving	Bottom up	Qualitative	Processing effect, growth potential, cooking effect, infectivity, ability to sporulate, production of toxins	Literature review, available modelling tools	Decision tree
2.2	Meat inspection in poultry	Multiple hazards in single food (meat borne hazards)	Likelihood of transmission from meat to humans	Top down	Qualitative Tabulation	Human incidence Case fatality rate (lethality) Prevalence on poultry carcases Source attribution from pork	Literature review, EFSA/ECDC zoonoses report EU/EFSA Baseline studies	Decision tree

Ref. in the text	Opinion	What was ranked	Metrics	Approach	Model structure	Model variables	Data collection	Data integration
2.3	Meat inspection in swine	Multiple hazards in single food (meat borne hazards)	Likelihood of transmission from meat to humans	Top down	Qualitative Tabulation	Human incidence Case fatality rate (lethality) Prevalence on pig carcases Source attribution from pork	Literature review, EFSA/ECDC zoonoses report EU/EFSA Baseline studies	Decision tree
2.4	Targets for reduction of *Salmonella* in poultry[12]	Single hazard in single food (*Salmonella* serovars of public health significance linked to certain poultry populations)	Strength of the association of particular *Salmonella* serovars found in humans to exposure to poultry foodstuffs (e.g. eggs, meat)	Top down	Qualitative	Data on: (1) prevalence in humans , animals and derived foodstuffs, (2) virulence of different serovars, (3) Resistance to AM treatments.	EFSA/ECDC zoonoses report EU/EFSA Baseline studies Literature review	Expert synthesis and opinion

[12] This point refers to four different outputs

Ref. in the text	Opinion	What was ranked	Metrics	Approach	Model structure	Model variables	Data collection	Data integration
2.4	Quantitative estimation of the public health impact of setting a new target for the reduction of *Salmonella* in broilers/turkey	Multiple hazards in multiple foods (*Salmonella* serovars)	Percent transmission from different reservoirs True number of human salmonellosis cases per serovar	Top down	Quantitative	Output variable: True number of human salmonellosis cases per serovar in food/animal source; Input variables: Number of reported human cases of *Salmonella* serovar i in country k; Underreporting factor in country k; Outbreak factor in country k; Prevalence of *Salmonella* serovar i in all putative food reservoirs j; Amount of food from reservoir j available for consumption in country k (accounting for trade); Estimated by the model: Serovar and food reservoir specific parameters	EFSA/ECDC zoonoses report EU/EFSA Baseline studies EUROSTAT	Bayesian inference

Ref. in the text	Opinion	What was ranked	Metrics	Approach	Model structure	Model variables	Data collection	Data integration
2.5	Association between TSEs in animals and humans	Multiple hazards in multiple foods Zoonotic potential of multiple TSE agents in different animals	Likelihood of transmission to humans	Top down	Qualitative Tabulation	Bradford Hill criteria	Literature review	Reasoned opinion
2.6	Quantification of the risk posed by broiler meat to human campylobacteriosis in the EU	Single hazard in single foods One hazard in multiple exposure pathways	Percent transmission via different pathways	Top down	Review of different models: 1) outbreaks; 2) case-control studies 3) molecular typing	1) number of outbreaks; 2) attributable fractions; 3) MLST types in different reservoirs	1) EU SR 2) literature review 3) literature review	Reasoned opinion
2.7	RA of parasites in fishery products	Multiple hazards in multiple foods Parasites of public health importance in fishery products	Likelihood of transmission of parasites of public health importance to aquaculture species	Bottom-up	Qualitative, tabulation	Aquaculture practices	Expert opinions, literature data	Tabulation

Ref. in the text	Opinion	What was ranked	Metrics	Approach	Model structure	Model variables	Data collection	Data integration
2.8	Foodborne AMR as biological hazard	Multiple hazards in multiple foods Risk of food as a source of AMR bacteria for humans	Probability of the food being contaminated with AMR bacteria	Bottom up	Semi-quantitative cross-tabulation	prevalence of bacteria in food at retail probability of bacteria to be resistance to AM class	available data or expert opinion	Tabulation
2.9	Geographical BSE risk assessment (GBR) methodology	Single hazard in single food Presence of BSE in a given country system	Likelihood of presence of BSE presence in a given country	Bottom up	Semi-quantitative	Level of external challenge (import of bovine animals or MBM) Level of internal challenge (SRM removal, rendering, feeding)	Governmental reports of a given country	Calculation on spreadsheet table
2.10	*Salmonella* in foodstuffs (SCVMPH)	Single hazard in multiple foods High risk food categories	Risk of illness per serving of a foodstuff	Top down and bottom up	Qualitative	the reported prevalence of salmonellae, the incidence of human salmonellosis including the serotypes implicated, the food technologies and/or preparation and handling applied.	Literature and zoonosis reports	Expert synthesis and opinion
2.11	*E. coli* (VTEC) in foodstuffs	Single hazard in multiple foods High risk food categories	Higher risk of illness per serving of a foodstuff	Top down and bottom up	Qualitative	risk factors for human exposure to HP-VTEC are linked to either direct or indirect exposure to ruminants and ingestion of food commodities contaminated by faecal contents from ruminants or humans.	Literature review	Expert synthesis and opinion

3. Development of the conceptual risk ranking framework for BIOHAZ Panel

Based on the conclusions from the comparative study of the available BIOHAZ opinions containing risk ranking, and based on the need for harmonisation a conceptual risk ranking framework is proposed and illustrated in Figure 10. The framework consists of nine conceptual stages involved in risk ranking, from defining of what to be ranked to presenting the results of risk ranking. The first two stages (i.e. the definition of what to be ranked and the selection of the risk metrics) reflect the risk management objectives of the organisation which has commissioned the risk ranking exercise and thus should, in most cases, be defined by the European Commission. The next six stages refer to the development of the risk ranking model and should be defined by the BIOHAZ Panel. Each of the stages in the framework is discussed in more detail in the following paragraphs and specific examples are drawn from the literature review for illustration.

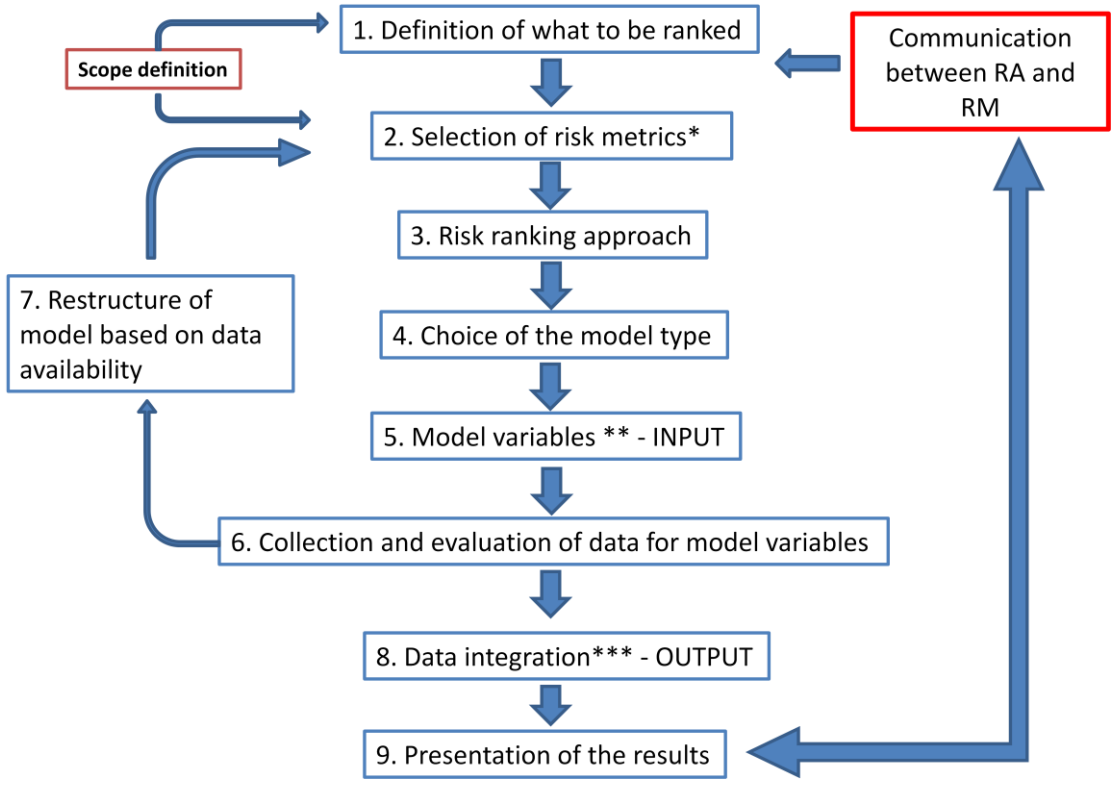


Figure 10: The proposed conceptual risk ranking framework for BIOHAZ Panel

* "Risk metrics" is the expression of the risk (DALY, QALY, incidence, etc.)
** Model variables" are the indicators used for risk ranking (prevalence, epidemiological data)
***"Data integration" is the combination of model inputs and formulas to produce model outputs

3.1. Definition of what to be ranked

Risk ranking models may be developed to fulfil a wide variety of purposes. In the initial stages of developing a model, it is essential to have a clear conception of what the model is intended to achieve and to define what to be ranked. The fundamental purpose for which the model is required will essentially determine which factors should be considered in the ranking process.

The following three levels can be identified in a risk ranking process based on hazard-food combinations:

- Level 1: Single hazard in multiple food products (ranking of foods)
- Level 2: Multiple hazards in a single food product (ranking of hazards)
- Level 3: Multiple hazards in multiple food products (combined ranking of hazards and foods)

The selection among the above levels is very important since it will determine the variables and data required for the risk ranking. For example in the case of single hazard in multiple food products (Level 1) the risk can be ranked without taking into account the severity of the hazard while information on the consumption of the different food are important. In contrast, for multiple hazards in a single food product (Level 2) risk ranking is not affected by consumption but severity of the hazard must be taken into account. In general as the level increases the risk ranking exercise is getting more difficult.

Often the number of hazards and foods which the risk managers are responsible for may be too large to make overall risk ranking feasible. This problem can be overcome by categorisation of the hazards and/or foods under consideration, followed by ranking of categories on a single or number of axes. Any practical process of risk ranking must group hazards into a manageable number of categories. Defining such categories requires value choices that can have important implications for the rankings that result. The development of an explicit basis for the selection of the risk-categorisation scheme is very important for using the results of a risk ranking project as an input into risk management.

Morgan et al. (2000) addressed the problem of grouping risks into categories and presented the following requirements to categorisation of hazards which could be also applied for the categorisation of foods, see Table 9:

Table 9: Desirable Attributes of an Ideal Risk-Categorization System for Risk Ranking (Morgan et al., 2000)

Categories for risk ranking should be:
Logically consistent
• Exhaustive so that no relevant risks are overlooked.
• Mutually exclusive so that risks are not double-counted.
• Homogenous so that all risk categories can be evaluated on the same set of attributes.
Administratively compatible
• Compatible with existing organizational structures and legislative mandates so that lines of authority are clear and management actions at cross purposes are avoided.
• Relevant to management so that risk priorities can be mapped into risk-management actions.
• Large enough in number so that regulatory attention can be finely targeted, with a minimum of interpretation by agency staff.
• Compatible with existing databases, to make best use of available information in any analysis leading to ranking.
Equitable
• Fairly drawn so that the interests of various stakeholders, including the general public, are balanced.
Compatible with cognitive constraints and biases
• Chosen with an awareness of inevitable framing biases.
• Simple and compatible with people's existing mental models so that risk categories are easy to communicate.
• Few enough in number so that the ranking task is tractable.
• Free of the "lamp-post" effect, in which better understood risks are categorized more finely than less understood risks.

EFSA has recently published a report describing steps towards a hierarchical food classification system that appears to be a useful starting point for future BIOHAZ mandates (EFSA (European Food Safety Authority), 2011a). As the system is hierarchical, it can be applied at different levels of detail without loosing consistency. It is expected that food consumption data in the EU, an important element of exposure assessment, will increasingly become available in the proposed format.

The top-level categories are shown in Figure 11 and they include 3 subcategories.

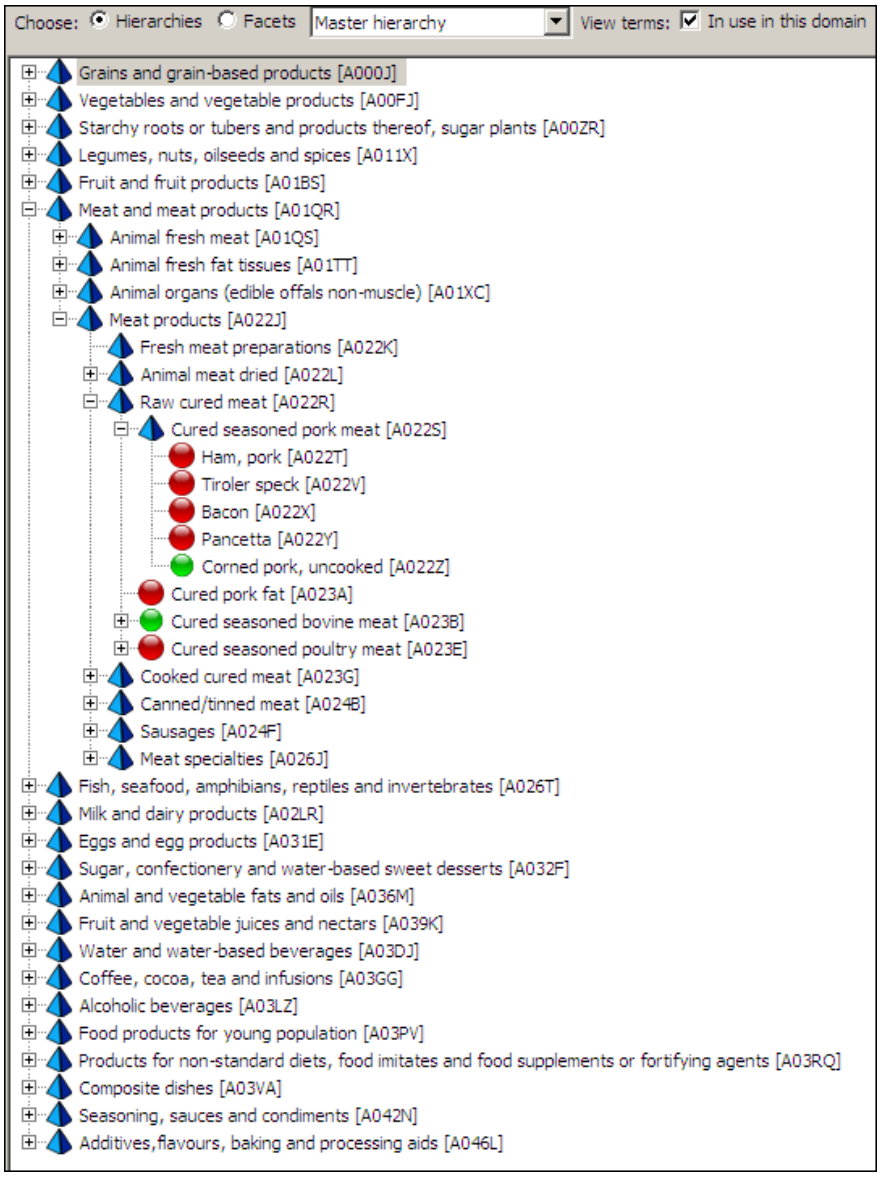


Figure 11: The exposure hierarchy is aggregated at the top level into 20 categories (the blue pyramid indicates that these are hierarchy elements)

3.2. Risk metrics

There are different ways of expressing risk in a risk ranking process. Codex Alimentarius defines risk as "a function of the probability of an adverse health effect and the severity of that effect, consequential to a hazard(s) in food". The simplest metric that can be used to account for the probability of an adverse effect in risk ranking is the number of adverse outcomes (e.g. illnesses, hospitalizations, and deaths) associated with a single hazard in multiple foods. In the case of ranking multiple hazards the challenge is to find metrics to characterize the severity of the health outcomes associated with these hazards in order to compare their overall health and/or economic impact. Indeed, the public health and economic burden of a gastrointestinal infection is not the same as an infection that requires frequent hospitalization or causes permanent disability or death. Similarly, an illness, disability, or death experienced by a child may have a different public health and economic impact than one experienced by adults of various ages. Thus, the selection of the risk metrics is of great importance in risk ranking. There are different metrics that have been developed to characterize and compare risk including the number of adverse outcomes, the quality-adjusted life year (QALY), the disability-adjusted life year (DALY) as well as metrics for monetary valuation of public health. Each of these metrics has some pros and cons, and there is no preferable choice for all scenarios. Each individual metric provides a different perspective on the public health risk of foodborne pathogens. A more detailed analysis of the main available risk metrics is presented in the following paragraphs. However, depending on data availability some of the model variables could be also used as risk metrics (see paragraph 2.5).

3.2.1. Number of adverse outcomes (e.g. illnesses, hospitalisations, deaths)

The number of adverse outcomes (e.g. illnesses, hospitalisations, deaths) is the simplest metric that can be used in risk ranking. This simple approach is appropriate for the evaluation of the relative public health impact associated with a single hazard in multiple food products (Level 1). This number of adverse outcomes can be estimated as "per serving" or "per annum (and standardised for population size (e.g. per 100,000 per year)". The "per serving" likelihood can be viewed as the risk that individual consumers face when they eat a serving of a food. The "risk per annum" on the other hand is a measure of the risk faced by a certain population (e.g. a country). The risk per annum is greatly affected by the number of servings per year. Thus, a food that has a relatively high risk on a per serving basis but is seldom consumed may have a relatively low per annum risk. Conversely, a food with a relatively low risk on a per serving basis that is consumed extensively is likely to have a higher risk on a per annum basis. In general, the per annum relative risks inherently have a greater degree of uncertainty than the corresponding per serving relative risk because of the additional uncertainty associated with the number of annual servings. Another factor that affects relative risk on a per annum basis is the size of the susceptible subpopulations, in proportion to the total population which are substantially different, i.e., YOPIs (young, old, pregnant, immunocompromised).

The number of illnesses has been used as a risk metric in the quantitative assessment of the risk to public health from foodborne *Listeria monocytogenes* among selected categories of ready-to-eat foods performed by FDA/FSIS (2003). Figure 12 shows the results of the latter study expressed as number of listeriosis per serving and per annum.

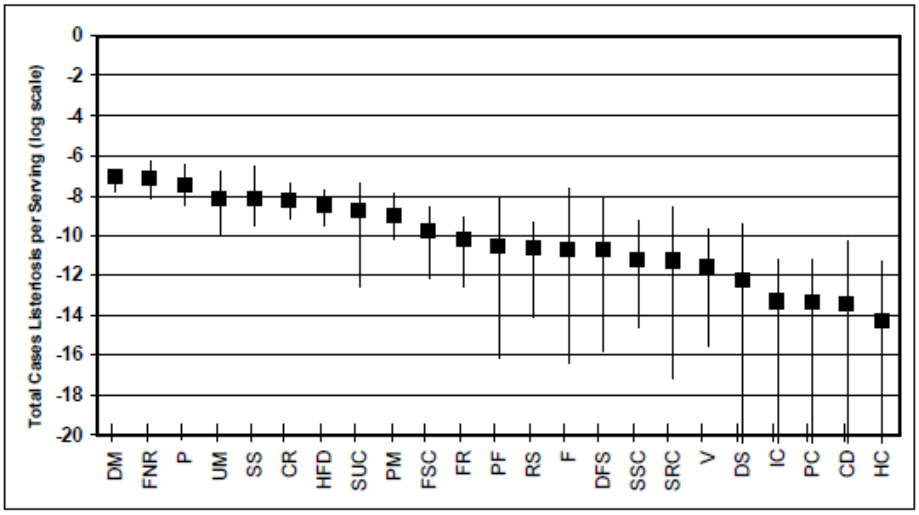
3.2.2. Cumulative exposure

Cumulative exposures are an issue if expressing the risk per serving. For chemical hazards the exposures can be cumulative. Therefore tools such as NOAEL (No Observed Adverse Effect Level), acceptable daily intake (ADI= NOAEL/safety factor) and maximum residue limits (MRL) in foodstuffs have been developed to deal with chronic cumulative risks.

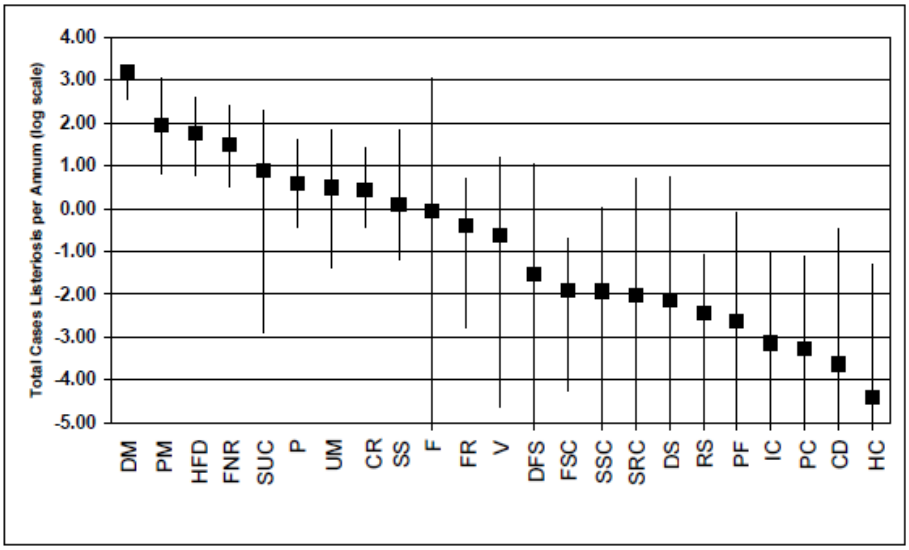
For repeated microbial exposures immunity can be a result with the consequence of higher infectious dose (right skewed dose response curve) exposures to catch disease.

Until now, immunity is not taken into account in risk assessment studies. Recently, Swart et al. (Swart et al., 2012) have developed a dynamic model and demonstrated that even short-lived immunity (protecting against disease upon re-exposure for e.g. a year) significantly affects the incidence of illnesses such as campylobacteriosis. Further work to incorporate such dynamic models in risk assessment studies is needed.

(a)



(b)



DM = Deli meats; FNR = Frankfurters (not reheated); P= Pâté and Meat Spreads; UM= Unpasteurized Fluid Milk; SS= Smoked Seafood; CR = Cooked Ready-To-Eat Crustaceans; HFD = High Fat and Other Dairy Products; SUC = Soft Unripened Cheese; PM = Pasteurized Fluid Milk; FSC = Fresh Soft Cheese; FR = Frankfurters (reheated); PF = Preserved Fish; RS = Raw Seafood; F = Fruits; DFS= Dry/Semi-dry Fermented Sausages; SSC = Semi-soft Cheese; SRC = Soft Ripened Cheese; V = Vegetables; DS = Deli-type Salads; IC= Ice Cream and Frozen Dairy Products; PC = Processed Cheese; CD = Cultured Milk Products; HC = Hard Cheese.

Figure 12: Predicted cases of listeriosis (log scale) associated with food categories for the total United States population on a "per serving" (a) and "per annum" (b) basis. The box indicates the median predicted number of cases of listeriosis (log scale) and the bar indicates the lower and upper bounds (i.e., the 5th and 95th percentiles).

3.2.3. Summary measures of public health

In the case of ranking of multiple hazards the challenge is to find metrics to characterize and compare the health impact of diverse risks and health outcomes. Different methods have been developed that provide a common metric for more fully valuing and comparing health risks. Health-adjusted life years (HALYs) are summary measures of population health permitting morbidity and mortality to be simultaneously described within a single number (Gold et al., 2002). They are useful for overall estimates of burden of disease, comparisons of the relative impact of specific illnesses and conditions on communities, and in economic analyses.

There are three steps in calculating a HALY (Gold et al., 2002):

- Describing health as a state or disease condition;
- Developing weights (or utilities) for the health state or condition (typically on a 0 – 1 scale);
- Combining incidence and weights for different health states or conditions with estimates of life expectancy, thus creating a measure of the health-related quality of life (HRQoL) and the period over which that quality of life is experienced.

HALYs are used in economic cost-effectiveness analyses, also sometimes referred in the literature as cost-utility analysis or weighted cost-effectiveness analysis (Mangen et al., 2010). The two most prominent HALYs are quality-adjusted life years (QALYs) and disability adjusted life years (DALYs). In the QALY approach, each health state is assigned a value (called a utility) that reflects the desirability of that health state; health states are valued between 0 (for death) and 1 (for perfect health). The QALY loss associated with an adverse health state is measured as the difference between QALYs with and without the condition. A number of different methods have been developed to estimate utility values for health states by defining different sets of descriptive domains that comprise quality of life (e.g., mobility, self-care ability, pain, anxiety in the EuroQol-5D). The next step is then to assign a utility weight to each health state. Different methods are available, including Visual Analog Scale, Person Trade-Off, Time Trade-Off, Standard Gamble and Pairwise Comparison). Different methods estimate different utility weights for the same health state, but the results are correlated. The QALY model requires utility independent, risk neutral, and constant proportional trade-off behaviour (Pliskin et al., 1980). QALYs are frequently used to support decisions about allocation of resources to health programmes (curative and preventive).

The DALY approach was first developed by the World Health Organization's Global Burden of Disease (GBD) program to compare the risk of specific diseases in different countries, and is increasingly used by the international infectious disease community. The DALY method is based on the same principles of the QALY, but it additionally requires definition of an idealised life expectancy. The DALY method then presumes perfect health for the entire life span, and therefore measures the loss due to ill health. Death, the worst possible health state, is assigned a disability weight of 1 and 0 represents the best health state. To calculate the burden due to premature mortality, the number of life years lost compared to a standard life table is calculated. In the original GBD project, age weighting was applied to reflect the fact that individuals have different roles and changing levels of dependency and productivity with age, though this choice is controversial. Furthermore, discounting was applied to account for the fact that good health in the near future is preferred to good health in future. Also, this choice is controversial and DALYs may be presented both discounted and undiscounted. The DALY method is considered by some to be preferable to the QALY method for making societal resource allocation decisions.

A strong point of the HALY approach is that utilities and disability weights are not income constrained. However, HALYs do not capture non-health effects and HALY impacts cannot be compared to other non-health projects (as would be the case if all effects would be expressed in monetary values). HALYs are based upon the assumption that a life-year is the appropriate metric for

measuring health; as a result, the valuation of permanent disability and mortality is linearly valued by age of patients.

3.2.4. Monetary risk metrics

The public health impact of foodborne disease can also be characterized using monetary metrics. However, health economics is a branch of economics with additional complexities (Arrow, 1963). Factors that distinguish health economics from other areas include extensive government interventions, uncertainty in several dimensions, asymmetric information (the physicians know more than the patients), barriers to entry, externalities (communicable diseases, fear of catching disease) and the presence of a third-party agent (professional health care provider). In healthcare, the third-party agent is the physician, who makes purchasing decisions (e.g., whether to order a lab test, prescribe a medication, perform a surgery, etc.) while being insulated from the price of the product or service.

A number of different approached has been developed for the monetary valuation of risk (Mangen et al., 2010). There are three general approaches: (1) the human capital approach, measuring a person's production in the marketplace; (2) and cost of illness (COI) methods and (3) revealed or stated preferences which also include intangibles (not measurable) factors such as suffering and pain.

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

A second approach to measuring the public health impact of disease is the cost of illness (COI) method. The COI approach does not measure intangible costs but traces the economic flow associated with an adverse health outcome through the quantification of measurable monetary costs. There are four components to COI: (1) direct health-care costs (DHC), which include medical services such as general practice (GP) consultations, specialists' consultations, hospitalisation, drugs, rehabilitation and other medical services; (2) indirect health-care costs (IHC), which are the future health care costs due to a life-saving intervention; (3) direct non-health-care costs (DNHC), which include such items as travel costs and informal care (e.g., by family members); and (4) indirect non-health-care costs (INHC), which include productivity losses due to lost work or the costs of special education due to chronic disability. Most COI studies include DHC and INHC. DHNC are typically low compared to other cost categories. IHC are controversial and rarely computed measure but recently, their inclusion in full economic evaluations of health care programmes is more frequently advocated (van Baal et al., 2011).

The willingness to pay (WTP) approach measures what individuals would be willing to pay or actually pays to obtain health improvements or to avoid adverse health states or, less commonly, what individuals would be willing to accept (WTA) for a health decline. In contrast to the human capital approach, the WTP approach is based on the tradeoffs that individuals must make between health and other goods, and is therefore consistent with the theoretical foundation of welfare economics.

WTP can be measured by evaluating the tradeoffs people actually make (revealed preference) or by presenting people with hypothetical choices (stated preferences). The use of stated preferences methodology can be fraught with problems such as free rider, while revealed preferences (experimental economics) measures what people actually do.

3.3. Ranking approach

Based on the features of the data sources used in model construction risk ranking models can be differentiated in "top-down", "bottom-up" and combined approaches.

In the surveillance based or "top-down" approach (or backward, Figure 13), the level of risk associated with specific foods, hazards, or their combinations is based on information gathered from epidemiological systems such as disease reporting and outbreak databases. It can be argued that these are the best sources of information for public health–based risk ranking because they reflect illness at the point of consumption. However, good epidemiologically based foodborne illness attribution data are not available at this time for the vast majority of hazard–food combinations. Another concern with this approach is that it represents disease risk only at the "point of consumption," which is the net sum of contamination occurring at the pre-harvest, processing, and final preparation stages. This does not necessarily translate directly to an understanding of the possible source of contamination in the supply chain, including a source at the point of processing.

The alternative or "bottom-up" (or forward, Figure 13) approach to public health risk ranking adheres roughly to the standard microbial risk assessment paradigm and follows the agent through the food chain to produce a prediction of risk to human health relative to other agents and/or foods. This approach is based on research data supplemented by expert judgment, and therefore can be resource-intensive and subjective. It frequently presupposes an understanding of the behaviour of microorganisms in complex and changing environments, complexities that may be very difficult to model. It could be argued that some combination of both approaches (bottom-up and top-down) would be better than either one alone.

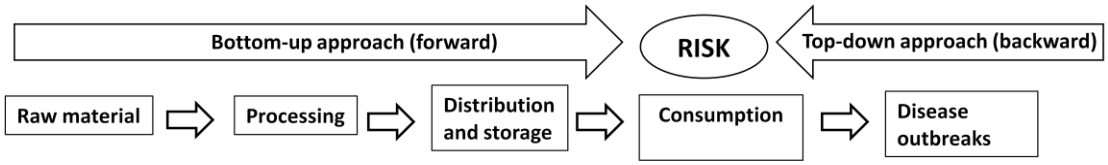


Figure 13: Possible combination of risk ranking approach (top-down and bottom-up) along the food chain.

3.4. Model type

As in the case of risk assessment, risk ranking methods span a continuum from qualitative through semi-quantitative to quantitative. Qualitative assessments are descriptive or categorical treatments of information, whereas quantitative assessments are mathematical analyses of numerical data. It should be noted that there is a gradation of model types from qualitative to quantitative and while such classifications may be helpful, they are not strict defined categories. All are valid approaches to food safety risk assessment and the appropriateness of a particular method ultimately depends on its ability to match the general principles of MRA (CAC, 1999) and the purpose of risk ranking.

3.4.1. Qualitative approach

The risk ranking generated by a qualitative risk assessment is generally of descriptive or categorical nature that is not directly tied to a more precisely quantified measure of risk. The Codex Alimentarius Commission (CAC, 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"

The reasons for selecting a qualitative approach in risk ranking are the same for those applied for risk assessment including:

- a perception that a qualitative approach is much quicker and much simpler to complete;
- a perception that a qualitative risk ranking will be more accessible and easier for the risk manager or policy-maker to understand and to explain to third parties;

- an actual or perceived lack of data, to the extent that the risk manager believes that a quantitative assessment will be impossible;
- a lack of mathematical or computational skills and facilities for risk ranking, coupled with a lack of resources or desire to involve an alternative or additional source of expertise.

A qualitative risk ranking model may provide the risk managers or policy-makers with all the information they require. Using a qualitative approach, risk can be effectively ranked based on a risk analysis matrix which categorizes the risk to low, moderate, high and very high (Table 1). However, assessing the risk, in these terms, is subjective and arbitrary. This is one of the major criticisms at qualitative risk assessments in general. However, these final risk estimates should never be viewed in isolation, just as numerical outputs from quantitative risk assessments should not, and reinforces the need for transparent documentation of the data and logic that lead to the assessor's estimate of the risk (WHO, 2009).

A qualitative risk ranking should take uncertainty and variability into account. Since in a qualitative approach there is no specific way in which uncertainty and variability in anyone input parameter is retained and reflected precisely in the final risk estimate, the overall assessment of uncertainty and variability can be evaluated in narrative terms such as 'much', 'little', etc, or can be scored according to the available evidence like in evidence-based medicine. Another option for the inclusion of uncertainty and variability is to include a number of scenarios that reflect the uncertainty and variability, evaluate each as a separately measured risk scenario, and compare the results. In general, the influence of key factors in the risk ranking model should be discussed in considerable detail where the uncertainty or variability in the factor is sufficient to change the ranking. This is particularly important where, within the range of uncertainty and variability, the risk ranking result could potentially surpass a key decision-making threshold (Table 10).

Table 10: Examples of categories of uncertainty

Evaluation	Score	Explanation
low	1	Solid and complete data available: strong evidence in multiple references with most authors coming to the same conclusions (e.g. in a meta-analysis).
medium	2	Some or only incomplete data available: evidence provided in small number of references; authors' conclusions vary.
		Solid and complete data available from other species which can be extrapolated to the species considered.
high	3	Scarce or no data available: evidence provided in unpublished reports, or based on observation or personal communications; authors' conclusions vary considerably

3.4.2. Quantitative approach

Quantitative risk ranking approaches provide numerical expression of risk. Quantitative measures of risk must combine in some form an expression of the two quantitative components of risk, namely some measure of the probability of the risk occurring; and the size of the impact should that risk occur (Kaplan and Garrick, 1981). Quantitative assessments require the development of mathematical models in which all relationships between factors affecting risk are described mathematically. The selection of quantitative models must be based on how well the model is supported by the available data, how effective the outputs are in informing decision-makers, and how many assumptions have been made in creating the model and the robustness of those assumptions (WHO, 2009).

Quantitative assessments are divided into two categories: deterministic and stochastic, which are also referred to as 'point-estimate' and 'probabilistic' assessments. In the deterministic assessment single values (average, highest level, most often observed value, 95th percentile, etc.) as the average or

'worst-case' to characterize each variable in the model (concentration in the food; effect of processing, growth during storage; amount of food serving; etc.). The point estimates are then combined using mathematical models to generate a point estimate of exposure and risk (worst case, best case, average, etc.). The effects of changes to model variables can then be evaluated using 'what-if' scenarios with different combinations of variables. In the probabilistic assessment, stochasticity is incorporated into these models by using probability distributions for variable or uncertain model parameters. In that case, the model is usually analysed by means of Monte Carlo simulation. The output of the stochastic approach yields a risk estimate that should correctly reflect the uncertainty and variability in the model for the used data.

Quantitative assessments must take into account both variability and uncertainty. The separation of uncertainty and variability as sources of variation of the model parameters is an important issue in quantitative assessments (Nauta et al., 2000). 'Uncertainty' represents the lack of perfect knowledge of the parameter value, which may be reduced by further measurements. 'Variability', on the other hand, represents a true heterogeneity of the population that is a consequence of the physical system and irreducible by additional measurements. Variability and uncertainty can all be described by distributions that, in essence, look the same. The difference is that the vertical scales describe different quantities. For variability distributions it is probability or probability density and for uncertainty distributions it is relative confidence. When variability and uncertainty are modelled together in one Monte-Carlo model, samples are taken from the different distributions, without a careful consideration of what the distributions stand for. The result of such a model will describe a mixture, which can be difficult to interpret. For these reasons, it is considered useful to separate them as far as possible. This can be achieved in a number of ways including second-order modelling.

3.4.3. Semi-quantitative approach

Semi-quantitative risk assessment provides an intermediary level between the textual evaluation of qualitative risk assessment and the numerical evaluation of quantitative risk assessment (FAO/WHO 2009). The difference with the qualitative assessment is that semi-quantitative assessment has a greater focus on attempting to evaluate the components of the risk to within defined quantitative bounds. Thus, semi-quantitative approaches are most useful in providing a structured way for risk ranking. Semi-quantitative risk ranking based on a scoring system does not require the same mathematical skills as quantitative assessment while at the same time avoids some of the greater ambiguities that a qualitative risk assessment may produce.

The basis for semi-quantitative assessment is the categorical labelling. It uses non-technical descriptions of model variables such as 'Very low', 'Low', Medium', 'High', and 'Very High', or some scaling like 0-5. In order for this type of labelling to be unambiguous and useful, a list of the non-overlapping, numerical categorical terms that are to be used must be provided, together with clear definitions of each term. This step is crucial, as a number of studies have shown that even professionals well-versed in probability ideas who regularly make decision based on risk assessments have no consistent interpretations of probability phrases ('likely', 'almost certain', etc.), which could lead to inconsistency and lack of transparency.

3.5. Model variables

After the definition of what to be ranked and the selection of the risk metrics and the ranking approach, it is necessary to determine which 'variables' are deemed to be important to the issues under consideration. The variables are basically the major factors that should be considered in decision-making regarding an issue and they define what is considered important in ranking one risk relative to another. The adoption of explicit variables allows participants in ranking exercises to make a series of incremental judgements which together can be combined to form an overall picture of the issues, rather than requiring them to make broad, complex and sweeping judgements. By identifying and explicitly defining variables, participants are forced to systematically think about their decisions and to justify the reasoning which underpins them. In the absence of explicit variables, the rationale behind

the rankings may be unclear. The ranking process, therefore, has to be centred on a set of agreed-upon variables.

In general the variables that can be used for risk ranking can be grouped in the following categories.

Hazard characterization is the qualitative and quantitative evaluation of the nature of the adverse effects associated with the hazard (refs general texts on risk assessment/ this is a standard risk assessment definition). However, the definition of hazard characterisation may vary and also the type of variables used. This needs to be clearly defined and stated in each particular risk ranking exercise. Hazard characterisation can be described by different types of variables describing different facets of the adverse effect of a hazard. In the following different types of variables are listed which can give information on the adverse effect of a pathogen such as epidemiological variables, disease severity and other characterization variables.

3.5.1. Epidemiological variables

An important element for deciding the qualitative or quantitative size of the risk is the magnitude of the disease (or other adverse health effect) in question. A commonly used measure for this is the number of reported cases in specific MSs and such figures may be found in national databases or annual reports. The reported incidence of common foodborne enteric diseases are also reported to ECDC and published by EFSA in the EU Summary Reports.

These data, however, have some limitations. Firstly, they only include the reported number of cases, which is well-known to be only a fraction of the illnesses occurring in the population. In addition, the degree of underreporting varies widely between MSs given a false impression of the real disease occurrence in EU. In a risk ranking exercise, it is considered important to consider underreporting to the extent possible in order to provide the best estimate for the true number of cases occurring in the population. Different approaches for estimating the burden of illness have been described (De Wit et al., 2001; Majowicz et al., 2010; Scallan et al., 2011; Tam et al., 2012). Also recently, Havelaar (Havelaar et al., 2012b) have estimated the true burden of illnesses in EU due to *Salmonella* and *Campylobacter* (Havelaar et al., 2012.

Secondly, for the vast majority of cases, the actual food source/vehicle carrying the pathogenic organism is not known. However, if different hazard-food pairs are to be ranked, it is important to have an estimate of the proportion of the total burden of illness that can be attributed to the different food sources and possible other sources such as water and direct contact with infected animals or humans. Different methods for source attribution are available and have been described by Pires et al. (EFSA, 2008b; Pires et al., 2009). Common for the methods are that they attempt to attribute the burden of disease at the population level, and do not describe causation of disease at the individual level. Methods for source attribution of foodborne diseases include e.g. use of microbial subtyping (Hald et al., 2007; Little et al., 2010; Mullner et al., 2009a), comparative exposure assessment (Evers et al., 2008; FDA, 2003), analysis of foodborne disease outbreak data (Pires et al., 2010a; Pires et al., 2012) and systematic review of case-control investigations of sporadic illness (Domingues et al., 2012) (Domingues et al., 2011). However, for many pathogens sufficient data for source attribution are missing. In such situations, expert elicitation can be used (Havelaar et al., 2008; Hoffmann et al., 2007).

At the EU level, source attribution estimates for human salmonellosis based on the subtyping approach (Hald et al., 2012; Pires et al., 2011) and estimates for human salmonellosis and campylobacteriosis using outbreak data (Pires et al., 2011; Pires et al., 2010b) are available. The microbial subtyping approach involves characterization of isolates of the pathogen by phenotypic and/or genotypic subtyping methods. The principle is to compare the distribution of subtypes in potential sources (e.g. animals and food) with the subtype distribution in humans and it is enabled by the identification of strong associations between some of the dominant subtypes and a specific reservoir or source, providing a heterogeneous distribution of subtypes among the sources. Depending on the purpose of

the risk ranking, a limitation of the subtyping approach is that human cases are attributed to the reservoir level i.e. food animals (e.g. pigs) or a broad food category (e.g. imported pork) and not to a specific food item (e.g. pork chops) consumed, making it impossible to assess the impact of specific foods. The approach requires a collection of temporally and spatially related isolates from various sources and humans, and is consequently facilitated by an integrated foodborne disease surveillance programme focused on the collection of isolates from the major food animal reservoirs of foodborne diseases and from humans (Pires et al., 2009).The latest study conducted so far at the EU level has applied data from the harmonised *Salmonella* monitoring in poultry - laying hens, broilers and turkeys- (EFSA Panel on Biological Hazards (BIOHAZ), 2010a, 2012a), the EU wide *Salmonella* baseline study in pigs (EFSA (European Food Safety Authority), 2009) and human salmonellosis data for both sporadic cases and outbreaks and other food/animal data reported in the EU summary reports (EFSA and ECDC, 2011). The data quality and requirements are considered the biggest limitation of this approach.

In contrast to the subtyping approach, an advantage of using data from outbreak investigations is that these data are observed at the public health endpoint and thereby provide a direct link between the foods consumed at the observed illnesses i.e. the data may allow for an assessment of the impact of specific hazard-food combinations. The main limitations are that the method implicitly assumes that the importance of different foods are the same for sporadic occurring and outbreak related cases, which is not true for all pathogens e.g. *Campylobacter* (Pires et al., 2010; Pires et al., 2012). In addition, the approach requires that a sufficient amount of outbreaks are investigated and reported limiting the approach to rather large countries or to multi-state analyses. For the studies conducted at the EU level, foodborne disease outbreak data reported by the MSs to EFSA (BIOMO unit) have been applied.

Source attribution estimates are often requested in the work of the BIOHAZ Panel and have recently been used in several BIOHAZ opinions (EFSA Panel on Biological Hazards (BIOHAZ), 2011a, 2011b, 2011c, 2012b).

3.5.2. Disease severity variables

Variables for the severity of human disease have been measured in the clinical setting for medical reasons that include essential diagnostic, therapeutic and prognostic considerations in individual patients or patient groups. For these purposes including the risk ranking of food-borne hazards, the many very specific medical scoring systems of disease severity in individual patients have little or no use. Rather, simple descriptors of outcome variables, such as hospitalisation rates and duration, and mortality rates are commonly used to account for disease severity.

To inform estimates of disease burden in a given population in DALYs, generic instruments to measure health related quality of life are available. These include instruments such as the SF-36 and the Euroqol-5D, which have been calibrated in population panels. Based on these data, regression models are available to transform any set of scores on these instruments into disability weights. Furthermore, for many disease outcomes of interest, disability weights are available from a variety of sources including WHO and different national projects. Further information on a European approach to estimate the burden of infectious disease can be found on the ECDC website: http://ecdc.europa.eu/en/healthtopics/burden_of_communicable_diseases/project/pages/project.aspx.

3.5.3. Dose-response variables

Description of the dose-response variables involves consideration of the factors related to the pathogen, the host and the matrix which affect the dose required for infection (WHO, 2009). Pathogen-related factors should be analysed with a view to determining the characteristics of the pathogen that affect its ability to cause disease in the host. The analysis should take into account the relevant mechanisms that cause illness (infectious, toxico-infectious, toxigenic, invasive or not, immune-mediated illness, etc.). There is huge variation in the dose response among pathogens (Table 11), which can affect the risk ranking of biological hazards. Host-related factors are the characteristics

of the potentially exposed human population that may influence susceptibility to the particular pathogen, taking into account host intrinsic and acquired traits that modify the likelihood of infection. Finally, the factors related to the food matrix are principally those that may influence the survival of the pathogen through the hostile environment of the stomach. Such effects are related to the composition and structure of the matrix (e.g. highly buffered foods; entrapment of bacteria in lipid droplets) and to the food-induced stress tolerance which can lead to protection of the pathogen against physiological challenges, such as gastric acid or bile salts.

Table 11: Variation across pathogens in the number of cells required to successfully infect a host, with examples of Dose-1% and P1 values (EFSA Panel on Biological Hazards (BIOHAZ), 2012b), modified.

Pathogens	**Population exposure**	**Dose-1% value[§]**	**P1 value[¥]**	**References**
Salmonella (salmonellosis)	any exposed people	4.1	$2.5 \cdot 10^{-3}$	(FAO/WHO, 2002)
Shigella	any exposed people	8.8	$1.2 \cdot 10^{-3}$	(Cassin et al., 1998)
Campylobacter jejuni (diarrheal disease)	adults	2.9	$3.5 \cdot 10^{-3}$	(FAO/WHO, 2009)
EHEC *(e.g. E. coli* O157*)* (haemolytic uremic syndrome)	children < 6 years	8.4	$1.2 \cdot 10^{-3}$	(Delignette-Muller and Cornu, 2008)
	children 6-10 years	41.9	$2.4 \cdot 10^{-4}$	
Yersinia enterocolitica	no dose-response model available involved in water-borne infections and growth in water does not seem possible			(Eden et al., 1977; Han et al., 2003; Keet, 1974; Lund, 1996; Ostroff et al., 1994; Ramalho et al., 2001; Thompson and Gravel, 1986)
Listeria monocytogenes (severe listeriosis)	more susceptible sub-population	$9.5 \cdot 10^{9}$	$1.1 \cdot 10^{-12}$	(FAO/WHO, 2004)
	less susceptible sub-population	$4.2 \cdot 10^{11}$	$2.4 \cdot 10^{-14}$	
Vibrio parahaemolyticus (enterocolitis)	adults	$2.2 \cdot 10^{4}$	$4.6 \cdot 10^{-7}$	FDA
Clostridium perfringens		$1.45 \cdot 10^{6}$	$6.93 \cdot 10^{-9}$	(Golden et al., 2009; Jaloustre, 2011)
Bacillus cereus (diarrhoeic)	no dose-response model available at least 10^{5}-10^{6} cells per serving of foods causing illness			(EFSA, 2005)

[§]: Dose-1% value: estimated dose (total number of cells) that causes a certain effect in 1% of the individuals exposed.
[¥]: P1 value: estimated probability of a certain effect when the ingested dose is represented by one cell.

3.5.4. Exposure variables

The level of exposure or dose is one of the most important factors affecting safety risk. For foodborne hazards, the level of exposure is a function of the following variables:

3.5.4.1. Probability and level of contamination

The exposure to foodborne pathogens is directly related to the probability that the product is contaminated and the level of this contamination. This type of information can be captured by examination of the prevalence and concentration of the pathogen in the food of concern. For describing exposure, estimates of prevalence and concentration of the pathogen at any stage of the food chain can be used, from primary production to the final product. Contamination may be determined as a percentage of contaminated samples (the prevalence) and/or the number of microorganisms (concentration). It is important that the detection level and sample size are known, as well as the sensitivity and selectivity (or specificity) of the detection method(s) utilized. In general, prevalence and concentration are uncertain parameters within the model. The data collected should, ideally, enable any variation in the likelihood and numbers to be fully characterized. Both prevalence and concentration may vary between products, producers, seasons and regions.

3.5.4.2. Processing variables

Food processing operations aim to minimize microbial growth and/or to maximize microbial inactivation or removal through cleaning and sanitation. The effect of food processing operation to the prevalence and concentration of pathogens will affect significantly the final risk of the product. There is an increased number of treatments that can be applied in foods during processing. The extent of inactivation during these treatments as well as the potential of recontamination after processing depends on the duration, the severity and the conditions of the treatment. However, the type and the conditions of the processing treatments can vary significantly between products and/or processors. An added difficulty in describing the effect of processing in the final risk is elaborating processing scenarios that are both representative of the majority of processors, yet take into account differences in processors (WHO/FAO, 2008).

3.5.4.3. Post-processing variables

The post-processing environment includes storage, distribution, retail display sale, food service operations and consumer handling. A list of the post-processing factors affecting the prevalence and concentration of pathogens at the time of consumption is presented in Table 12. Depending on the storage conditions and their characteristics, certain products support the growth of pathogens, while others do not support their growth. In the former case, the extent of growth is also important since higher numbers of pathogens correlate with higher risk. The extent of pathogen's growth mainly depends on the storage conditions and time, the product's formulation but also on other factors including the presence of antagonistic flora in the food and physiological state of the pathogen. The effect of spoilage bacteria on the shelf life of the product should also be considered. Conditions that lead to rapid growth of pathogens may also lead to rapid microbial spoilage. Contaminated products that are obviously spoiled are less likely to be consumed, and thus not lead to foodborne disease, despite that fact that they contain a microbiological hazard.

Other post-processing factors that affect the prevalence and concentration of pathogens at the time of consumption include cross-contamination during handling, cleaning and sanitation treatments and cooking practices. Post-processing environments are very complex because of the variety of conditions involved. For example, food handling practices vary by geographical region or even within the same country, based, for example, on ethnicity, gender and education. The data gaps on consumer storage times, extent of cross-contamination, cooking times and temperatures, food handling practices by restaurant and food service operations, etc. may increase significantly the uncertainty of the risk estimations.

Table 12: Post-processing factors affecting the prevalence and concentration of pathogens at the time of consumption

Factor	Description
Storage conditions	Temperature, packaging atmosphere
Storage time	Shelf life of product
Product formulation	pH, a_w, presence and concentration of antimicrobials, (sorbate, lactate, nitrite, nisin, etc.)
Physiological state of pathogen	Conditions before contamination (history)
Antagonistic microflora	Presence of organisms (i.e Lactic acid bacteria) that inhibit growth of pathogen
Cross-contamination	Contamination from, surfaces, equipment, hands etc
Treatment before consumption	Cleaning (washing), Sanitizing (chlorine, acetic acid)
Spoilage microflora	Discarding spoiled products
Cooking	Cooking method, time and temperature

3.5.4.4. Consumption variables

The level of exposure is also a function of the frequency of consumption of the foods and the quantity of food consumed. Products that are consumed frequently or in high volume are more likely to cause widespread outbreaks or multiple cases than are products consumed less often or eaten by only a limited segment of the population. Thus to characterize the risk from exposure to microbiological hazards in food, it is necessary to know the amount of food consumed and how often it is consumed. The amount of food consumed can be expressed as "per capita amount" which is calculated by dividing the total amount of a food by the total number or "per-eater amount" which is calculated by dividing the total amount of food only by the number of people who actually consumed the food. The frequency of consumption can be expressed as the amount of consumption per year, per day or per eating occasion.

3.6. Collection and evaluation of data for the model variables

After the selection of the variables for the risk ranking model, the data for describing the effect of these variables to the safety risk of the products of concern must be collected and evaluated. Data required for risk ranking may come from a wide variety of sources. In general these sources can be categorized three main categories including i) literature review, ii) predictive microbiology and iii) expert opinion.

3.6.1. Data from national or international databases

Various international agencies manage different databases that represent some of the sources for data for risk assessment studies. Here below some examples about database on food safety, public health are described in the EU and worldwide.

3.6.1.1. EFSA

EFSA founding regulation (Art. 33) states that EFSA shall search for, collect, analyse and summarise particularly data on:

- food consumption,
- incidence and prevalence of biological risks, and
- occurrence of contaminants and chemical residues.

For food consumption data, the Comprehensive Food Consumption Database is a source of information on food consumption across the European Union (EU). It contains detailed data for a number of EU countries. Concerning data on zoonoses, the Directive 2003/99/EC assigns EFSA the task of examining data submitted annually by Member States on zoonoses, zoonotic agents, food-borne outbreaks and antimicrobial resistance. Finally the Regulation 396/2005 requires that EFSA collate and analyse results of national controls on pesticide residues in food and feed. A consumer exposure assessment has to be carried out by EFSA before concluding on the safety of a maximum residue level.

3.6.1.2. ECDC

The European Surveillance System (TESSy), managed by ECDC, is a highly flexible metadata-driven system for collection, validation, cleaning, analysis and dissemination of data. Its key aims are data analysis and production of outputs for public health action. All EU Member States and EEA countries report their available data on communicable diseases as described in Decision No 2119/98/EC to the system.

3.6.1.3. Eurostat

Eurostat database is kept by the homonymous EC Directorate General which provides the European Union with statistical information at European level and to promote the integration of statistical methods across the Member States of the European Union, candidate countries and EFTA countries. The organisations in the different countries which actively cooperate with Eurostat are summarised under the concept of the European Statistical System.

3.6.1.4. FAO

FAOSTAT provides time-series and cross sectional data relating to food and agriculture for some 200 countries. The national version of FAOSTAT, CountrySTAT, is being developed and implemented in a number of target countries, primarily in sub-Saharan Africa. It will offer a two-way data exchange facility between countries and FAO as well as a facility to store data at the national and sub-national levels.

3.6.1.5. WHO

WHO manages the Global Database on Child Growth and Malnutrition is a standardized compilation of child growth and malnutrition data from nutritional surveys conducted around the world since 1960. Scientists have been using growth assessment because it best defines the health and nutritional status of children while serving as a useful indirect measurement of a population's overall socioeconomic status.

3.6.2. Literature review

Literature review is the main source for data collection in risk assessment and risk ranking. EFSA recently published guidance on the "Application of systematic review methodology to food and feed safety assessments to support decision making" (EFSA (European Food Safety Authority), 2010). This Guidance aims to assist the application of systematic reviews to food and feed safety risk assessments in support of decision making, by describing a framework for systematic review generated by the risk assessment process. The Guidance provides suggestions and examples for the conduct of eight key steps in the systematic review process, including both the collection and evaluation of data (Figure 14).

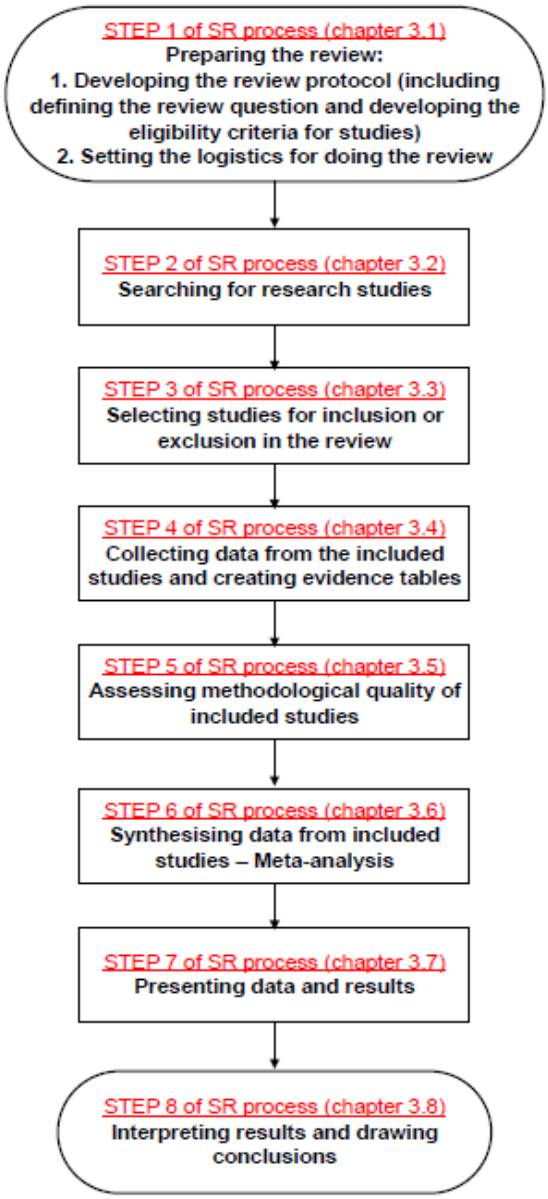


Figure 14: Core steps for performing a systematic review based on EFSA guidance (adapted from the Cochrane Handbook for Systematic Reviews of Interventions, Higgins and Green (editors), 2009)

3.6.3. Predictive microbiology

Predictive microbiology is another important source for data collection in risk ranking especially for models the exposure assessment model variables related to the behaviour of pathogens. Predictive microbiology has been established itself as a scientific discipline that uses mathematical equations to summarize and make readily available quantitative information on the microbial responses in various foods under different conditions (McMeekin et al., 2008). Development of models to predict survival, growth or inactivation of microorganisms in foods has been a most active research area within food microbiology during the last 25 years (Ross and Dalgaard, 2004). Microbial growth and inactivation models are now sufficiently detailed and accurate to make important contributions since scientists and regulators can make reasonable predictions of the relative risk posed by a hazard in a particular food or by a food process. However, predictive microbiology has limitations. Most of models have been developed based on laboratory media and the predicted values may not truly represent the real world if

models have not been validated. In addition not all hazards that are of interest have been characterized and uncertainties surrounding predictions are not always given.

Mathematical models have been incorporated into a considerable number of predictive microbiology software tools that are available to predict survival/growth of microorganisms in foods (see Annex).

3.6.4. Expert opinion

In some cases data are not available in the literature or other sources. When no data are found to describe a variable which is considered critical for the risk ranking, expert opinion can be used. In this case, expert opinions must be based on formalized and documented methods that avoid biasing (Gallagher et al., 2002; Morgan et al., 1992; Vose, 1996; Wooldridge et al., 1996) as much as possible. Ideally, the opinion of each individual expert, and the way whether and how a consensus was reached, should be documented and explained to the greatest extent possible in order to increase transparency, and minority opinions need to be included. When opinions between experts differ markedly, weighting methods can be used to integrate information in the most reliable manner.

One of the tools to potentially optimise results achieved by expert opinion, in particular when significant uncertainty is involved is the Cooke method of "expert elicitation" (Cooke, 1991). There, a two-step procedure first calibrates the individual expert's informativeness according to the response to "seed" questions in the field for which answers are already known, so that an individual weighting score is given for each expert; second, the answers to the real questions are collectively analysed according to the individual experts' performance, giving ranges of values that reflect the cumulative feeling of uncertainty for the specific problem. This procedure has been increasingly used, more recently for risk assessments ranging from volcanic eruptions to safety issues of river dams and prion disease risks (Aspinall, 2010; Tyshenko et al., 2011).

3.7. Restructure of model based on data availability

The risk metrics, ranking approach, model's type and variables during the stages 2 to 5 are selected based on the ideal approach for the purpose of risk ranking without taking into account the availability of data. During data collection and evaluation however (stage 6), data gaps can be identified. For example, although all variables that affect the final risk should ideally be included in the risk ranking model, data for a specific variable may be limited or even nonexistent. Similarly, gaps can be identified in data required for the risk metrics, ranking approach and model's type that have been initially selected as the ideal approach for the risk ranking purpose. When this is the case, it may be necessary to restructure the model and re-select the appropriate risk metrics, ranking approach, model's type and variables according to data availability. Restructure of the model may also be decided in order to reduce the uncertainty of the model output. In any case restructuring the model should always take into account the purpose of risk ranking and should be performed with caution since important factors that have an effect on the risk may be overlooked and lead to erroneous results.

3.8. Data integration

The data integration step combines information collected in previous stages to produce output results on the chosen risk metric. Depending on the metric and approach chosen, this step can take different forms.

- In qualitative risk assessment, the information is preferably combined using a set of logical rules to arrive at a final result. This can be in the form of a reasoned opinion[13] (e.g. the collected information is compared with a set of predefined criteria, without any hierarchy of these criteria) or in the form of a decision tree, a schematic tree-shaped diagram used to determine a course of action or show a statistical probability. Each branch of the decision tree

[13] A reasoned opinion, a term introduced in Regulation 396/2005 about pesticide residues, describes the comprehensive scientific evaluation of, and subsequent conclusions from, the consumer exposure assessment and the risk assessment of pesticide residues resulting from the use of pesticides.

represents a possible decision or occurrence. The tree structure shows how one choice leads to the next, and the use of branches indicates that each option is mutually exclusive. A decision tree can be used to clarify and find an answer to a complex problem. The structure allows users to take a problem with multiple possible solutions and display it in a simple, easy-to-understand format that shows the relationship between different events or decisions. The furthest branches on the tree represent possible end results (from www.investopedia.com/terms/d/decision-tree.asp#axzz1rfTGXiyo). In qualitative risk assessment, it is crucial that the approach used is transparent and repeatable.

- Multi-criteria analysis has been described in section 2.4.3. In the data integration step, scores for each scenario to be evaluated are combined with the appropriate weights and are combined to produce a final risk estimate using simple additive or multiplicative models. Scores can be presented as such, or can be normalized if the results are naturally bounded between a minimum and a maximum value.

- In quantitative approaches, model equations guide the integration of input parameters and other model factors to produce risk estimates. Uncertainty and variability are important factors to take into account in any risk assessment, be they qualitative, semi-quantitative or fully quantitative. Techniques include stochastic simulation, sensitivity and scenario analysis. Many guideline documents are available that provide detailed information on the importance and approaches to consider these aspects (EFSA Panel on Animal Health and Welfare (AHAW), 2009; WHO, 2009).

3.9. Presentation of the results

In the presentation of the results, the risk ranking exercise should be documented as fully as possible. It is imperative that all processes undertaken to produce the final output are fully documented in a transparent way such that the process of risk ranking is reproducible. The reason of the selection of the different options in each stage of the process must be explained in detail. Managers should be fully informed of the strengths and limitations of the risk ranking to ensure its best use. The risk ranking results should be presented in an objective manner with all assumptions fully acknowledged and their impact thoroughly considered or recognized. It is very important that the presentation of the risk ranking results explicitly address sources of variability and sources of uncertainties separately wherever possible. Finally, the need for additional data to improve the risk ranking output should be explicitly discussed.

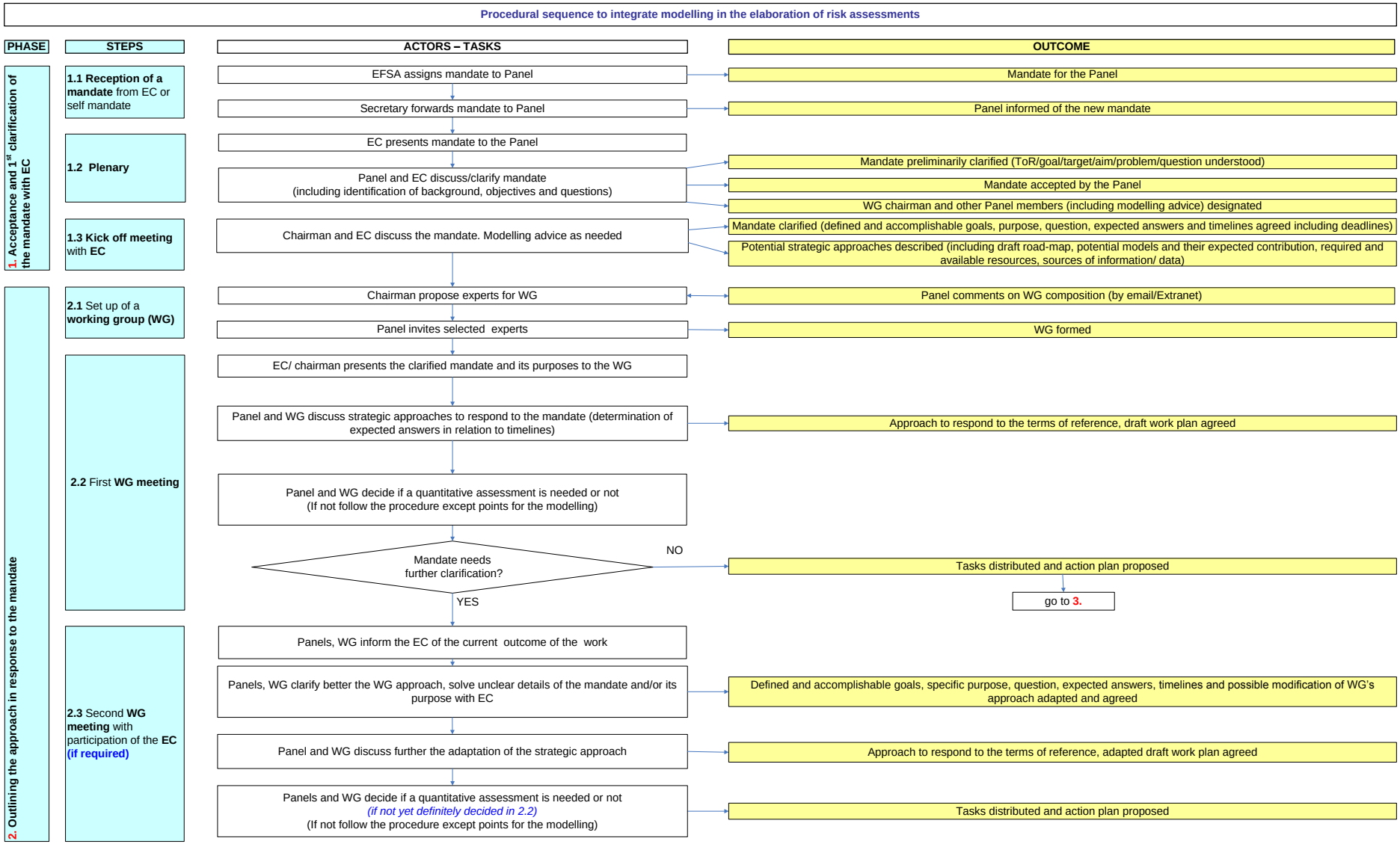
3.10. Interaction between managers and risk assessors

As in any risk analysis process, risk ranking applied to food safety requires continuous exchange of information between risk assessors and risk managers. The interfacing between the risk manager, the requestor and the risk assessor, should be done at the early stage of presenting the scientific request, in order to clarify the purpose, the assumptions and the methodology applied.

Once available information has been used to fully identify the hazards, and decide on and assess the appropriate risks, this may be followed by further discussion with stakeholders, leading to corrections, amendments, and additions as appropriate, resulting in the final risk assessment.

3.11. Application of the conceptual risk ranking framework

The application of the risk ranking framework can be done according to the steps shown in the diagram in Figure 15 from the BIOHAZ scientific opinion on reflecting on the experiences and lessons learnt from modelling on biological hazards, which has been modified from the flowchart based on the guidance on good practice in conducting scientific assessments in animal health using modelling by EFSA Panel on Animal Health and Welfare (EFSA Panel on Animal Health and Welfare (AHAW), 2009).


Procedural sequence to integrate modelling in the elaboration of risk assessments
PHASE
STEPS
ACTORS – TASKS
OUTCOME
1. Acceptance and 1st clarification of the mandate with EC
1.1 Reception of a mandate from EC or self mandate
EFSA assigns mandate to Panel
Mandate for the Panel
Secretary forwards mandate to Panel
Panel informed of the new mandate
1.2 Plenary
EC presents mandate to the Panel
Panel and EC discuss/clarify mandate (including identification of background, objectives and questions)
Mandate preliminarily clarified (ToR/goal/target/aim/problem/question understood)
Mandate accepted by the Panel
WG chairman and other Panel members (including modelling advice) designated
1.3 Kick off meeting with EC
Chairman and EC discuss the mandate. Modelling advice as needed
Mandate clarified (defined and accomplishable goals, purpose, question, expected answers and timelines agreed including deadlines)
Potential strategic approaches described (including draft road-map, potential models and their expected contribution, required and available resources, sources of information/ data)
2. Outlining the approach in response to the mandate
2.1 Set up of a working group (WG)
Chairman propose experts for WG
Panel comments on WG composition (by email/Extranet)
Panel invites selected experts
WG formed
2.2 First WG meeting
EC/ chairman presents the clarified mandate and its purposes to the WG
Panel and WG discuss strategic approaches to respond to the mandate (determination of expected answers in relation to timelines)
Approach to respond to the terms of reference, draft work plan agreed
Panel and WG decide if a quantitative assessment is needed or not (If not follow the procedure except points for the modelling)
Mandate needs further clarification?
NO
Tasks distributed and action plan proposed
go to 3.
YES
2.3 Second WG meeting with participation of the EC (if required)
Panels, WG inform the EC of the current outcome of the work
Panels, WG clarify better the WG approach, solve unclear details of the mandate and/or its purpose with EC
Defined and accomplishable goals, specific purpose, question, expected answers, timelines and possible modification of WG's approach adapted and agreed
Panel and WG discuss further the adaptation of the strategic approach
Approach to respond to the terms of reference, adapted draft work plan agreed
Panels and WG decide if a quantitative assessment is needed or not (if not yet definitely decided in 2.2) (If not follow the procedure except points for the modelling)
Tasks distributed and action plan proposed

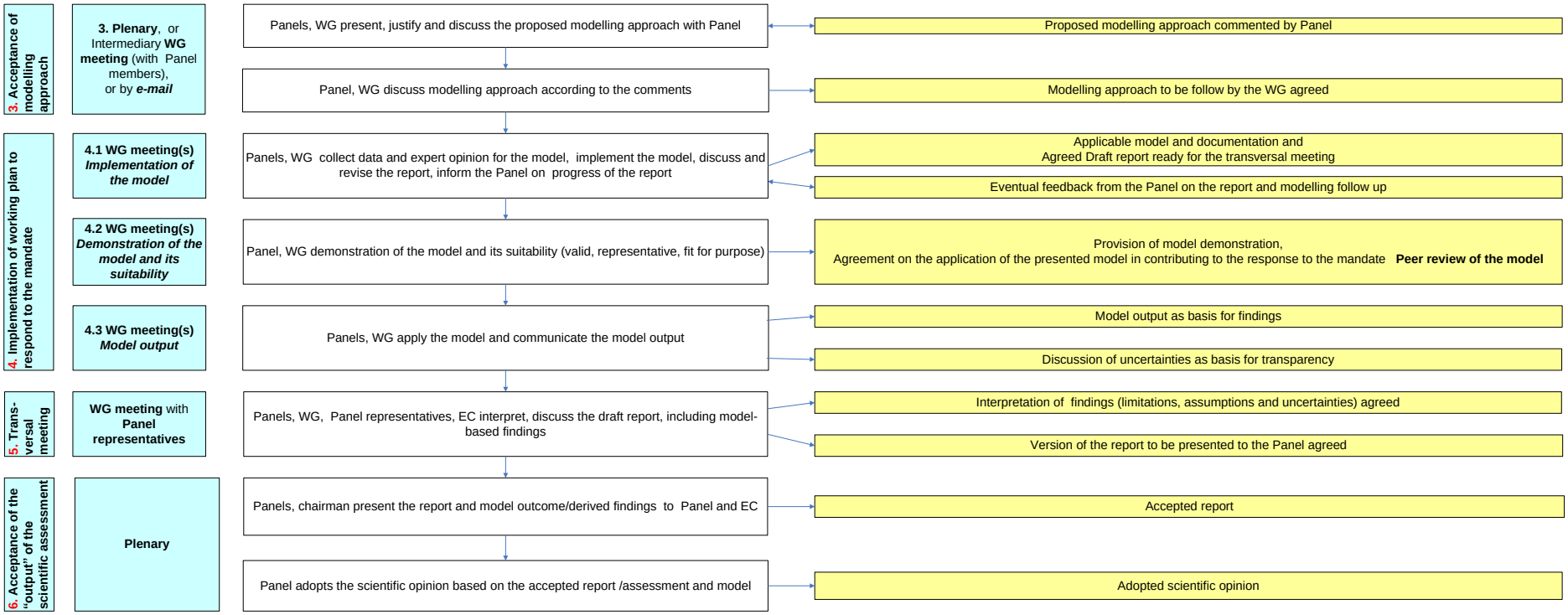


Figure 15: Process of risk assessment modelling (EFSA Panel on Animal Health and Welfare (AHAW), 2009).

4. Available Risk Ranking tools related to biological hazards developed worldwide

In this chapter the risk ranking prototypes developed by different food safety agencies worldwide are presented, considering the approach taken, the data and criteria used and the risk metrics.

4.1. Risk Ranger from Australian Food Safety Centre

The Risk Ranger tool[14] developed by the Australian Food Safety Centre is in Microsoft Excel spreadsheet software format and embodies established principles of food safety risk assessment, i.e.

- the combination of probability of exposure to a food-borne hazard;
- the magnitude of hazard in a food when present and
- the probability and severity of outcomes that might arise from that level and frequency of exposure.

The tool requires the user to select from eleven qualitative statements and/or to provide quantitative data concerning factors that that will affect the food safety risk to a specific population, arising from a specific food product and specific hazard, during the steps from harvest to consumption.

The spreadsheet converts the qualitative inputs into numerical values and combines them with the quantitative inputs in a series of mathematical and logical steps using standard spreadsheet functions. Those calculations are used to generate indices of the public health risk (Ross and Sumner, 2002). The approach taken in the development of the tool is bottom-up, so that the model has a predictive capacity risk levels. The eleven statements and weighting values used in the current model are:

1. Hazard severity
2. How susceptible is the consumer?
3. Frequency of consumption
4. Proportion of population consuming
5. Size of population of interest
6. Proportion of product contaminated
7. Effect of process
8. Is there a potential for recontamination?
9. How much increase from level at processing is required to reach an infectious or toxic dose for the average consumer?
10. How effective is the post-processing control system?
11. Effect of preparation for meal

[14] www.foodsafetycentre.com.au/docs/RiskRanger.xls

The risk is calculated as:

Risk ranking = Probability of illness per day per consumer of interest X Hazard severity X Proportion of population consuming X Proportion of total population in population of interest

The tool has some advantages, it is simple to use and intuitive tool and it does not requires installing specific software. However some limitations include the lack of evaluation of the model's performance has not been evaluated because of lack of detailed data sets describing exposure and food-borne disease incidence and some of the weighting factors employed in the model are arbitrarily derived. The tool provides an estimate of the most probable outcome, but it does not provide information about the level of confidence we have in that estimate, and the probable range of illnesses for different scenarios.

4.2. Ranking tool developed by EmZoo consortium of national institutes for human and animal health (the Netherlands)

In order to support the development of early warning and surveillance systems of emerging zoonoses, a general method to prioritize pathogens using a quantitative, stochastic multi-criteria model[15], parameterized for the Netherlands was presented (Havelaar et al., 2010).

A risk score was based on seven criteria, reflecting assessments of the epidemiology and impact of these pathogens on society (Figure 16). Criteria were weighed, based on the preferences of a panel of expert with a background in infectious disease control. The quantitative method is based on the well-established multi-criteria analysis (MCA) method.

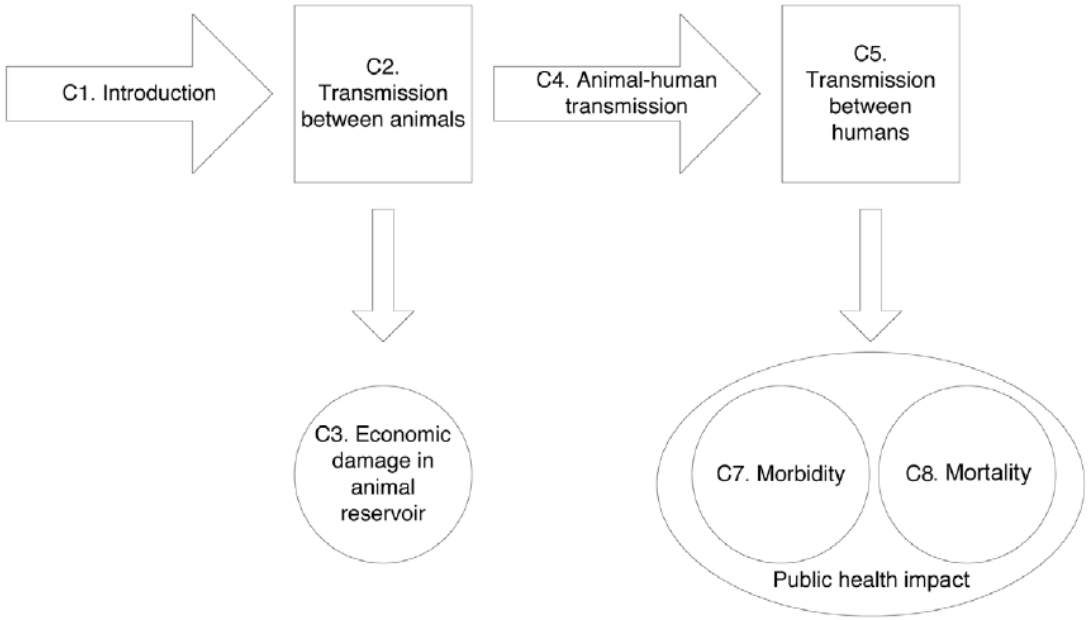


Figure 16: Flow chart of the pathway from introduction of a zoonotic pathogen to public health impact, represented by seven criteria (C1–C7) from which the risk to public health of emerging zoonoses was derived.

All criteria were scored on a natural scale, and were divided into 4-5 levels; often covering several orders of magnitude in terms of effects. Levels were assigned to pathogens based on published literature, and values were to reflect the situation in the Netherlands in 2010. For the ranking exercise, five groups of seven scenarios were generated. Each scenario represented a hypothetical zoonotic agent, by randomly choosing a level for each criterion, subject to certain constraints: scenarios were

[15] Available at http://ezips.rivm.nl

chosen as not to 'majorize' each other, and implausible scenarios (i.e. with low animal prevalence yet very high costs) were omitted. Then different scenarios were ranked by the judges' panel and check for consistency. Data-analysis was carried out by probabilistic inversion (Kurowicka et al., 2010). A linear model was applied, which combined the mean weights from the panel session with transformed values for all 86 zoonotic agents. These results were then normalized to a value between 0 and 1 by calculating the scores for the pathogen with the highest and lowest theoretical risk.

The advantages of the present tool are that the criteria use associated numerical scales, rather than non-informative *ad-hoc* scales. This forces explicit consideration of the available scientific evidence so to make the approach less arbitrary in assigning values to possible levels that a criterion can take, than a semi-quantitative approach. Further the number of criteria is limited, so it is relatively easy to develop validated databases in which pathogens are assigned to multiple possible values. Finally preference-based weights in the calculation of the pathogen scores were used. The weights are reflecting the preferences of a panel of decision makers, in this case professionals involved in infectious disease control. Using weights affects ranking to a lesser extent than introducing numerical scales.

4.3. Risk Ranking Tool for fresh produce from FDA

A semi-quantitative risk ranking tool[16] was created to identify priority pathogen-produce commodity combinations based on explicit data-driven risk criteria. To identify candidate pathogen-commodity pairs, a database was created that included all reports of outbreaks associated with fresh produce from the Annual Listing of Foodborne Disease Outbreaks compiled by the U.S. Centre for Disease Control and Prevention (CDC) from 1996 to 2006 (CDC, 1996 - 2006).

Additional information was sought from peer-reviewed literature and publicly accessible databases. Reliable epidemiological outbreak data were available for 51 pathogen-commodity pairs. The approach taken was top-down, considering epidemiological data from outbreaks associated with fresh produce.

Eight variables were used (see below), for each criterion, the data were grouped or categorized into four scoring bins, which were defined and assigned a numerical, ordinal score from 1 to 4.

- Epidemiological Link;
- Disease Multiplier;
- Hospitalization and Death Rates;
- Susceptible Population;
- Prevalence of Contamination;
- Relative Infectivity;
- Consumption;
- Shelf-Life/Growth Potential

A model was constructed so that the scores for each of the nine criteria could be combined to produce a single score for each pathogen-commodity pair for the purposes of risk ranking.

The result is an overall numerical score for each pathogen-commodity pair that is produced by first multiplying each criterion's score by its weight and then adding each of these nine values:

[16] http://foodrisk.org/default/assets/File/FDA_Risk_Ranking_Tool.mdb

$Rank = \Sigma Score_i \times Weight_i$

The purpose of this tool was to build a relational database of information relevant to ranking risks for pathogens and categories of fresh produce. The relational database is grounded in foodborne disease outbreak (epidemiological) data supplemented with information on disease severity, population susceptibility, prevalence of contamination, likelihood of pathogen growth, and human consumption patterns. The advantages of the present tool are its simplicity and transparency, the tool could be used to rapidly identify priority pathogen-commodity pairs based on risk criteria and user specified weighting preferences. Further, the tool is flexible, allowing the user to choose both the criteria and weights that reflect specific preferences. On the other side, this approach was not quantitative and lacked the resolution necessary to compare risks with similar likelihood of occurrence or overall public health impact.

4.4. iRisk: a RR framework prototype from IFT

The Institute of Food Technologists (IFT) developed a risk-ranking tool to enable comparison of microbiological and chemical hazards in foods (Newsome et al., 2009). The initial concept for the framework, which contributed to deliberations and subsequent tool development, included an expert elicitation framework and envisioned information from several sources: expert panel opinion, evidence databases, value models, assessment assumptions, and policy options.

The tool exists on two platforms: a web-based user interface, implemented in Visual Basic language and an Analytica model. The web-based platform allows users to explore the complex ranking hierarchy, view the current evidence, edit evidence, and update assumptions. The Analytica model, which complements the web-based prototype application, facilitates visualization of the logic flow and interrelationship of input and output variables. It also allows inspection and auditing of the calculations comprising the prototype.

The tool is a bottom-up system based on assumptions that incorporate expert opinion/insight with a number of exposure and hazard-related risk criteria variables, which are propagated forward with food intake data to produce risk-ranking determinations.

Two main risk criteria modules were developed: exposure (farm-to-fork) and hazard characterization (health impacts). The exposure module contains questions grouped into three food system stages: primary production; processing; and distribution, storage, retail, foodservice, and home.

For a specific hazard–food combination the prototype can produce a single metric: a final risk value expressed as annual pseudo-disability adjusted life years (pDALY).

The pDALY concept is modified slightly from the general use of DALY (IOM 2005) to allow for a semi-quantitative characterization of the disease burden of health impacts. The pDALY approach allows for the characterization of a standard health outcome (such as mild illness) without further definition of the exact impact. Users create pDALY templates by assigning a fraction of cases to appropriate health impacts, such as mild, moderate, or severe pathogen, and short-term, adult, elderly, or childhood mortality.

4.5. Foodborne Illness Risk Ranking Model (FIRRM) from Food Safety Research Consortium

The Foodborne Illness Risk Ranking Model (FIRRM)[17] is a decision tool used to examine the public health burden of foodborne illnesses due to microbiological hazards from specific food commodities. Users can rank pathogen-food combinations by different measures of annual disease burden, including estimated cases, hospitalizations, and deaths, as well as by estimated costs of illness and QALY loss. FIRRM is an open model designed in Analytica, a Monte Carlo simulation environment with a visual

[17] www.thefsrc.org/firrm.htm

interface built on functional influence diagrams. Due to the visual programming nature of Analytica, much of the model documentation is built directly into the model itself (Batz et al., 2004).

FIRRM focuses solely on microbiological foodborne hazards. FIRRM uses a "top-down" epidemiological approach rather than a "bottom-up" microbiological approach to estimating illnesses. To estimate illnesses due to pathogen-food combinations, FIRRM uses surveillance data on pathogen illnesses and then traces these illnesses back to food origin. This is distinguished from conventional risk-assessment approaches, which use food contamination data, predictive microbiology, and consumption patterns to estimate illnesses. A top-down approach ensures identical methodology across pathogen-food combinations; individual risk assessments are not nearly so directly comparable. Although the top-down approach is preferable for a big-picture comparison of foodborne risks, it is inadequate to isolate the causes of illness along the farm-to-table pathway.

FIRRM is composed of three major modules: incidence, valuation of health impacts, and food attribution. In the first module, the annual number of cases, hospitalizations, and deaths from foodborne pathogens are estimated from public health surveillance data. In the second module, the economic cost and QALY loss associated with a single case of illness are computed for individual pathogens. The third module consists of pathogen-specific food attribution percentages; illnesses from each pathogen are attributed, by percentage, to some set of food vehicles.

The model includes two approaches and data sources: i) outbreak data, which are easily accessible but can offer a distorting picture of risks as cases not tied to an outbreak are ignored and ii) an expert elicitation, which develops attributions based on judgments of food safety experts and may, to some extent, depend on outbreak data.

This model shows some limitations because it is applicable to ranking risks by major commodity group (for example, comparing fresh produce to beef), but epidemiological attribution data currently lacks resolution when attempting to compare, or rank, specific individual food items (such as different types of fresh produce) to one another. This model also does not take into account aspects that might tangentially influence risk such as product shelf-life, likelihood of pathogen contamination, or relative infectivity.

4.6. Food Safety Universe Database from Ontario Min. of Agriculture and Foods

A method of systematically ranking food-safety-risks is needed to help prioritize the allocation of food safety resources. This document describes a Food Safety Universe Database (FSUDB)[18], developed by the Ontario Ministry of Agriculture and Food (OMAF) that may be used as a semi-quantitative tool to rank food-safety-risks.

The FSUDB may be used to assess and rank food-safety-risks across various foods and hazards, at various points along the food-chain. It assesses risk from a "societal" point of view, as influenced by differences in consumption patterns of various foods. It also assesses risk from a "per-serving" point-of-view, as influenced by differences in contamination rates of various foods. Furthermore, the FSUDB assesses risks of accidental contamination, and risks of deliberate contamination from acts of sabotage or terrorism (McNab, 2003).

Each food-hazard location- of-entry combination presents a different likelihood and consequence (risk) of harm. In theory, every possible combination of food-hazard-location-of-entry could be defined and assessed in terms of its likelihood and consequence. This theoretical complete data set of all possible combinations could be thought of as the "universe" of food safety data. Therefore, the database designed to capture and analyze these data was named the Food Safety Universe Database (FSUDB).

[18] www.ontla.on.ca/library/repository/mon/7000/10318750.pdf

The specific combination of food, hazards and location of hazard-entry are captured in each database record. Then, ordinal scores of 1 to 10 are captured to describe the probability (or likelihood) and impact (or consequence) components of the food-safety-risk. Scores are assigned for the risk believed to be presented to consumers by the specific hazard, entering the specific food, at the location along the food-chain described by each specific record in the database. Table 13 summarizes the type of data captured in the database.

Table 13: Summary of FSUDB Data Capture and Risk Scoring

Food-Hazard-Location Data: Food: e.g. meat, chicken, fresh (i.e. 3 levels of detail) Hazard: e .g. biological, bacteria, pathogenic S*almonella* Location: e.g. production (broiler chicken barns) (i.e. location along food-chain that contamination occurred)
Probability Sub-Scores: Pa) scale of consumption score (based on amount consumed per person per day) 1 - 10 Pb) of (Pa), the "proportion" contaminated with this hazard at this location; modified 1-10 Pc) of (Pb), the "proportion" that lead to consumer exposure to that hazard; 1 - 10
Impact Sub-Scores: Ia) of those exposed (Pc), the "proportion" of consumers that become ill 1 – 10 (based on toxicity of chemicals, but inversely related in infective dose of organisms) Ib) the severity of illness among consumers who become ill 1 -10 (based on acute and chronic health impacts) Ic) difficulty to reduce or limit impact 1 - 10
Overall Risk-score: (for this food-hazard-location combination) Risk "score" = Pa x Pb x Pc x Ia x Ib x Ic = range from 1 to 1,000,000

Table 14 summarizes the bases on which probability and impact scores are assigned to each food-hazard-location combination captured in the FSUDB.

Table 14: Summary of Scoring Principles

Sub-Score	Type of Information Used
Probability "Pa" or "6a" Scale of Consumption	Based on amount consumed of the respective food per person per day using data from Canadian and American studies; The greater the consumption, the higher the score
Probability "Pbi" or "6bi" Accidental Contamination	Based on frequency of chemical use and frequency of contamination with biological hazards. The greater the frequency and amounts, the higher the score
Probability "Pbii" or "6bii" Deliberate Contamination	Based on expert opinion of the sabotage appeal, influenced by logistical ease and expected terror; The greater the sabotage appeal, the higher the score
Probability "Pc" or "6c" Consumer Exposure	For biological hazards, based on likelihood of organism surviving to consumption, given the location of its introduction relative to inactivation steps (e.g. thermal or chemical treatments). For chemical hazards, based on processing steps that would reduce concentration, chemical half-life, pre-harvest intervals, drug withdrawal periods. The greater the likelihood of exposure, the higher the score.
Impact "Ia" or "7a" Consumer Illness	For biological hazards related to the amount relative to the infective-dose. For chemical hazards, related to the amount of exposure relative to maximum residue limits (MRLs) The greater the amount relative to infective-dose or MRL, the higher the score.
Impact "Ib" or "7b" Severity of Illness	For biological hazards, based on data of average health costs per case including treatment, hospitalization, lost days and statistical values of life. For chemical hazards based in toxicity including acute and chronic impacts The greater the health impacts, the higher the score.
Impact "Ic" or "7c" Difficulty to Limit Impact	Based on the difficulty to detect contamination, the distribution of the food, difficulty to determine and eliminate the source, the amount of secondary spread and indirect economic impacts. The greater the difficulty to limit impact, the higher the score.
Overall risk-score	Pa x Pb x Pc x Ia x Ib x Ic

4.7. A Multi-Factorial Risk Prioritization Framework for Food-borne Pathogens

The Multi-Factorial Risk Prioritization Framework considers four factors that may be important to risk managers: public health, consumer risk perceptions and acceptance, market-level impacts, and social sensitivity. Canadian case studies are presented for six pathogen-food combinations: *Campylobacter* spp. in chicken; *Salmonella* spp. in chicken and spinach; *Escherichia coli* O157 in spinach and beef; and *Listeria monocytogenes* in ready-to-eat meats (Ruzante et al., 2010). Risk ranking is facilitated through the development of a knowledge database presented in the format of info cards and the use of multi-criteria decision analysis (MCDA) to aggregate the four factors. The framework is based on the systematic organization and analysis of data on these multiple factors. The basic building block of the information structure is a three-dimensional cube based on pathogen-food-factor relationships. Each cell of the cube has an information card associated with it and data from the cube can be aggregated along different dimensions (Henson et al., 2007).

4.8. Disease burden of foodborne pathogens

Ranking of foodborne pathogens in the Netherlands was performed using DALYs as the risk metrics (Havelaar et al., 2012a). The model estimates the incidence and duration of acute disease by fourteen pathogens, as well as the incidence and duration of sequelae and fatalities. Disability weights were elicited in a specific study, using a representative panel of lay persons from the Netherlands (Haagsma et al., 2008). DALYs are calculated in the Analytica software. Results are combined with data from an expert elicitation to attribute cases and DALYs to major pathways and food groups (Havelaar et al., 2008).

The approach taken in the development of the tool is top-down, based on surveillance data, cohort studies and registries in the Netherlands, as well as data from the international literature. A large set of data were integrated in a single, consistent framework. The model uses parameter values reflecting the state of public health and health care in the Netherlands. Ideally, specific data would be included when extrapolating to other countries, but this is a demanding task. Results are assumed to be appropriate for countries with a similar health infrastructure as the Netherlands. ECDC is currently developing the "Burden of Communicable Diseases in Europe" project to provide national estimates of the burden of disease of a large number of pathogens, including food-and waterborne diseases (see 4.10.1.2 for further details). On a global scale, WHO (Foodborne Epidemiology Reference Group) is aiming to estimate specifically the global burden of foodborne disease.

The criteria and variables considered in the tool are many and include:

- Incidence and duration of acute disease
- Incidence and duration of sequelae
- Disability weights
- Incidence of fatal cases
- Idealised life expectancy
- Attribution to major pathways (food, environment, human-human contact, animal-human contact and travel)
- Attribution to 11 food groups within the food pathway.

Results are presented as DALYs at population level as well as at individual level, see Figure 17.

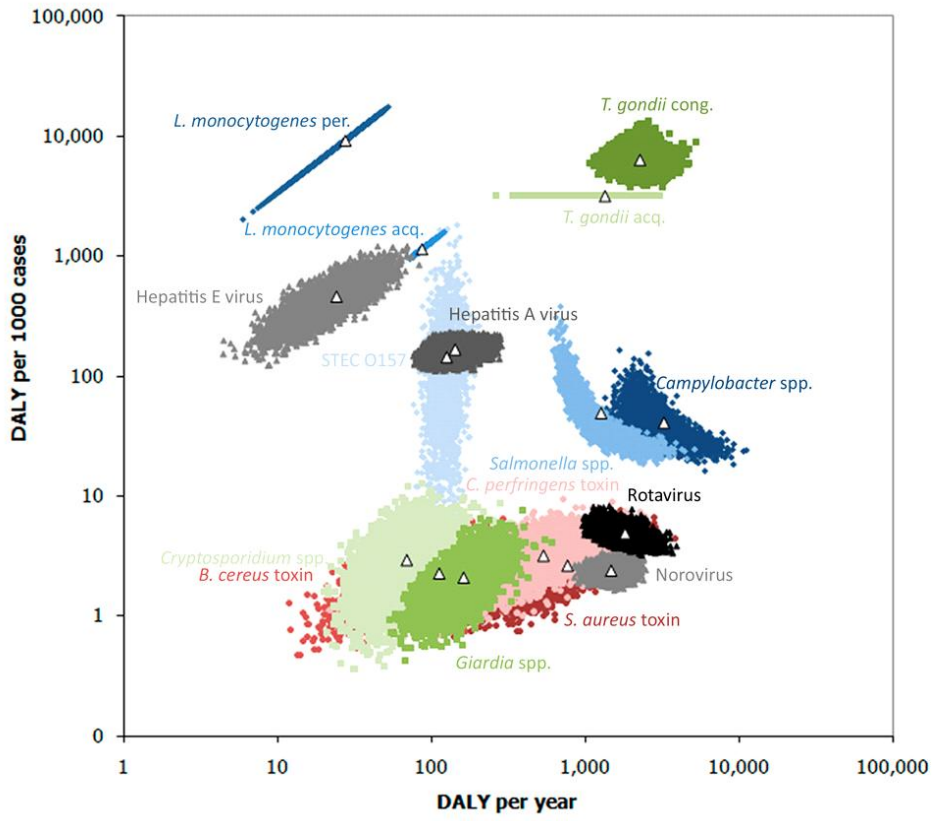


Figure 17: Ranking of pathogens by burden (undiscounted) at population and individual level (Scatter plot of 10,000 samples per pathogen from the joint uncertainty distributions of DALY per year in the Netherlands, 2009 and DALY per 1,000 cases. Data reflect transmission by all pathways. Note both axis are on a logarithmic scale (Havelaar et al., 2012a).

Results after attribution are available at different levels of aggregation, primarily by major transmission pathways and by food group, see Figure 18.

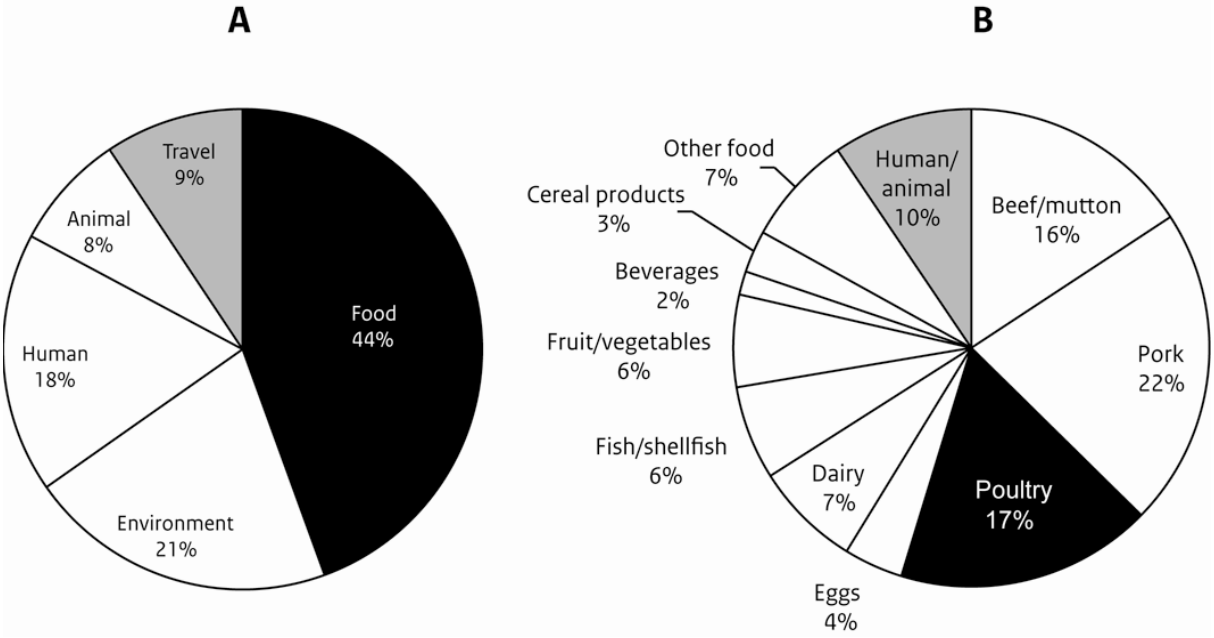


Figure 18: Breakdown of total disease burden (undiscounted) of fourteen pathogens in the Netherlands, 2009 (YLD: Years Lived with Disability; YLL: Years of Life Lost. Figure reproduced from Havelaar et al., in press).

4.9. sQMRA tool

The swift Quantitative Microbiological Risk Assessment (sQMRA) tool is a simplified QMRA model especially aimed at comparing the risk of pathogen–food product combinations. Like in full-scale QMRA, the model applies a top-down approach by tracking pathogen prevalence and numbers through the food chain, which in this case starts at retail and ends with the number of cases of human illness. The model in its currently available stage is deterministic and includes cross-contamination and preparation (heating) in the kitchen and a dose–response relationship (Evers and Chardon, 2010) The paper is downloadable from http://foodrisk.org/exclusives/sQMRA .

A second version of the tool is ready and a paper will be submitted this year. Main changes are the inclusion of variability (optional), growth/inactivation during storage, D/z-inactivation modelling (optional), two dose response models and expansion of relative risk references.

The sQMRA – tool is implemented in Microsoft Excel. Special attention is given to make the sQMRA tool insightful, for educational purposes. The general setup of the sQMRA tool consists of consecutive questions for values of each of the 11 parameters, always followed by intermediate model output broken down into categories of contamination, cross-contamination and preparation. In a separate sheet, model input and output are summarized and exposures as well as cases are attributed to the distinguished categories. As a relative risk measure, intermediate and final model outputs are always compared with results from a full-scale QMRA of *Campylobacter* on chicken fillet.

The following 11 questions have to be answered:

- Consumption data
  - How many portions are consumed in the population per consumption period?
  - What is the average size of one portion?

- Retail
  - What percentage of the portions is contaminated at retail?
  - What is the average concentration of the pathogen in contaminated portions?
- Kitchen – cross contamination
  - Given contaminated portions: what percentage of the portions contaminate the environment?
  - Given cross-contamination: what percentage of the CFU on a portion will contaminate the environment?
  - Given cross-contamination: what percentage of the CFU in the environment ends up being ingested?
- Kitchen – preparation
  - What percentage of the portions is prepared done, half-done or raw?
  - What percentage of the CFU on a portion will survive for each of these categories?
- Infection and illness
  - At which dose (no. of CFU) per portion will half of the exposed population get infected?
  - What percentage of infected people will get ill?

The necessary data for the 11 questions will partly be data that are country-specific, possibly vary per year and have to be obtained from national authorities (consumption and retail data). The other part (kitchen-cross contamination/preparation, infection and illness) are data from scientific literature.

The calculations are simple and consist mainly of simple multiplications and divisions, with the exception of the dose-response relationship. Being a simplified model, the relative (and not the absolute) risk, compared with *Campylobacter*-chicken filet, is considered the most important model output, which can be compared between pathogen-food product combinations. It is estimated at a number of points along the food chain.

By implementing different scenarios (i.e. sets of parameter values), the model can be used for different risk ranking scenarios: comparing multiple pathogens in one food, comparing one pathogen in multiple foods or comparing multiple pathogens in multiple foods.

4.10. Risk ranking tools developed by other EU and international agencies

4.10.1. ECDC

4.10.1.1. Operational guidance on rapid risk assessment methodology

This guidance document develops a methodology for rapid risk assessments undertaken in the initial stages of an event or incident of potential public health concern. It describes an operational tool to facilitate rapid risk assessments for communicable disease incidents at both Member State and European level. The tool comprises information tables and risk-ranking algorithms to give an estimate of risk posed by a threat (ECDC (European Centre for Disease Prevention and Control), 2011; Kretzschmar M et al., 2012).

4.10.1.2. Burden of Communicable Diseases in Europe (BCoDE) project

The Burden of Communicable Diseases in Europe (BCoDE) is a project funded by an ECDC grant, implemented by a European Consortium lead by the Dutch National Institute for Public Health and the Environment (RIVM) including both academic centres and national health institutes with experts from all around Europe. The aim is to estimate the burden of communicable diseases applying composite health measures (DALYs: Disability Adjusted Life Years) in order to summarize the overall burden in one single metric and therefore to compare the relative burden of each communicable disease.

In the first months the project estimated DALYs for measles, hepatitis B, influenza and salmonellosis and reviewed the methodology. Later, estimates for all other communicable diseases of the four

countries included in the field test study will become available. Disease reports outlining the methodological choices, the data sources and the variables selected (e.g. multiplication factors adjusting for under-estimation, disability weights) are being developed for presentation at a workshop involving Member States. Based on the results from the field test study, a toolkit will be developed and distributed to interested EU Member States to facilitate calculation of their national burden of disease.

One of the important outcomes of the study, beyond generation of disease burden estimates, will be the identification of gaps in data availability and quality, proposals for ways to improve in these areas and improvement of methodology to adjust for underreporting in notification data. Moreover, once the baseline DALY estimates will be computed, it will be possible to expand to dynamic studies and develop sensitivity analysis depending on different variables (e.g. risk factors, interventions to name some) and to develop forecasting scenarios. Up-to-date information can be found on the ECDC website:
http://ecdc.europa.eu/en/healthtopics/burden_of_communicable_diseases/project/pages/project.aspx.

4.10.2. WHO

4.10.2.1. Initiative to estimate the Global Burden of Foodborne Diseases

The WHO Department of Food Safety and Zoonoses (FOS) launched an Initiative to Estimate the Global Burden of Foodborne Disease in collaboration with multiple partners in October 2006 with the Foodborne Disease Burden Epidemiology Reference Group (FERG) as its advisory body. The FERG is an independent expert group charged with assembling estimates of the global burden of foodborne disease by 2013 (according to age, sex and region) and operates through several task forces. Three task forces assemble burden estimates in the areas of enteric diseases, parasitic diseases and diseases caused by the ingestion of chemicals and toxins through systematic reviews; a fourth task force aims to attribute the burden of diseases to food and specific food sources; and a fifth task force focuses on supporting countries with tools and capacity building to estimate the national foodborne disease burden. A recently established sixth task force is to convert results of (a) the global epidemiological reviews for mortality, morbidity and disability in each of the major foodborne diseases and (b) epidemiological data resulting from the FERG country studies into DALYs. This task force will also develop tools for countries to estimate the national burden of foodborne disease. More information can be found at: http://www.who.int/foodsafety/foodborne_disease/ferg/en/index.html.

4.11. Conclusions from the review of the available risk ranking tools: the need for developing a risk ranking toolbox for EFSA

Nine available risk ranking tools were identified and reviewed (Table 15). Some of them are general and can be used to various hazards-foods combination while some others are specific to certain food categories. They differ in their degree of complexity, level of quantification, and approach to model construction. Various methodologies were applied in each tool using different risk metrics, ranking approaches, model types, variables and data integration methods.

Among the tools adopting a bottom-up approach, the majority of them were based on a semi-quantitative structure of the model (Risk Ranger, iRisk by IFT, Food Safety Universe Database), and expressing the risk with numerical scores. Only iRisk used a different metrics based on annual pseudo-disability adjusted life years (pDALY). The example of risk ranking tool with a quantitative structure was the stochastic multi-criteria model developed by the EmZoo consortium.

Five tools were based on a top-down approach (the Risk Ranking Tool for fresh produce from FDA, the Foodborne Illness Risk Ranking Model (FIRRM), the Multi-Factorial Risk Prioritization Framework for foodborne pathogens, the Disease burden for food pathogens, the swift sQMRA tool). Among these, DALY metrics was used in the Multifactorial Risk Prioritization, in the FIRRM model and in the Disease Burden for food pathogens developed in the Netherlands. The latter two examples

was characterised by a quantitative model structure, as the swift sQMRA tool which also differently adopted the expression of relative risk as metrics.

As in the case of all risk ranking models the appropriateness of each of the available tools to answer a risk ranking question depends on the purpose of risk ranking and the availability of the data. Regarding future risk ranking exercise on biological hazards, the possibility to use some of the presented available tools with proper adjustments to answer specific questions could be considered. The selection of an available risk ranking tool for EFSA opinions should be based on whether all appropriate variables have been included in the model, whether the data underlying is reliable, how uncertainty and variability is managed, how probabilities are inferred and the degree on which the results fit the purpose of the risk ranking. However, none of the available tools could be recommended to be used as a general risk ranking tool for biological hazards due to the differences in purpose and data availability of the risk ranking questions received by the Panel.

The conceptual risk ranking framework presented in this opinion (Figure 10) can be used as the basis for the development of a risk ranking toolbox. Such a toolbox should be generic and allow the adoption of different risk ranking methodologies in order to fit the variety of risk ranking purposes of the received mandates. The toolbox should be based on different modules that correspond to the nine stages of the framework with each module providing different option on risk metrics, ranking approaches, model types, variables and data integration methods. The above structure will allow the design and construction of risk ranking models targeted to the purpose of each mandate. Developing such a tool and getting to the point of being able to apply it will be complex and time-consuming but it will significantly increase consistency and transparency related to risk ranking.

Table 15: Table about comparison of risk ranking tool developed worldwide

Reference to the text	Tool	What was ranked	Metrics	Approach	Model structure	Model variables	Data collection	Data integration
4.1	Risk Ranger from Australian Food Safety Centre	Food product/hazard combination	Numerical scores related to risks	bottom-up	Semi-quantitative	• Hazard severity • Susceptibility of the consumer • Frequency of consumption • Proportion of population consuming • Size of population of interest • Proportion of product contaminated • Effect of process • potential for recontamination • increase from level at processing to reach an infectious or toxic dose for the average consumer • effectiveness of the post-processing control system • Effect of preparation for meal	Qualitative and quantitative inputs from the users	Tabulation
4.2	Ranking tool developed by EmZoo consortium	Emerging foodborne zoonosis	Normalized scores related to emerging zoonotic pathogens	bottom-up	Quantitative (stochastic multi-criteria model)	• Probability of introduction into the Netherlands • Transmission in animal reservoirs • Economic damage in animal reservoirs • Animal-human transmission • Transmission between humans • Morbidity (disability weight) • Mortality (case-fatality ratio)	published literature internet sources of public health and veterinary organizations expert opinions	Normalised MCA score

Reference to the text	Tool	What was ranked	Metrics	Approach	Model structure	Model variables	Data collection	Data integration
4.3	Risk Ranking Tool for fresh produce from FDA	Pathogens/fresh produce categories	Numerical scores of pathogen-commodity pairs	Top-down	semi-quantitative	• Epidemiological Link; • Disease Multiplier; • Hospitalization and Death Rates; • Susceptible Population; • Prevalence of Contamination; • Relative Infectivity; • Consumption; • Shelf-Life/Growth Potential	Foodborne disease outbreak (epidemiological) data	Tabulation
4.4	iRisk: a RR framework prototype from IFT	Hazards/food combination (both microbiological and chemical hazards)	Annual pseudo-disability adjusted life years (pDALY)	Bottom-up	semi-quantitative	User inputs about hazard prevalence, concentration, and changes in concentration at each of the 3 food system stages: 1- primary production; 2- processing; 3- distribution, storage, retail, foodservice, and home	Expert elicitation framework and envisioned information from several sources: expert panel opinion, evidence databases, value models, assessment assumptions, and policy options CSFII (Continuing Survey of Food Intakes by Individuals) data	Tabulation
4.5	Foodborne Illness Risk Ranking Model (FIRRM) from Food Safety Research Consortium	pathogen-food combinations	Costs of illness and QALY loss	Top down	quantitative	Incidence, valuation of health impacts, and food attribution	Surveillance data on pathogen illnesses Outbreak data Expert elicitation	Tabulation

Reference to the text	Tool	What was ranked	Metrics	Approach	Model structure	Model variables	Data collection	Data integration
4.6	Food Safety Universe Database from Ontario Min. of Agriculture and Foods	Pathogen-food combinations	Risk scores	bottom-up	Semi-quantitative	• Scale of Consumption • Accidental or deliberate Contamination • Consumer Exposure • Severity of Illness • Difficulty to Limit Impact	• Data from Canadian and American studies about food consumption • Expert opinion	Tabulation
4.7	Multi-Factorial Risk Prioritization Framework for foodborne pathogens	Pathogen-food combination	DALY and cost of illness	Top down	Semi-quantitative	• public health impact • market impact, • consumer risk acceptance and perception, • social sensitivity	• Data from Public Health Agency of Canada • data from the Ontario Ministry of Agriculture and Food. • Canadian studies	Tabulation, MCDA
4.8	Disease burden for food pathogens	foodborne pathogens in the Netherlands	DALY	Top down	quantitative	• Incidence and duration of acute disease • Incidence and duration of sequelae • Disability weights • Incidence of fatal cases • Idealised life expectancy • Attribution to major pathways (food, environment, human-human contact, animal-human contact and travel) • Attribution to 11 food groups within the food pathway	• Surveillance data • Cohort studies in the Netherlands, international literature • Expert opinion	Quantification of DALYs

Reference to the text	Tool	What was ranked	Metrics	Approach	Model structure	Model variables	Data collection	Data integration
4.9	sQMRA tool	Pathogen–food product combinations	Relative risk	Top-down	quantitative	• Portions consumed /time • % contaminated portions at retail • Contamination load at retail • % Kitchen cross contamination • % of done, raw portions • % surviving CFU on portions • Dose per portion for infecting 50% of exposed population • % of infected got ill	Data from national authorities Scientific literature	Quantification of relative risk

CONCLUSIONS AND RECOMMENDATIONS

Conclusions

General conclusions:

- Risk ranking has been recognized as the proper starting point for risk-based priority setting and resource allocation.
- Due to its significance in priority setting risk ranking has been established as an important component of risk management frameworks.

ToR 1. To reflect on the lessons and experiences from risk ranking exercises undertaken by the BIOHAZ Panel, in particular describing successful approaches and challenges

- Fourteen opinions of the BIOHAZ Panel in which a risk ranking was used were reviewed as examples. Based on this review it was concluded that:
  - The risk ranking purposes in most of these opinions were different (e.g. single hazard in single food, multiple hazards in multiple foods, single hazard in different countries).
  - The risk ranking exercises differed widely in methodology emphasising the fact that models are tailored to fit for purpose.
  - The risks were expressed using a variety of risk metrics (e.g. probability of illness per annum or per serving, incidence, QALY, DALY).
  - Most risk ranking models were qualitative using decision trees for data integration. In only two opinions a fully quantitative model was developed.
  - There is no universal methodology for risk ranking as each model has to be specifically tailored to each specific purpose, data availability and time frame.
  - The harmonization in model structure and presentation of results will increase consistency and transparency of the risk ranking models and remains an important challenge.
- In order to ensure harmonisation a conceptual risk ranking framework comprising nine separate stages has been developed in this opinion.

ToR 2. To suggest risk ranking tools related to biological hazards to be used in risk assessments

- Nine risk ranking tools were identified and reviewed. They differed in their degree of complexity, level of quantification, and approach to model construction. Various methodologies were applied in each tool using different risk metrics, ranking approaches, model types, variables and data integration methods.
- None of the available tools could be recommended as universal use risk ranking tool for biological hazards due to the differences in purpose and data availability of the risk ranking exercises usually requested to the BIOHAZ Panel.
- For future risk ranking exercises on biological hazards, the possibility to use some of the available tools with proper adjustments to answer specific questions could be investigated.

ToR 3. To analyse strengths and weaknesses of different approaches to risk ranking on biological hazards

- The identification of successful risk ranking approaches and tools among those examined in this opinion requires a comprehensive review of each model taking into account its purpose, the available data and the time frame of each mandate. This is a very time consuming process which was not feasible under the timeline of this mandate.

- Overall, the strengths and weaknesses of a risk ranking method depend on whether all appropriate variables have been included in the model, whether the data underlying is reliable, how uncertainty and variability are managed, how probabilities are inferred and the degree on which the results fit the purpose of the risk ranking.

Recommendations

- The risk ranking exercise should take a structured approach and be documented as fully as possible. It is imperative that all processes undertaken to produce the final output are fully documented in a consistent and transparent way such that the whole risk ranking process is reproducible.

- The conceptual risk ranking framework presented in this opinion should be used in future risk ranking exercises in order to increase consistency and transparency.

- The proposed framework provides the ability of adopting the appropriate risk ranking methodology by selecting different options at each stage. The appropriate option should be selected based on the risk ranking purpose and the available data.

- Whenever possible quantitative risk ranking approaches are preferable.

- The given time frame should be in correspondence with the requirements of the risk ranking exercise.

- All the components of the risk ranking models should be clearly defined, the reasons for the selection of each component and how the final conclusions were reached should be described.

- The interaction between the risk managers and the risk assessors in the definition of the risk ranking purpose and the communication of the risk ranking results should be encouraged.

- The conceptual framework proposed in this opinion could be translated into a document with more details on the risk ranking methodology, providing tools for future risk ranking exercises. This could be useful for future opinions.

- The development of a risk ranking toolbox based on the proposed framework should be investigated, since such a toolbox would support the construction of consistent and transparent risk ranking models.

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APPENDIX

A. EXAMPLES OF AVAILABLE SOFTWARE TOOLS ON PREDICTIVE MICROBIOLOGY

- **Pathogen Modeling Program (PMP)**: The PMP is available for use free of charge (http://portal.arserrc.gov/) and, with more than 5000 downloads per year, it is probably the most widely used predictive microbiology application software. PMP has been available for close to 20 years and it is regularly being updated and expanded. The present version includes more than 40 models for different bacterial pathogens. The software allows growth or inactivation of pathogens to be predicted for different combinations of constant temperature, pH, NaCl/a_w and, in some cases, other conditions such as organic acid type and concentration, atmosphere, or nitrite. In addition, PMP includes models that predict the effect of cooling temperature profiles on growth of *C. botulinum* and *C. perfringens* after cooking. Predictions can be exported and the software contains references to studies from which the models were developed. In 2007 PMP was integrated with the Predictive Microbiology Information Portal (PMIP).

- **Combined database on predictive microbiology information (ComBase)**: ComBase (www.combase.cc) is a web-based resource for quantitative and predictive food microbiology. Its main components are: a database of observed microbial responses to a variety of food-related environments and a collection of relevant predictive models. ComBase is managed by the ComBase Consortium consisting of the Institute of Food Research (IFR) in the United Kingdom, the USDA Agricultural Research Service (USDA-ARS) in the United States, and the University of Tasmania Food Safety Centre (FSC) in Australia. The ComBase predictive models are a collection of software tools based on ComBase data to predict the growth or inactivation of microorganisms. Currently available predictive tools include the following online applications:

  - *ComBase Predictor*, a set of 23 growth models and 6 thermal death models for predicting the response of many important food-borne pathogenic and spoilage microorganisms to key environmental factors. A Microsoft Excel version of this web application can also be found in the ComBase Excel Demo provided in the website.

  - *Perfringens Predictor*, an application specially designed for predicting the growth of *C. perfringens* during the cooling of cooked meats. A Microsoft Excel AddIn version of the program can also be found in the Downloads section of the web site.

- **Sym'previus**: Sym'previus (www.symprevius.org) is an extensive decision support system developed in France that includes a database and simulation tools for growth, survival, inactivation and growth/no growth interface of pathogenic bacteria and some spoilage microorganisms. Evaluation of consumer exposure can be done by means of a probabilistic module. Information from Sym'previus is available on a commercial basis through contact centres as indicated on the homepage cited above.

- **Seafood Spoilage and Safety Predictor (SSSP)**: The SSSP software has been developed by Danish Technical University (http://sssp.dtuaqua.dk/HTML_Pages/Help/English/Index.htm) to facilitate the practical use of mathematical models to predict shelf life as well as growth of spoilage and pathogenic bacteria in seafood. The SSSP v. 3.1 released August 2009 includes: four product-specific relative rate of spoilage (RRS) models, three generic RRS models, four product-specific microbial spoilage models, a generic model to predict microbial growth and shelf-life, modules to compare predictions from SSSP with users own data of shelf-life or growth of bacteria, models to predict growth and histamine formation by *M. psychrotolerans* and *M. morganii*, growth and growth boundary model for *L. monocytogenes* and a model to predict the simultaneous growth of *L. monocytogenes* and lactic acid bacteria in lightly preserved seafood.

- **Microbial Responses Viewer (MRV):** The MRV (http://cbnfri.dc.affrc.go.jp/) is a new database consisting of microbial growth/no growth data of nineteen different microorganisms derived from ComBase. The specific growth rate of each microorganism is modelled as a function of temperature, pH and a_w using a Poisson log-linear model, which is a family of generalized linear models (GLMs). The specific growth rate is illustrated using a two-dimensional contour plot with growth/no growth data. The software allows the user to rapidly view growth/no growth contour plots superimposed by actual ComBase data. Contours of any two of three variables (temperature, pH and a_w) can be visualized, while the third is held constant.

- **Refrigeration index (RI) calculator**: The RI calculator was developed by Meat & Livestock Australia Limited (www.foodsafetycentre.com.au/refrigerationindex.php). It predicts the expected growth of *E. coli* on meat from temperature and other data. The model has values for pH, a_w and lactate concentration, which, in addition to temperature, all affect the growth rate of *E. coli*. The current RI model allows for the user to enter data on temperatures of the product over time. Choosing the type of product sets the other parameters.

- **Opti-Form@ Listeria control model 2007 (PURAC)**: This software predicts the effect of organic acids, temperature, pH and moisture on growth of *L. monocytogenes* in meat products. It can be requested (www.purac.com/purac_com/d9ed26800a03c246d4e0ff0f6b74dc1b.php) from the PURAC company.

- **Websim-MILQ**: WebSim Milq is a web implementation of predictive models designed to optimise heat treatment processes in dairy companies. Information about the software can be obtained (http://websim.milq.org/websim/milq/LoginForm.aspx) through NIZO Food Research in the Netherlands.

- **Shelf Stability Predictor**: The software has been developed by the Center for Meat Process Validation at the University of Wisconsin - Madison (http://meathaccp.wisc.edu/ST_calc.html/) and provides a set of models for predicting the growth of *L. monocytogenes* and *S. aureus* on ready-to-eat meat products as a function of pH and a_w.

- **Temperature History Evaluation for Raw Meat (THERM)**: Developed by the Center for Meat Process Validation at the University of Wisconsin – Madison (http://meathaccp.wisc.edu/). THERM is an online tool designed for evaluating the safety of meat or poultry at temperatures between 50°F and 115°F (10°C to 46°C).

- **Process Lethality Determination Spreadsheet**: Developed by AMI Foundation, USA (www.amif.org/ht/d/sp/i/26870/pid/26870). This tool provides processors with a science-based validation tool that can be used to demonstrate the effectiveness of a specific heat process to destroy a microorganism of concern. Specifically, the interactive model allows the user to input actual in-process data from a given cook cycle and determine if the process achieves the required log reduction for the microorganism of concern. The goal is to define or map the heating and cooling profile of the product by observing the temperature characteristics of the product during heating and cooling.

GLOSSARY AND ABBREVIATIONS[19,20]

- **Benefit:** A function of the probability of positive welfare consequences and the magnitude of those consequences, following exposure to a particular factor or exposure scenario, in a given population

- **DALY**: Disability Adjusted Life Years

- **Decision tree model:** The model translation of a decision tree or risk pathway diagram. Usually applied as unidirectional evaluation of a sequence of alternative (stochastic) events that contribute to the final outcome of the tree (end-point calculation).

- **Deterministic model:** A model (or system) in which no random process is involved in the derivation of future states of the model. Deterministic models thus produce identical outputs (results) for a given unchanged set of input values (starting conditions). (Wikipedia)

- **Expert elicitation**: A multi-disciplinary survey of expert opinion that can inform decision making by characterising uncertainty and filling data gaps where traditional scientific research is not possible or data are not yet accessible or available.

- **Expert opinion** (judgement): The views on particular issues of those who have experience on farming procedures, such as veterinarians in practice or practising farmers, particularly for welfare consequences.

- **Exposure assessment**: The qualitative or quantitative evaluation of the level, duration, and variability of exposure to the identified factors.

- **Monte Carlo simulation** Iterative technique applies in modelling (with Markov chain Monte Carlo or MCMC sampling as a common example) to estimate the range of possible output (i.e. a distribution) that involves repeatedly drawing random numbers from input (parameter) probability distributions. The technique usually is applied in stochastic models in which the exact parameterisation cannot be taken for granted (substantial uncertainty in input values).

- **Qualitative Risk Assessment:** An assessment that generates an estimate of categorical nature or based on an ordinal scoring system. The outcome of such an assessment is a classification of output into descriptive categories.

- **Quantitative Risk Assessment:** An assessment that generates an estimate of a numerical nature directly tied to a measurement or calculation. Depending on the type of model tool used, an indication of the associated uncertainties - expressed either as extreme values, → confidence intervals or → prediction intervals are needed.

- **Semi-quantitative or qualitative risk scale:** probabilities of an event are assessed and described textually on a scale from negligible, indicating that the probability of an event or the estimated risk cannot be differentiated from zero (and in practical terms can be ignored) to extremely high.

- **Semi-quantitative risk assessment**: A risk assessment based on data which, while forming an adequate basis for numerical risk estimates, nonetheless, when conditioned by prior expert

[19] Most of the definitions here reported are quoted by EFSA Panel on Animal Health and Welfare (AHAW) 2011. Guidance on risk assessment for animal welfare. EFSA Journal 2012;10(1):2513, 30 pp.

[20] Recently the Scientific Committee of the European Food Safety Authority (EFSA) reviewed the use of risk assessment terminology within its Scientific Panels and recommended to improve the clarity, consistency and where possible the harmonization of risk assessment terminology within and across EFSA's scientific opinions (EFSA Scientific Committee 2012. Scientific Opinion on risk assessment terminology. EFSA Journal 10(5):2664, 84 pp.).

knowledge and identification of attendant uncertainties, permits risk ranking or separation into descriptive categories of risk.

- **Sensitivity Analysis:** A method to qualify the output of a model by measuring the variation in model outputs resulting from changes in inputs. Through this, the "sensitivity" of a model to the respective changes can be assessed, and work can be focussed onto those input parameters that have substantial impact on the model output. Testing changes in model output caused by changing certain structural aspects of the model usually may be referred to as Robustness Analysis.

- **Stochastic models:** A model in which randomness is involved in the derivation of future states of the model. Stochastic models thus produce distributions as output even for a given starting condition. Randomness might be incorporated via stochastic parameterisation i.e. accounting for variability and uncertainty of event occurrence**.**

- **Uncertainty**: Uncertainty is the expression of lack of knowledge that can be reduced by additional data or information.

- **Variability**: The heterogeneity of the subjects modelled, including both stochastic variability (randomness) and inter-individual variability. Variability cannot be reduced by additional data or information.