EFSA Panel on Biological Hazards (BIOHAZ); Scientific Opinion on Reflecting on the experiences and lessons learnt from modelling on biological hazards

EFSA Publication

Link to article, DOI:
10.2903/j.efsa.2012.2725

Publication date:
2012

Document Version
Publisher's PDF, also known as Version of record

European Food Safety Authority

EFSA Journal 2012;10(6):2725

SCIENTIFIC OPINION

Scientific Opinion on Reflecting on the experiences and lessons learnt from modelling on biological hazards[1]

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

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ABSTRACT

Quantitative analysis of scientific evidence involves the collection of data and modelling of a situation or process under consideration and this protocol is the basis of quantitative microbial risk assessments (QMRA). The lessons and experiences from quantitative risk assessments and modelling undertaken by the BIOHAZ Panel are reviewed. Quantitative models in risk assessments were found to be essential for providing an output that could be used by risk managers to support a proportionate response to a situation and/or to balance risks and costs. QMRA is a developing field which creates methodological uncertainties, and therefore, preferences for types of models cannot be specified. Newer approaches need to be identified and considered. Fit for purpose and simplicity are key issues when developing QMRA models. However, limits on time and resources may restrict the model selection. At the start, preferably before accepting the mandate, a scoping exercise is recommended. The scoping exercise could include an assessment of the mandate, possible interpretations of the terms of reference, deadlines, the modelling approaches possible and the data requirements. To support this process, a model catalogue could be developed. The choice of modelling approach is guided by the available data and cause-effect relationships. The basis/assumptions of each quantitative expression should be clearly stated as well as the associated uncertainties. Certain expressions such as "negligible", "concern" and "unlikely" should be used carefully, with scientific criteria and context clearly defined, or avoided.

KEY WORDS

Biological hazards, guidelines, modelling, QMRA, quantitative risk assessment, review.

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[3] Acknowledgement: The Panel wishes to thank the members of the Working Group on Reflecting on the experiences and lessons learnt from modelling on biological hazards: Boris Antunovic; Tine Hald, Arie Havelaar, James Hope; Christine Müller-Graf and Ivar Vågsholm for the preparatory work on this scientific opinion and EFSA staff: Michaela Hempen for the support provided to this scientific opinion.

Suggested citation: EFSA Panel on Biological Hazards (BIOHAZ); Scientific Opinion on Reflecting on the experiences and lessons learnt from modelling on biological hazards. EFSA Journal 2012;10(6):2725. [44 pp.] doi:10.2903/j.efsa.2012.2725. Available online: www.efsa.europa.eu/efsajournal

SUMMARY

The European Food Safety Authority (EFSA) asked the Panel on Biological Hazards (BIOHAZ) to provide a scientific opinion reviewing the lessons and experiences from quantitative risk assessments and modelling undertaken by the BIOHAZ Panel.

Quantitative analysis of scientific evidence involves the collection of data and modelling of a situation or process under consideration and this protocol is the basis of quantitative microbial risk assessments (QMRA). A quantitative assessment should be used whenever feasible and practical to get more precise answers on microbial risks for food safety. The mandates given to EFSA's BIOHAZ Panel by the European Commission increasingly ask for a quantitative evaluation of public health benefits and risks, and the results should be the basis for cost-benefit analyses. Therefore, mathematical models are often necessary for answering the mandates and questions in sufficient depth.

In this opinion the lessons and experiences from quantitative risk assessments and modelling undertaken by the BIOHAZ Panel are reviewed, in particular, describing successful approaches and challenges, suggesting practical improvements, and developing guidelines for a transparent and consistent description of the models. Moreover, it is based on the discussions, lessons learnt and afterthoughts when developing opinions in the Biological Hazards Panel during the three mandate periods 2003-2012 as well as the report commissioned by EFSA on QMRA at the European level, the guidance on modelling by the EFSA Animal Health and Welfare Panel, answers to a questionnaire by BIOHAZ Panel members who chaired at least one working group involving QMRA modelling, a review of the risk assessment work in other EFSA Panels and the work by EFSA's Scientific Committee on harmonisation of risk assessments both on transparency and risk assessment terminology and the EFSA Science Strategy 2012-2016.

Quantitative models in risk assessments were found to be essential for providing an output that could be used by risk managers to support a proportionate response to a situation and/or to balance risks and costs. Therefore, models and modelling activities are likely to be at the core of the future EFSA scientific risk assessments, including those by the BIOHAZ Panel.

Compared to qualitative models, QMRA models have given better insights into and enabled quantitative predictions of the impact of interventions within the food chain. Expertise, data, as well as time and resources, have been limiting factors for QMRA exercises.

QMRA is a developing field which creates methodological uncertainties and therefore preferences for types of models cannot be specified. New approaches need to be identified and considered.

Fit for purpose and simplicity are key issues when developing QMRA models. However, limits on time and resources may restrict the model selection.

A common approach is needed for documentation and quality assurance of the models, and guidelines for documentation and communication should be developed as a priority.

Critical control points for risk assessments were a) the process where mandates are defined and distributed to Panels, b) the selection of modelling approaches to support answering the mandate, c) the decisions on the criteria for data inclusion/exclusion, the review of the output of the QMRA and e) the communication of the opinions to risk managers. With regard to the interface between risk management and assessment, the mutual understanding of quantitative risk expressions and their associated uncertainties by both risk assessors and risk managers are crucial for the ability to ask informed risk assessment questions and to take informed risk management decisions.

In order to better allocate resources for future QMRA models, it is essential to be pro-active. A dialogue between BIOHAZ Panel, EFSA, and EC on future biological hazards/food commodities combinations for risk modelling activities is therefore advantageous. This needs to be done before mandates are received, to facilitate the planning and allocation of resources for foreseen QMRA

exercises. Therefore, EFSA needs an early notification of mandates in which QMRA will be included, as the QMRA process needs careful planning. Moreover, appropriate time for considering various modelling approaches and reviewing the model output should be foreseen and planned for.

At the start, preferably before accepting the mandate, a scoping exercise is recommended. The scoping exercise could include an assessment of the mandate, possible interpretations of the terms of reference, deadlines, the modelling approaches possible and the data requirements. To support this process, a model catalogue could be developed

The modelling approach, including the results of the scoping exercise, should be discussed in the Panel early in the process. In particular the Panel has to be able to evaluate the approach before models are implemented. The choice of modelling approach is guided by the available data and cause-effect relationships. When giving advice on proportionate response and/or balancing risks and costs, quantitative approaches should be preferred.

The following is suggested for developing a transparent and consistent description of the models: The EFSA Scientific Committee's recommendations for harmonisation of risk assessment terminology are endorsed. EFSA models should be archived and, where appropriate, made available for scientific use. The basis/assumptions of each quantitative expression should be clearly stated as well as the associated uncertainties. Certain expressions such as "negligible", "concern" and "unlikely" should be used carefully with scientific criteria and context clearly defined or avoided. Standard protocols for documentation and reporting should be developed and used when describing models, model input and output, and assumptions.

At the end of their mandates it is suggested that the future EFSA Biological Hazards Panels reflect on the lessons learnt from the modelling and risk assessments. Both, QMRA as well as risk ranking exercises should be reviewed to create a learning process.

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BACKGROUND AS PROVIDED BY EFSA

Models enable a quantitative analysis of the scientific evidence often in the form of quantitative risk assessments (QRAs). As outlined in the recommendations for addressing quantitative microbiological risk assessments (QMRAs) at the European level (Havelaar, 2005[4]) a quantitative assessment should be used whenever feasible and practical to get more precise answers on microbial risks for food safety. The mandates given to EFSA's Biological Hazards (BIOHAZ) Panel by the European Commission increasingly ask for a quantitative evaluation of public health benefits and risks, and the results should be the basis for cost-benefit analyses. Therefore, mathematical models are often necessary for answering the mandates and questions in sufficient depth.

Moreover, models identify important data gaps or lacks of knowledge thereby indicating future research priorities. Nevertheless, learning by doing has been important for the use of modelling to support the work of the BIOHAZ Panel. It is now an appropriate point in time for reviewing and reflecting upon the experiences gained and suggesting ways forward.

The BIOHAZ Panel has used quantitative risk assessment (QRA) and modelling to address questions related to food-borne pathogens (*Salmonella* and *Campylobacter*) in pigs, in the poultry pyramid and prion diseases (BSE in cattle and TSE diseases in small ruminants). In the experiences of the BIOHAZ Panel, models have been useful tools but their use present challenges including:

- Models are often novel, complex and not always peer-reviewed before being presented.
- They are often developed by contractors and are described in a report.
- A report, however, is often not detailed enough to understand a complex model and to carry out a peer-review.
- The Panel has had difficulties peer-reviewing the models used, as the time between delivery of the model by the contractors and adoption deadline for the opinion is not long enough to allow a thorough validation and evaluation of a complex model. The consequence could be that mistakes in the model code are only discovered after the adoption of the opinion.

The proposal is that the BIOHAZ Panel provides a review of the lessons and experiences from quantitative risk assessments and modelling undertaken by the BIOHAZ Panel. This review should include a description of successful approaches and challenges and suggest practical improvements, e.g. development of technical guidelines and a standard checklist for the technical specifications for outsourced modelling work. The BIOHAZ Panel should also develop guidelines for a transparent and consistent description of quantitative models.

A possible approach for the latter is the guidance developed by the Animal Health and Welfare (AHAW) Panel in 2009[5]. The guidance suggests using a standard operating procedure (SOP) for the use of modelling tailored to support animal health decisions or to inform scientific risk or benefit assessments. Although these guidelines were about the procedure to include models rather than the QMRA modelling itself, the approach can be useful for describing quantitative models transparently.

[4] www.efsa.europa.eu/en/af060303/docs/af060303-ax2.pdf
[5] www.efsa.europa.eu/en/efsajournal/pub/1419.htm

TERMS OF REFERENCE AS PROVIDED BY EFSA

EFSA requests the BIOHAZ Panel to:

Provide a scientific opinion reviewing the lessons and experiences from quantitative risk assessments and modelling undertaken by the BIOHAZ Panel. The BIOHAZ Panel is in particular requested to:

- Describe successful approaches and challenges
- Suggest practical improvements, e.g. development of technical guidelines or a standard checklist for the technical specifications for outsourced modelling work
- Develop guidelines for transparent and consistent description of the models.

ASSESSMENT

1. Introduction

According to Regulation (EC) 178/2002[6], EFSA should take on the role of an independent scientific point of reference in risk assessment and can be requested to give opinions on scientific issues, thereby enabling the Community institutions and Member States to take informed risk management decisions necessary to ensure food and feed safety.

The challenge when addressing the terms of reference given to EFSA's Scientific Panels and previously DG SANCO Scientific Committees is to make a synthesis and assessment of the current state of knowledge, but also the lack of knowledge and uncertainties. The synthesis and assessment of knowledge has usually been in the form of a scientific review resulting in an opinion with conclusions and recommendations addressing the terms of reference. The recommendations would often include suggestions for filling the knowledge gaps. A quantitative risk assessment is a structured method of incorporating current knowledge enabling more precise quantitative answers, which in particular are needed when discussing proportionate risk management responses and/or balancing risks and costs. Other complementing approaches could be systematic literature reviews and meta-analyses.

Since EFSA's Biological Hazards (BIOHAZ) Panel was established in 2003, at least ten mandates, all received from the European Commission, have asked for quantitative evaluations in their scope. An overview of these mandates can be found in Appendix A. The deadlines, limited resources, and the complexities of risk assessment models used, have created challenges for all involved. Are there any lessons from the experiences gained during three mandate periods of the BIOHAZ Panel, i.e. the last nine years?

This opinion is based on the discussions, lessons learnt and afterthoughts when developing opinions in the Biological Hazards Panel during the three mandate periods. The purpose of this exercise is to be as helpful as possible and to give some advice to the renewed BIOHAZ Panel whose mandate commences in June 2012. However, this opinion is not about giving advice on modelling in general.

Important documents considered when developing this opinion were the report commissioned by EFSA on QMRA at the European level (Havelaar, 2005); the guidance on modelling by the EFSA Panel on Animal Health and Welfare (AHAW, 2009); answers to a questionnaire by BIOHAZ Panel members who chaired at least one working group involving QMRA modelling; a review of the risk assessment work in other EFSA Panels; and the horizontal work by EFSA's Scientific Committee on harmonisation of risk assessments both on transparency and risk assessment terminology (EFSA Scientific Committee, 2009, 2012), as well as the EFSA Science Strategy 2012-2016[7].

The BIOHAZ Panel received many mandates asking for quantitative assessments and risk ranking and it is anticipated that this trend will continue or even increase. A complementary opinion on the development of a risk ranking framework on biological hazards (EFSA Panel on Biological Hazards (BIOHAZ), 2012) has been concurrently adopted by the Biological Hazards Panel. One of the purposes shared by both opinions is to reflect on experiences with QMRA and risk ranking that the BIOHAZ Panel gained during the last three mandates and to advice the renewed Panel. However, given the time constraints, this opinion can only provide some guidance and rules of thumb. It is suggested that the renewed Panel also reviews its risk assessment experiences at the end of its mandate period.

In this document the term QMRA (quantitative microbiological risk assessment) is used consistently and includes QRA (quantitative risk assessment) of prion diseases.

[6] OJ L 31, 1.2.2002, p. 1–24
[7] www.efsa.europa.eu/en/corporate/doc/sciencestrategy12.pdf

2. Summary of experiences gained

The experiences gained are presented in this Chapter as a synthesis of a questionnaire sent to the Panel working group chairs (Appendix B). Moreover, a brief overview of models and their purposes are presented, and a follow-up of the Havelaar (2005) report's most salient conclusions and recommendations. It is noted, that the report from the EFSA Panel on Animal Health and Welfare (AHAW, 2009), where the process of risk assessment modelling is outlined by the Figure in Appendix C, could inform the work of assessments in the biological hazards sphere too. An overview of the risk assessment approaches taken by other EFSA Panels and Units appears in Appendix D.

2.1. Synthesis of questionnaire sent to BIOHAZ Panel members chairing WG using modelling

The questionnaire was developed for the purpose of this opinion and completed by five BIOHAZ Panel members who have chaired at least one working group using modelling. The questionnaire, (shown in Appendix B) reflects the broad diversity of risk questions posed to the Biological Hazards Panel. A synthesis of responses is provided here.

2.1.1. Please list the major strengths and weaknesses of using quantitative analyses and modelling for developing the opinion:

Strengths of a QMRA model

- Helps understanding and gives perspective on the complex and/or dynamic relationships between components of the biological system modelled;
- Quantitative models are well documented with assumptions that can be tested;
- Integrates data and biological insights;
- Identifies and clearly defines data and knowledge gaps, and indicates their importance, thereby suggesting research priorities;
- Quantitative answers are more objective than qualitative and use all available information;
  - Less dependent on individual judgements;
  - Better able to consider variability and uncertainty;
- Enables judgements on the relative importance of parameters and thereby risk management interventions, thereby revealing which management interventions appear to be the most effective;
- Separates science from opinions and advocacy.

Weaknesses of a QMRA model

- Is time consuming and resource and labour intensive;
- May be difficult to understand for non-modellers and requires extensive explanations;
- Results and approaches may be difficult to communicate to non-experts;
- Can include numerical and code errors in the model;
- Can have incomplete considerations of uncertainty;
- Can give false impression of accuracy or precise knowledge;
- Is hard to fully validate with regard to all results and assumptions, difficult even for experienced modellers to fully understand unless they spend a lot of time;
- Is often frustrated by lack of data.

2.1.2. Please list the major opportunities and threats you experienced when using quantitative analyses and modelling for developing the opinion

Opportunities of a QMRA model

- A structured approach and logical layout that enhances structured thinking through a question;

- Revealing the complexities of a food chain or biological system
  - Can identify associations not recognised previously – generate hypotheses;
  - Develop new visions of a question;
  - Promote interdisciplinary approaches;
- Quantitative conclusions on risk management interventions;
- Better use of available data.

Threats of a QMRA model

- Complex project structures with many bureaucratic obstacles;
- Difficulties with interactions and communications between modellers and subject specialists;
- Lack of data, or sources of data not reliable;
- Too ambitious and too complex terms of reference;
- Too complex models; thereby reducing transparency;
- Too short time available for modelling and validating the model;
- Use of non-established modelling methods.

2.1.3. Could you suggest criteria for deciding when quantitative modelling is appropriate for answering a biological hazards question?

A **quantitative** microbial risk assessment is preferable:

- Whenever the mandate requires a quantitative answer, i.e. evaluation of risk. This could be
  - when risk management intends to balance risks, benefits and costs, doing a benefit cost analysis, a risk benefit analysis – i.e., proportionate risk management responses are considered. This is possible even with few data, provided appropriate uncertainty and sensitivity analysis can be performed;
  - when different risks must be compared;
  - when comparing different control options;
- If the data, resources, expertise and sufficient time are available;

2.1.4. Could you suggest criteria for deciding when qualitative approach is better suited for answering a biological hazards question?

A **qualitative** microbial risk assessment is preferable:

- For questions with a very limited time frame;
- When hardly any data are available or scientific knowledge is ambiguous or missing;
- When precautionary risk management measures are considered, in particular as an urgency;
- As a scoping exercise to see if a quantitative assessment is warranted.

Figure 1 shows a diagram suggesting different approaches to risk assessment based on knowledge about likelihoods and outcomes (Stirling and Scoones, 2009), reflecting the two classical dimensions of risk, i.e. likelihoods ("probabilities") and outcomes ("severity"). It is recognised, however, that knowledge about either of these may be imperfect. Depending on the level of knowledge on likelihoods (based on data availability) and outcomes (based on understanding of causal relationships), four broad categories of approaches are proposed:

(1) If knowledge about likelihoods and outcomes are not problematic, i.e. sufficient quality data are available and causal relationships are established, standard risk assessment methodologies including probabilistic modelling can be applied.

(2) If knowledge on likelihoods is problematic, i.e. sufficient data are not available and/or of insufficient quality (uncertainty about risks);

(3) If knowledge on outcomes is problematic, i.e. if causal relationships are not well established (ambiguous risks)

In both cases (2) and (3), quantitative approaches are still recommended, but these should now explore uncertainties in the available information beyond statistical confidence intervals;

(4) If knowledge on both domains is problematic (ignorance), quantitative approaches are of limited use and more exploratory, qualitative approaches are suggested with the acknowledgement that the output will likely support a precautionary rather than a proportionate response.

Hence, the choice of modelling approach is guided by the available data and cause-effect relationships.

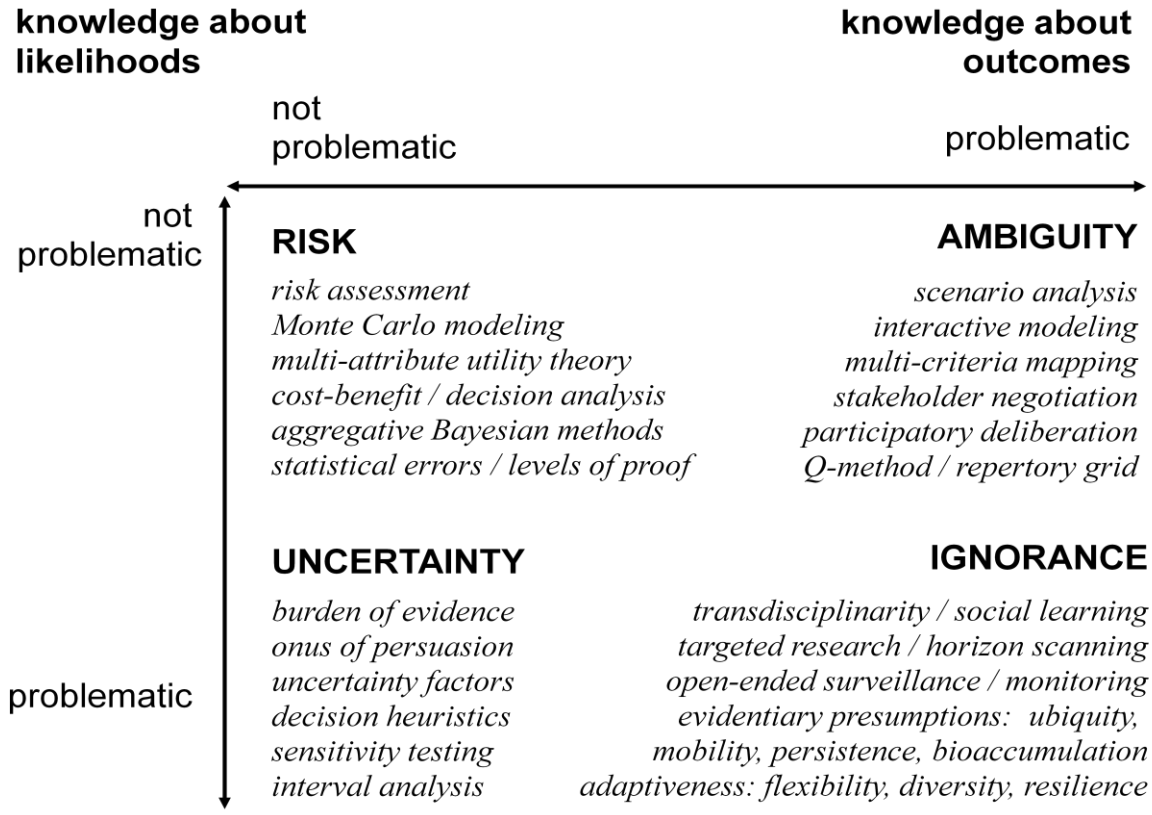

Figure 1: Possible approaches for when using qualitative or quantitative approaches based on knowledge about outcomes and probabilities (Stirling and Scoones, 2009).

2.1.5. Please, indicate how much you agree on the statement by a number from the scale 1 (fully agree) to 4 (fully disagree).

The WG chairs **agreed** on the following statements: (*with some qualifications and comments in parenthesis and italics)*

- A quantitative assessment should be used whenever feasible to get more precise answers on microbial risks for food safety. *(The term feasible should be interpreted widely: from a technical and organisational point of view as well as time frame).*

- A simple model is always preferable to the complex (Occam's razor). *(It should be recalled that quantitative models are not by definition more complex than qualitative approaches.)*

- Models identify important data gaps and thereby indicate future research priorities.

- The period between delivery of the model by a contractor and the deadline for adoption of the opinion should be sufficient for a review of the model *(For very complex and/or novel models, it could be considered also to commission an external review, that the Panel can use to inform its review).*

The chairs **disagreed** with the following statement:

- The modelling results and uncertainties are understood by risk managers. *(One of the difficult issues is to explain the models' inherent uncertainties which are important in relation to the management decision making process.)*

There was **no common agreement or disagreement** on the following statements

- A qualitative assessment should be used whenever expedient answers on microbial risks for food safety are required.

- The state of modelling used for risk assessments on biological hazards is sufficiently well established for producing guidelines. *(This is still a developing field. Perhaps it never will be as type of questions will differ).*

- Launching a modelling task is justifiable only if the resources and time are commensurate with the magnitude and complexity of the task. *(True, but it is not always apparent how complex the task is until it has been started. This is an important message for the process of accepting the mandate. Furthermore, the nature of the modelling task should primarily be defined by the risk management needs. Resources and time should be matched to those needs).*

- The peer-review should be the responsibility of the Panel. *(This puts high demand on the composition of the Panel. Often only one or two members are sufficiently well versed in modelling expertise to carry out the review. For very complex and/or novel models, it could be considered also to commission an external review that the Panel can use for guidance.)*

- Only peer-reviewed models should be used *(Ideally yes, but it would be difficult in most circumstances as almost all models need to be tailored to the specific questions. However, a catalogue of published models should be developed and they may then become useful for future mandates addressing similar questions)*

- The Panel review of a model should be split into a technical part and a biological part. *(The model should be evaluated in its entirety, and specialists in different disciplines should make an effort to bridge their worlds. The review team should include both modellers and subject experts, but the review should be done as a single process.)*

- Risk managers use the modelling results when making decisions

- Communication is the biggest challenge in modelling.

2.1.6. Which are the critical control points of a modelling exercise when using quantitative analyses and modelling for developing the opinion:

The respondents were asked to choose those points that they think are critical. The following control points were suggested:

a) The acceptance of the mandate and its deadline
b) The design of the modelling exercise (interpretation of terms of reference, terms of reference for outsourcing, selection of the contractor, composition of WG, interface between contractor and WG) after accepting the mandate
c) Preparatory work (obtaining data, reviewing literature, team assignment...)
d) Mathematical work (choosing the parameters, distribution curves, algorithms...)
e) Drafting, reviewing and publishing the results (agreement on the outputs, conclusion...)
f) Progress reports to the panel
g) First reading of draft opinion
h) Final conclusions and recommendations

It appears that all aspects are important as control points, but b) design of the modelling exercise appears to be the most crucial, and unique to the QMRA process.

2.1.7. Based on your experience, what would be your advice to the renewed BIOHAZ Panel in order to use modelling in the best way?

- The Panel should have the right skills mix and would have to thoroughly discuss the need for, and resource demands of, quantitative approaches during the mandate acceptance process. Risk managers should be actively involved in all stages of the work. If a cost benefit analysis is undertaken, communication between risk assessors, risk managers, and the group carrying out the cost benefit analysis should be established early on. A standard procedure for QMRA should be developed in which the Panel has the possibility to provide scientific input in all stages.

- Consider having a permanent modelling group in the Biological Hazards Panel tasked with supporting EFSA in the process in particular on accepting mandates and choice of strategies for answering the questions (in-house, ad-hoc WG, outsourcing, etc.), critical peer-review of models used and interpretation of their results.

- EFSA needs to expand its in-house capacity for modelling, both doing the modelling and critical review of modelling, its capabilities for outsourcing, and creating a network of excellence among EU food safety agencies, research institutes and universities for risk assessment.

2.1.8. Have you experienced difficulties in understanding or communicating quantitative risk assessments? Why? And what would you suggest to improve it?

- Yes, models may appear too complicated. The basis / assumptions of the model have to be understood. Difficulties can arise if 1) the models are very complex and therefore less transparent making it difficult for to see the logic behind the model, which can also be difficult to explain, and/or 2) the results are very different from what was expected based on e.g. “common knowledge” or opinions. The problems we are dealing with are often dynamic and a risk assessment made at some point in time may provide different results than a risk assessment performed at another time.

- A challenge is the interaction between risk assessors and managers. Possibilities for improving this communication should be explored, including that WG chairs should if invited explain the opinions to risk managers as well as findings ways to improve the possibilities for interactions and clarifications of questions during the risk assessment process. All without prejudice to the

scientific integrity and independence of risk assessment process. The Panel should be multidisciplinary in terms of members. The modelling approach taken should be discussed and agreed upon by the Panel at an early stage and not only in the working group. It is also important that the interpretation of the terms of reference is agreed with both the Panel and the Commission before the modelling task begins, and the risk managers should be given a clear view of what output can be expected.

- To improve understanding of QMRA, clearer explanations of the assumptions and outcome of the model could be provided. More detailed documentation of what went into a model, with a clearly defined scheme of documentation, could help when looking for certain type of information. Risk assessors should be very structured and decide in a very clear way whether to use a model or not, taking into account the time frame for the opinion, and provide a dummy answer so that everybody agrees at the beginning on the likely answer. They should also make sure that the question and aim is very clearly defined.

2.2. Description of models

Models (be they mathematical or otherwise, e.g. animal or *in vitro* models) are simplifications of the real world and will always reflect an imperfect understanding thereof (EFSA Panel on Animal Health and Welfare (AHAW), 2009). The type of models used (quantitative or qualitative) will be determined by their purposes (terms of reference), the availability and the type of data, and the available expertise, time and resources. Models can be either qualitative or quantitative, while quantitative models can be deterministic or stochastic.

There are, in general, three purposes for modelling a biological system: description, understanding and prediction (Hall and DeAngelis, 1985).

Data driven models are used for **description.** Their purpose is to extract information from available data, and of their inherent uncertainties. Models applied for descriptive purposes can indicate relationships and the outcome of descriptive models may be hypotheses, which can then be tested when new data become available. It is not appropriate to test the hypothesis on the same data from which the model was derived. These models describe what is observed very well, but are not based on the understanding of the biological system. Examples are polynomial and regression models. There is great uncertainty when using black box models for predicting outside the data intervals from which the model was derived, which is therefore not recommended.

Knowledge driven modelling is used to improve the **understanding** of a system. The modelling can result in comparisons, and show variability in outcomes given different assumptions. Accuracy is often a less important issue when modelling relative or worst case scenarios in order to aid decision making. Examining the complexity of a system and its internal relationships can generate emergent findings, leading to improved system understanding and generating new hypotheses.

Combined data and knowledge driven models are concerned with **prediction** of future consequences based on current data or outside the domain of these data. Models intended for predictive purposes often attempt to mimic nature in great detail. However while high accuracy, high predictive value and minimal uncertainty are desired one should keep in mind that on the other hand unpredictable changes can have a great impact on the precision of the forecast.

The terms of reference given to EFSA often appear to focus on predictions and priorities

2.3. Reconsidered recommendations for addressing quantitative microbiological risk assessment at European level

In 2005, the Executive Director of EFSA requested for recommendations on the implementation of quantitative microbiological risk assessment (QMRA) at the European level (Havelaar, 2005). The recommendations were based on consultations with risk managers in the European Commission and in

Member States, as well as with scientists in the Biological Hazards (BIOHAZ) Panel. This report suggested that the scientific opinions should be supported by quantitative assessments whenever feasible. Different possible strategies for EFSA to include QMRA in its scientific work were evaluated. It was suggested that EFSA developed a guidance document, and increased the capacity for quantitative risk assessments either through in-house, networking or decentralised strategies. The recommendations from Havelaar (2005) are reproduced below, followed by an evaluation of the experiences in the past years (*in italics*).

- EFSA is advised to develop its capacity to include QMRA in its scientific advice to the European Commission and other clients with high priority (Havelaar, 2005).

  The BIOHAZ Panel agrees that when time, resources and data permit, preference should be given to quantitative methods. However, qualitative risk assessment may be appropriate for specific problems, or when time, resources or data are not sufficiently available, as discussed above.

- EFSA is recommended to work towards an iterative process with the Commission (and other clients) to accurately define the risk management questions and to decide on the appropriate type of assessment, taking into account the available resources and time. Risk profiles could be a useful instrument in this process (Havelaar, 2005).

  Getting the question right and involvement of risk assessors in the communication process in an early stage is one of the most critical moments. Currently, the communication between EFSA and the risk managers involves many players and is mainly internal in EFSA. The BIOHAZ Panel is indirectly involved through the BIOHAZ Unit, the Panel (vice) chair and possibly Panel members with specific expertise. Risk profiles are not included in this process, but their use could lead to a more structured process (see Havelaar 2005, page 12, Figure 4-1). The duration of the entire process would become longer, though.

- EFSA may consider developing a guidance document on the appropriate use of different types of (microbiological) risk assessment to support food safety management at the European level. This document can be used within its own organisation; the BIOHAZ Panel included, and also communicated to EFSA's clients, in particular the European Commission. It can also be used as a module in training programmes for risk managers and risk assessors (Havelaar, 2005).

  The field is still developing, and it is currently not clear if such a guidance document can indeed be developed. Structuring the process discussed in the previous bullet may be a next step towards this goal.

- EFSA, the BIOHAZ Panel included, has final responsibility for the scientific advice based on QMRA but is advised not to carry out all technical work itself. It could aim to ensure the soundness and transparency of the whole process by developing expertise to manage and interpret QMRA studies. Outsourcing is expected to continue to be an important part of larger QMRA projects and optimising the process is a critical success factor (Havelaar, 2005).

  There are different possible strategies for the actual performance of QMRA projects including an in-house strategy, a networking strategy, and a decentralized strategy. Each strategy has specific advantages and disadvantages. EFSA's management is recommended to consider a strategy that combines the advantages of the in-house and networking strategies (Havelaar, 2005).

  EFSA has chosen for the third option discussed in Havelaar (2005), i.e. a decentralized strategy. Some problems identified in the QMRA models identified in this Opinion were indeed predicted in the report: "a low degree of continuity and limited capacity building within EFSA itself and this may lead to difficulties in supervising and interpreting the

assessments", "no creation of more or less permanent teams, so each project may suffer from initial delays" and "least likely to develop a Community perspective in the project teams, and will not easily lead to harmonisation activities". Therefore, reconsideration of this recommendation is suggested.

- To support the implementation of QMRA in EFSA, new tasks will prove necessary. These include a coordinating function in the BIOHAZ Unit and database management in the Unit on Monitoring of Zoonoses. Other identified tasks include QMRA project management, QMRA team leadership, risk assessment modelling, data analysis and QMRA model management. Specialised technical tasks should be outsourced and EFSA should assure sufficient funding and support for teams of scientists involved in the risk assessments (Havelaar, 2005).

  The coordination functions and database management have been realized within EFSA. Other tasks have been performed by the contractors. Considerable budgets have been allocated to several QMRA projects. It should be recommended that tenders take into account that modelling is resource intensive and that QMRA models require good documentation, and possibly a user friendly interface, etc. In this respect the use of the models by EFSA staff is also valuable.

  Another point is that the long lag time when outsourcing necessitates a planning horizon that is longer than the planning horizons implicit for the mandates given to EFSA.

  There is a need for a strategic long term planning and proactive management of QMRA tasks.

  Close interaction between EFSA staff and the BIOHAZ Panel is necessary in all steps of incorporating QMRA in the scientific opinions. The Panel should be able to review and interpret QMRA studies, and use these results in a broader context. EFSA may need resources to hire specialised support for this purpose.

  Reviewing QMRA models has turned out to be a major task. The Panel and the BIOHAZ Unit have limited expertise and resources for such tasks. Nevertheless, the support provided to the Panel by the BIOHAZ secretariat has proved highly useful, by using the model to produce output required for answering the mandates. By doing so, a quality control of the provided models was also possible. In some cases, other EFSA Units have supported the review, but more detailed peer-review of both the model code and the contractor's report would improve the credibility of the QMRA models and their use by EFSA. This appears to be a promising way forward.

- EFSA should give consideration to the requirements of all Panels together, rather than the BIOHAZ Panel in isolation. In particular the experiences from those undertaking risk assessments for the AHAW Panel should be considered (on a formally included basis) along with the BIOHAZ study, in considering EFSA's future strategy (Havelaar, 2005).

  The Scientific Committee has discussed multi-sectoral issues. In case EFSA receives a request concerning a multi-sectoral matter, the Scientific Committee is responsible for adopting the final opinion, either via a dedicated Scientific Committee working group(s), composed of members of different Scientific Panels and/or external experts possessing the knowledge and expertise needed to address the said matter or via the relevant Scientific Panel(s) to preparing a draft opinion to be discussed and adopted by the Scientific Committee. The AHAW Panel has developed Guidance on Good Practice in Conducting Scientific Assessments in Animal Health using Modelling" (EFSA Panel on Animal Health and Welfare (AHAW), 2009).

- To support the implementation of QMRA, it is suggested that EFSA develops structured databases. Furthermore, EFSA may promote additional data generation by direct funding or by influencing priorities of other national and international funding agencies. EFSA may also promote the further development of QMRA as a discipline in cooperation with European and national research funding agencies (Havelaar, 2005).

  A brief overview of some EFSA activities since 2005:

  EFSA has developed a preliminary standardised food classification and description system called FoodEx2. The system consists of descriptions of a large number of individual food items aggregated into food groups and broader food categories in a hierarchical parent-child relationship. The DCM published in 2008 the Concise European Food Consumption Database, which gathers data on food consumption for adults in Europe according to these broad categories. These data can be used for exposure screening. The Comprehensive European Food Consumption Database provides detailed information for a number of EU countries in refined food categories and specific population groups, also partly covering children. Summary statistics from the database enable quick screening for chronic and acute exposure to substances that may be found in the food chain. The EU Menu project that is co-ordinated by EFSA, and in close co-operation with Member States, *aims at harmonising data collection on food consumption in Europe. The objective is to provide standardised information on what people eat in all countries and regions across the EU in detailed categories and including all population groups. It will allow more efficient and accurate overall exposure assessment in Europe and support risk managers in their decision making on food safety.*

  EFSA' in collaboration with the European Centre for Disease Prevention and Control (ECDC), collect and analyse the data on zoonoses, zoonotic agents, antimicrobial resistance, microbiological contaminants, food-borne outbreaks and animal populations and produces an annual European Union Summary Reports. EFSA also analyses the results from EU-wide baseline surveys on zoonotic agents in animals and food. Data from the baseline surveys were used in several BIOHAZ QMRAs.

  EFSA) is building systematic literature review databases to extract data for their risk assessments in animal health and welfare. This could be extended into biological hazards area.

- To reduce the different abilities across Europe to produce quantitative risk assessment studies and to effectively use the results in the risk management process, training and capacity building, including the development of guidelines and glossaries, was encouraged (Havelaar, 2005) .

  A brief overview of some EFSA activities since 2005:

  EFSA published in 2010 a guidance document on the application of systematic review methodology to food and feed safety assessments to support decision making. Training sessions on systematic literature review are organised twice a year for EFSA staff and Panel members.

  EFSA's Animal Health and Welfare Panel (AHAW) published in 2009 Guidance on Good Practice in Conducting Scientific Assessments in Animal Health using Modelling. In this document, an 'operating procedure' (OP) is presented for the use of modelling. The OP provides a detailed flowchart enabling modelling to be transparently and consistently integrated in the assessment and appear in Appendix C of this opinion. The development of a dynamic wiki-like web-based glossary for terminology used in modelling is recommended. It is concluded that adherence to the OP will improve transparency and acceptability of models in EFSA outputs, and it is recommended to adopt the flowchart as a

standard procedure when responding to AHAW mandates. The EFSA scientific Committee has published opinions on transparency of risk assessments (2009) and risk assessment terminology (2012).

2.4. Animal Health and Welfare Panel's Guidance on Good Practice in Conducting Scientific Assessments in Animal Health using Modelling

The "Guidance on Good Practice in Conducting Scientific Assessments in Animal Health using Modelling" (EFSA Panel on Animal Health and Welfare (AHAW), 2009) originated from problems encountered during the development of AHAW opinions. A number of scientific assessments in animal health were carried out using modelling.

It was thought more guidance could help to avoid repeatedly encountered problems, such as whether to use a model or not, was discussed at the end of an opinion and not at the beginning, which either resulted in having wasted a lot of time on a model which was deemed then not appropriate for the answering the question or in being in a situation that at the end of an opinion it was discovered a model could have answered that question in an appropriate way.

To deal with these problems during the initial stages of an opinion and to deal with the acceptance of using models as well as with the communication during the development of models as well as the communication with the risk managers, this guidance was formulated to give some guidance, for instance to new experts. The guidance can help risk managers to understand the risk assessment process and proposes to present them with the type of expected results in the initial stages in order to check whether this is the answer they need. Furthermore, during scientific assessments, the danger may exist that good practice may be overlooked when models are developed and used under time pressure. Experience in the AHAW Panel also showed that sometimes communication between so called "subject" and "modelling" experts was poor, creating unnecessary misunderstandings or delays in the possible development of a model, if the decision was taken to do one. The respective roles of subject and modelling experts are discussed and a list provided.

A central part of the guidance was the description of an "operating procedure" for the use of modelling within an animal health working group. A detailed flowchart is provided to help to make the modelling more transparent, as well as text explaining the "operating procedure" in detail. The "operating procedure" points out the importance of clarifying the terms of reference very carefully and introduces the discussion of the use of modelling very early in the development of the opinion. This is done to avoid the discussion of the usefulness of the modelling at the very end and also to give a clear idea of the result at an early stage of the opinion.

The flow chart allows experts to check whether they are following a suggested procedure without re-reading the text. The original flow-chart has been slightly modified according to the situation of the BIOHAZ Panel (Appendix C). Each phase shows the steps to be taken, the tasks involved and the outcome, as well as who is involved (Plenary, EC, Working group). The usage of the standard risk assessment terminology was discussed in the guidance document. However, "while identifying standard terminology, a recurrent problem of the absence of universally agreed definitions in risk or benefit assessment terminology was faced", a reason being that definitions may vary between disciplines, such as animal health and quantitative microbiology, also the verbal grading of risks and related parameters may vary.

As a solution, to define the precise interpretation of certain terms a dynamic approach in form of an electronic glossary was proposed, a so-called wiki approach (see Chapter 4.2). This could take into account the evolution of methods as well as the slightly different meaning of the same term in different fields. It would also make it easier to compare the outputs of different EFSA opinions. This was seen to be an improvement to define terms for each individual EFSA opinion, which of course has to be carried out at the moment, since there is no generally agreed EFSA terminology. A recent helpful development is the EFSA Scientific Committee's opinion on the risk assessment terminology.

Model characterisation, model selection and model transparency were also discussed. It was specifically avoided to go into technical details or recommend one modelling technique over another, since it was felt that models had to be fit for purpose and that approaches to categorising models lead to non-productive discussion as to which is the "right" approach. The emphasis was put on a frame-work to understand the different option for the model characterisation and model selection. Model implementation and model evaluation referred to the transparency and documentation of the model and the technical analysis of the implemented models such as verification, uncertainty analysis, validation and peer-review. Model application and communication deal with the discussion of the model output referring to sensitivity analysis, robustness and threshold analysis as well as to the transparent and complete explanation of the results.

Overall, this AHAW guidance deals with almost the same problems faced also in the BIOHAZ Panel. It is therefore recommended as a useful background document for future QMRA tasks and the Figure in Appendix C should inform the process and procedures in the BIOHAZ Panel.

2.5. The use of Q(M)RA models in other EFSA Panels

As a risk assessment tool, modelling has been used by different EFSA scientific Panels for different purposes as outlined in Appendix D. Due to the specificities of work, modelling approaches and methods and frequency of modelling differ between the Panels. Therefore, harmonisation cannot be envisaged and it could rather be suggested to develop and improve modelling tools within the Panels.

3. Horizontal considerations on QMRA

A frequent recommendation is to use quantitative microbiological risk assessments (QMRAs) whenever feasible to get more precise answers on microbial risks for food safety, which is endorsed. Moreover, the panel emphasizes the fit for purpose as the guiding principle for risk assessments.

In order to better allocate resources for future QMRA models, it is essential to be pro-active. A dialogue between BIOHAZ Panel, EFSA, and EC on future biological hazards/food commodities combinations for risk modelling activities is therefore advantageous. This needs to be done before mandates are received, to facilitate the planning and allocation of resources for foreseen QMRA exercises.

3.1. Scoping exercises

The beginning of a mandate is a critical control point where sufficient time should be taken to clarify a number of questions which will determine the planning of the opinion. These include the terms of reference, whether and what kind of model should be used, data requirements and whether the model should be outsourced.

It is suggested that a scoping or risk profile exercise is done at this stage looking into

- whether the risk management question is proportionate or precautionary
- which data are available
- whether there are peer-reviewed risk assessment models available
- whether outsourcing would be needed
- suggestions for approaches to be taken
- the time required
- expression of risk desired
- quantitative expressions of qualitative risk terms
- population to which you want to make inferences

- quantitative descriptions of the effect

Possibilities for the future EFSA Panels to support this preliminary step should be explored.

3.2. Documentation of quantitative models

Model documentation is an important part of describing the model and communicating the results. Only when the model is well documented can it be reviewed and validated by others and also be possibly reused if necessary. Only when the assumptions which went in the model and the data which are used for the different parameters are documented and clear, can the scope and the limits of the model be understood.

There are several reasons why models may not be understood. One reason is that scientists and risk managers may not have enough training to understand the mathematical concepts implemented in the model, another that the computer code is not given out so that the model cannot be evaluated or re-used and still another is that the model is not documented in a way that the structure, algorithms and data feeding into the model are clearly described. The lack of good documentation can be explained partly by the time pressures under which most models are developed. Documenting models in detail takes a lot of time and is a cumbersome task. Once the model is up and running and the results are available, there may be no more funding left or time to dedicate to this task or perhaps not a lot of interest since the primary goal has been accomplished. Furthermore, often there is not a lot of interest by the general reader or journal editors in the technicalities of the model, even though they describe the underlying assumptions and allow the used data to be checked by experts.

However, these details are an inherent part of risk assessment and need to be able to be scrutinized. This will become more important when more people start to read and understand the methods more carefully.

In the future guidelines or standards need to be developed by which the different steps of the model have to be clearly identified, the data which went into the model and the references on which these data are based. This will allow the validation and a discussion of the assumptions and data of the model. As discussed, under certain circumstances it may be a good option to use an already developed and validated model again or to re-use a model when the data situation has strongly changed and for this a good documentation is necessary. If there is consistency in model documentation it will make it easier to understand different models and to compare them.

There are attempts at model documentation such as the Interactive online Catalogue on Risk Assessment (ICRA) project (http://icra.foodrisk.org) or the risk project (www.bfr.bund.de).These could be helpful for future EFSA QMRA exercises.

3.3. Central database of definitions

As described for the AHAW guidance document (see Chapter 3.4) a dynamic glossary was suggested in order to keep up with the evolution of the methods and definitions and in order to account for slightly different definitions in adjacent fields for exactly the same term. This would allow comparing the outputs of the different EFSA models and to understand the slightly different connotations of the various terms.

Based on these suggestions, as well as in order to reduce ambiguity and improve the consistency and clarity of its technical risk assessments to risk managers, consumers and the wider scientific and stakeholder community, the Scientific Committee is planning the development of the central database of definitions (EFSA Scientific Committee, 2012). Such database would also make it easier for people to check in a single space rather than trying to look in several EFSA opinions as well as elsewhere (OIE, Codex Alimentarius, FDA, EPA etc) for definitions. It would also enable the risk managers to understand more easily the terms used. Eventually, it would also be helpful, if the definitions did not have to be redefined for each new opinion. However, this requires human resources, because a list

would have to be maintained by EFSA. "As consequence, definitions used in EFSA communication would be consistent at least within the Panel and preferably should be across all EFSA outputs" (EFSA Panel on Animal Health and Welfare (AHAW), 2009). The BIOHAZ Panel should support the development of the central database of definitions by giving suggestions on definitions that have been more in usage by BIOHAZ Panel and based on the experiences in understanding/misunderstanding of specific terms. The BIOHAZ Panel welcomes EFSA's initiative to establish a scientific network on the harmonisation of risk assessment methodologies.

The glossary of each scientific output should include the definition of the risk assessment terms used. If possible, these terms should be fed into a dynamic EFSA glossary as a first step towards a standard terminology in EFSA's risk assessments.

Three levels for harmonisation of terminology should be considered (EFSA Scientific Committee, 2012):

- Within each scientific opinion, one should ensure that the risk assessment terminology used is consistent within abstract, summary and conclusions on risk.
- Within each Panel risk assessment terminology should be used consistently across its opinions within the same scientific area.
- Within EFSA one should endeavour to improve harmonisation of risk assessment terminology across EFSA outputs.

Communication would be improved if terminology/terms (e.g. negligible) were more harmonised. The priority should be to harmonise terminology within the Panel. However, if more than one Panel is involved, it will be important for the communication with risk managers that the terminology is harmonised across the involved Panels

It is more important to harmonise terminology within Panels if more than one panel is involved. On the other hand for the risk management purposes the priority should be given to the harmonisation across the Panels. The glossary of each scientific output should include the definition of the risk assessment terms used. If possible these terms could be fed into the EFSA central database of definitions as a first step towards a standard terminology in EFSA's risk assessments.

The basis/assumptions of each quantitative expression should be clearly stated as well as the associated uncertainties, including whether it has been estimated subjectively by expert judgments, derived from mathematical models, and/or estimated statistically from empirical data.

It is noted that the understanding of quantitative risk expressions and their associated uncertainties by both risk assessors and risk managers, are crucial for the ability to ask informed risk assessment questions and to take informed risk management decisions.

In order to reduce ambiguity, it is recommended (EFSA Scientific Committee, 2012) to use quantitative expressions of risk whenever possible, i.e. quantitative expression of the probability of the adverse effect and of any quantitative descriptors of that effect (e.g. duration), or the use of verbal terms with quantitative definitions.

Certain words such as "negligible", "concern" and "unlikely" have risk management connotation in everyday language. The Scientific Committee recommends that, when used in EFSA opinions, they should be used carefully with objective scientific criteria (not involving value judgments) and be clearly defined (EFSA Scientific Committee, 2012). The historical context in each opinion needs to be considered to understand the risk assessments. For example 'negligible risk' has been a term in TSE risk assessments, with a clear definition in that context. If doing multi- or interdisciplinary risk assessments, this issue of terminology needs to be considered. This means that a Wiki glossary also has to include the contexts in which the terms such as 'negligible risk' are used.

3.4. Gain access to best expertise available

Currently, the most frequently used approach for accessing expertise on QMRA is ad-hoc tendering and outsourcing. One concern with this approach is the difficulty in creating a learning process where successes and failures can feed into a steadily improving scientific community and EFSA's ability to assess risks.

To gain access to the state of the art of risk assessment and models therein, it is suggested that EFSA initiates a framework agreement with consortia of leading food safety agencies and universities in the EU. This would develop strategic relationships where a learning process and continuous improvements to the QMRA exercises are a part of the package and reduce ad-hoc development of risk assessment models.

The continuous efforts of EFSA to increase its in-house capacities should be encouraged as it would enable EFSA to more critically review mandates and address questions concerning outsourcing and selecting the best contractors.

This is in line with EFSA science strategy 2012-1016 which aims at reducing external experts' workload related to routine activities by better utilising the internal scientific expertise among EFSA's scientific staff and outsourcing preparatory work. EFSA established dedicated units to provide preparatory scientific support at the various stages of the scientific work: collection and analysis of data and information including literature review and exposure assessment and modelling. However, there will be a need for enhanced developmental training on risk assessment for EFSA's staff, along with Panel members and external experts, including a need for greater engagement with the wider scientific community.

The conclusions in the EFSA scientific strategy are endorsed in particular the ones on the use of the expertise in the Panels focusing on the critical and novel scientific issues, as well as the ones for internal scientific expertise. In addition it is suggested that EFSA considers developing a network of excellence amongst EU food safety agencies, research institutes and universities for risk assessments.

3.5. Novel versus peer-reviewed models

QMRA is a developing field where methods can still change quickly, therefore guidelines for the type of models to be used cannot be given. Certain questions may be answered by different modelling approaches, so that it also depends on the experience of the modeller which approach is used.

Published models have the advantage of being peer-reviewed by other modelling experts, giving creditability to the data, assumptions and modelling approach used. However, existing (peer-reviewed) models are not easily accessible as in most cases model codes are not available and publications do usually not allow reconstructing of the model. In addition, peer-reviewed models will always need to be adapted to the specific purpose, which typically will include applying different data and making different assumptions than those presented in the published model. It is, therefore, important that the actual model used in an opinion is critically reviewed even if it is based on a peer-reviewed model. This review should include whether the model used is fit for purpose, the critical assumptions and data requirements. Novel (i.e. not peer-reviewed) models have the additional problem of using unpublished methodology, for which the Panel may not have the sufficient expertise or time to appraise thoroughly due to e.g. model complexity. In such situations, it could be considered to outsource the peer-review in e.g. a network of excellence in order to facilitate the Panels development of an opinion. External peer-review could also allow for increased use of quantitative and novel approaches and thus in general advance the development of QMRA methodologies which is desired.

Irrespective of the type of model used, it is important that the Panel is informed timely about the modelling approach, including the results of the scoping exercise, in order to be able to evaluate the approach (data, assumptions and methodology) before definitive conclusions are reached. Also peer-

reviewed models will need adaptations in order to be useful as they have been developed fit for purpose.

In conclusion, peer-review models are good but there is always need for new model development. Peer-review could be outsourced. While an open mind for new models is needed, a proper review of the modelling approach requires extra time. Hence, EFSA and its Scientific Panels and Committee should keep an open mind and welcome newer and smarter modelling approaches, and use them after a scientific review.

3.6. Data availability

The reliability of a QMRA also depends on the availability and quality of the data to be used as input parameters. Several methods have been described in literature to analyze the data quality. One approach, the Numerical Unit Spread Assessment Pedigree (NUSAP), has been applied in the study by Boone et al. (2009), for screening and evaluating the data quality of potential input parameters in a QMRA model on *Salmonella* in pork meat.

CONCLUSIONS AND RECOMMENDATIONS

GENERAL CONCLUSIONS:

- Models and modelling activities are likely to be at the core of the future EFSA scientific risk assessments, including those by the BIOHAZ Panel.

TOR 1: Describe successful approaches and challenges

- The use of quantitative models in risk assessments has enabled answers to questions linked to proportionate responses and/or balancing risks and costs.

- Compared to qualitative models, QMRA models have given better insights into and enabled quantitative predictions of the impact of interventions within the food chain. Expertise, data, as well as time and resources, have been limiting factors for QMRA exercises.

- QMRA is a developing field which creates methodological uncertainties and therefore preferences for types of models cannot be specified. New approaches need to be identified and considered.

- Fit for purpose and simplicity are key issues when developing QMRA models. However, limits on time and resources may restrict the model selection.

- A common approach is needed for documentation and quality assurance of the models, and guidelines for documentation and communication should be developed as a priority. The BIOHAZ Panel welcomes EFSA's initiative to establish a scientific network on the harmonisation of risk assessment methodologies.

TOR 2 - Suggest practical improvements, e.g. development of technical guidelines or a standard checklist for the technical specifications for outsourced modelling work

- Critical control points that should be considered in future risk assessment guidelines are

  - Process where mandates are defined and distributed to Panels;
  - Selection of modelling approaches to support answering the mandate
  - Decision on criteria for data inclusion and exclusion
  - Reviewing the results of the QMRA
  - Communication of the opinions to risk managers.

TOR 3 - Develop guidelines for transparent and consistent description of the models.

- The understanding of quantitative risk expressions and their associated uncertainties by both risk assessors and risk managers are crucial for the ability to ask informed risk assessment questions and to take informed risk management decisions.

RECOMMENDATIONS

- In order to better allocate resources for future QMRA models, it is essential to be pro-active. A dialogue between BIOHAZ Panel, EFSA, and EC on future biological hazards/food commodities combinations for risk modelling activities is therefore advantageous. This needs to be done before mandates are received, to facilitate the planning and allocation of resources for foreseen QMRA exercises.

- EFSA needs an early notification of mandates in which QMRA is considered to be included, as the QMRA process needs careful planning.

- Appropriate time for considering various modelling approaches and reviewing the model output should be foreseen and planned for.

- At the start, preferably before accepting the mandate, a scoping exercise is recommended. The scoping exercise could include an assessment of the mandate, possible interpretations of the terms of reference, deadlines, the modelling approaches possible and the data requirements. To support this process, a model catalogue could be developed.

- The modelling approach, including the results of the scoping exercise, should be discussed in the Panel early in the process. In particular the Panel has to be able to evaluate the approach before models are implemented.

- The choice of modelling approach is guided by the available data and insight in cause-effect relationships.

- When giving advice on proportionate response and/or balancing risks and costs, quantitative approaches should be preferred.

- The basis/assumptions of each quantitative expression should be clearly stated as well as the associated uncertainties.

- The model outputs should always be interpreted taking the assumptions and limitations into account.

- At the end of their mandates it is suggested that future EFSA Biological Hazards Panels reflects on the lessons learnt from the modelling and risk assessments. Both, QMRA as well as risk ranking exercises should be reviewed to create a learning process.

- EFSA models should be archived and, where appropriate, made available for scientific use.

- The EFSA Scientific Committee's recommendations for harmonisation of risk assessment terminology are endorsed.

- Certain expressions such as "negligible", "concern" and "unlikely" should be used carefully with scientific criteria and context clearly defined or avoided.

- Standard protocols for documentation and reporting should be developed and used when describing models, model input and output, and assumptions.

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APPENDICES

A. SCIENTIFIC OPINIONS ADOPTED BY THE BIOHAZ PANEL THAT USE QUANTITATIVE RISK ASSESSMENTS

1. Overview of BIOHAZ Opinions

Scientific Opinion on an estimation of the public health impact of setting a new target for the reduction of *Salmonella* in turkeys. Adopted: 08 March 2012. www.efsa.europa.eu/en/efsajournal/pub/2616.htm

Scientific Opinion on a quantitative estimation of the public health impact of setting a new target for the reduction of *Salmonella* in broilers. Adopted: 26 July 2011. www.efsa.europa.eu/en/efsajournal/pub/2106.htm.

Scientific Opinion on *Campylobacter* in broiler meat production: control options and performance objectives and/or targets at different stages of the food chain. Adopted: 10 March 2011. www.efsa.europa.eu/en/efsajournal/pub/2105.htm

Scientific Opinion on the revision of the quantitative risk assessment (QRA) of the BSE risk posed by processed animal proteins (PAPs). Adopted: 09 December 2010 www.efsa.europa.eu/en/efsajournal/pub/1947.htm

Scientific Opinion on a quantitative estimation of the public health impact of setting a new target for the reduction of *Salmonella* in laying hens Adopted: 11 March 2010 www.efsa.europa.eu/en/efsajournal/pub/1546.htm

Scientific Opinion on a Quantitative Microbiological Risk Assessment of *Salmonella* in slaughter and breeder pigs Adopted: 11 March 2010. www.efsa.europa.eu/en/efsajournal/pub/1547.htm

A quantitative microbiological risk assessment on *Salmonella* in meat Adopted: 24 January 2008. www.efsa.europa.eu/en/efsajournal/pub/625.htm

Opinion of the Scientific Panel on biological hazards (BIOHAZ) on the "Quantitative assessment of the human BSE risk posed by gelatine with respect to residual BSE. Adopted: 18 January 2006. www.efsa.europa.eu/en/efsajournal/pub/312.htm

Opinion of the Scientific Panel on biological hazards (BIOHAZ) on the on the “Assessment of the human and animal BSE risk posed by tallow with respect to residual BSE risk” Adopted: 28 April 2005 www.efsa.europa.eu/en/efsajournal/pub/221.htm

2. Terms of reference for some BIOHAZ opinions using QMRA

2.1. Scientific Opinion on an estimation of the public health impact of setting a new target for the reduction of *Salmonella* in turkeys.

The EFSA is asked:

- To indicate and rank the *Salmonella* serotypes with public health significance according to Appendix III of Regulation (EC) No 2160/2003,
- To assess the impact of a reduction of the prevalence of *Salmonella* in breeding flocks of turkeys on the prevalence of *Salmonella* in flocks of fattening turkeys,
- To assess the relative public health impact if a new target for reduction of *Salmonella* is set in turkeys being 1 % or less of flocks remaining positive for all *Salmonella* serotypes with public health significance.

The references for the two assessments mentioned above shall be:

- The theoretical prevalence at the end of the transitional period (1 % or less of flocks remaining positive for *Salmonella* Enteritidis and/or *Salmonella* Typhimurium), and
- The real prevalence in 2010 to be reported by the Member States.

2.2. Scientific Opinion on *Campylobacter* in broiler meat production: control options and performance objectives and/or targets at different stages of the food chain

EFSA is asked to further elaborate and update, in **a quantitative** way, its Opinion of the Scientific Panel on Biological Hazards related to *Campylobacter* in animals and foodstuffs, adopted on 27 January 2005 as regards broiler meat production.

In particular, EFSA is asked to:

1. Identify and rank the possible control options within the broiler meat production chain (pre-harvest, at harvest and post-harvest), taking into account the expected efficiency in reducing human campylobacteriosis. Advantages and disadvantages of different options should be considered.
2. Propose potential performance objectives and/or targets at different stages of the food chain in order to obtain e.g. 50% and 90% reductions of the prevalence of human campylobacteriosis in the EU caused by broiler meat consumption or cross-contamination. The performance objectives might include targets for reduction at pre-harvest and/or microbiological criteria for foodstuffs (qualitative or quantitative criteria for *Campylobacter* in general or for certain strains (e.g. species, resistant to certain antibiotics)). In addition, guidance should be given on a realistic time period needed to achieve these reductions, taking into account the outcome of (1).

2.3. Scientific Opinion on the revision of the quantitative risk assessment (QRA) of the BSE risk posed by processed animal proteins (PAPs).

In the summary to the opinion of the Scientific Panel on Biological Hazards (BIOHAZ) on the "**Quantitative risk assessment of the animal BSE risk posed by meat and bone meal with respect to the residual BSE risk**" (EFSA-Q-2003-099, July 2005) it was stated, that the QRA Report should be considered a dynamic document and, consequently, its content and data need to be reviewed periodically

The European Food Safety Authority is requested therefore to:

- To review and update the scientific input data of the **current QRA model**.
- If needed, to review the methodology and update the **current QRA model**.
- To review the cattle BSE risk posed by bovine derived processed animal proteins (PAPs) with respect to the residual BSE risk, based on the **outcome of the QRA**.

2.4. Scientific Opinion on a quantitative estimation of the public health impact of setting a new target for the reduction of *Salmonella* in laying hens

The EFSA is asked to **assess the relative public health impact** if a new target for reduction of *Salmonella* is set in laying hens being 1% or less remaining positive for all *Salmonella* serovars with public health significance, compared to:

- A theoretical prevalence of 2% of flocks remaining positive for *Salmonella* Enteritidis or *Salmonella* Typhimurium, and
- The real prevalence in 2008 to be reported by the Member States.

The *Salmonella* serotypes with public health significance should be determined by the EFSA taking into account the criteria laid down in Annex III to Regulation (EC) No 2160/2003.

2.5. Scientific Opinion on a Quantitative Microbiological Risk Assessment of *Salmonella* in slaughter and breeder pigs

The European Food Safety Authority is asked to carry out a **quantitative risk assessment** on *Salmonella* in slaughter and breeder pigs.

Slaughter pigs

The objective of this request is to carry out a quantitative assessment of the public health risk of the presence of *Salmonella* in slaughter pigs, including a quantitative estimation of the risk factors and the effect of mitigation options. The assessment should provide the input for a future cost/benefit analysis of setting a target for reduction in slaughter pigs at EU level.

A baseline study to collect comparable information on the prevalence of *Salmonella* in slaughter pigs in all Member States will be carried out from October 2006 until September 2007 in accordance with Decision 2006/668/EC8. The technical specifications were based on EFSA's proposal in Annex III to the opinion of the BIOHAZ Panel on *Salmonella* in pigs and involve bacteriological analyses of ileo-caecal lymph nodes at slaughter and serology on meat juice. The Community Reference Laboratory intends to also make comparative studies on different serological tests in 2007. Prevalence data from all Member States based on these two analyses seem therefore the most appropriate reference data if targets for reduction are considered. Using information from the baseline study, the data mentioned in section 1 and any other information considered relevant, a quantitative estimation at Community level is requested of:

- The relative contribution of *Salmonella* infections in slaughter pigs on *Salmonella* cases in humans. If an estimation of the influence of the prevalence of *Salmonella* in pigs at slaughter on human cases is not possible within the indicated time schedule, the influence on *Salmonella* prevalence in pig meat at retail should be estimated;
- The expected reduction of *Salmonella* cases in humans (or pig meat at retail) by a reduction (e.g. 5- or 10-fold) of *Salmonella* prevalence in slaughter pigs (based on bacteriology in lymph nodes or serology at slaughter);
- The sources of infection for fattening pigs at farm level;

- The reduction of the prevalence in slaughter pigs by the most important potential treatments or control measures at farm level:

- The impact of transport, lairage and slaughter processes on contamination of carcasses;

- The expected reduction of *Salmonella* cases in humans (or pig meat) by the most important potential control options during transport, at lairage or during the slaughter process.

All serotypes in pigs that are of human health significance should be considered together.

Breeder pigs

The objective of this request is to carry out a quantitative assessment on the risk of the presence of *Salmonella* in breeder pigs as a source of infection for slaughter pigs, including a quantitative estimation of risk factors and the effect of mitigation options. The assessment should provide the input for a future cost/benefit analysis of setting a target for reduction in breeder pigs at EU level.

A baseline study to collect comparable information on the prevalence of *Salmonella* in breeder pigs in all Member States is scheduled from October 2007 until September 2008. EFSA has been requested to propose technical specifications for such a baseline study. Using information from the baseline study and any other information considered relevant, a quantitative estimation at Community level is requested of:

- The relative contribution of *Salmonella* infections in breeder pigs on *Salmonella* prevalence in slaughter pigs (based on bacteriology in lymph nodes or serology at slaughter);

- The expected reduction of *Salmonella* prevalence in slaughter pigs (based on bacteriology in lymph nodes or serology at slaughter) by a reduction (e.g. 5- or 10-fold) of *Salmonella* prevalence in breeder pigs;

- The sources of infection for breeder pigs and piglets at farm level;

- The reduction of the prevalence in breeder pigs and piglets by the most important potential treatments or control measures at farm level.

All serotypes in pigs that are of human health significance should be considered together.

2.6. A quantitative microbiological risk assessment on *Salmonella* in meat

The European Food Safety Authority is asked to carry out a **quantitative risk assessment** and evaluate:

1. The relative contribution of different meat categories, such as carcasses, fresh meat and products thereof, minced meat and meat preparations to cases of food-borne *Salmonella* infections in humans, taking into account the occurrence of the pathogen in the food chain, risk factors, food production flows and food preparation and consumption habits. A distinction between meats derived from different species, such as bovine, porcine, poultry (if possible separately broilers and turkeys) and other possible species should be considered. In particular, the impact of the intended and common use of the abovementioned meat categories derived from different species should be taken into account as well as the impact of cross-contamination.

2. The impact of main factors along the food chain affecting the prevalence, growth and transmission of *Salmonella* in the above-mentioned meat categories and the related risk of human illnesses, in the light of prevalence data and epidemiological data to be supplied by the Member States.

2.7. Opinion of the Scientific Panel on biological hazards (BIOHAZ) on the "Quantitative assessment of the human BSE risk posed by gelatine with respect to residual BSE.

The European Food Safety Authority (EFSA) is invited to:

a) Assess the validity of the outcome of a **quantitative assessment of the residual BSE** risk in bovine derived products, carried out for gelatine, tallow and dicalcium phosphate from bones, tallow from fat tissues and tallow from rendered mixtures of tissues, and for the presence of small amounts of meat-and-bone meal in feeding stuffs intended for ruminants.

b) If the outcome is considered valid, review the following SSC opinions in the light of the QRA:

- Updated opinion and report on the safety of dicalcium phosphate (DCP) and tricalcium phosphate (TCP) from bovine bones, used as an animal feed additive or as fertiliser (submitted to the SSC at its meeting of 6-7 March 2003) (EC, 2003a).
- Updated opinion on the safety with regard to TSE risks of gelatine derived from ruminant bones or hides (adopted by the SSC at its meeting of 6-7 March 2003) (EC, 2003b).
- Opinion and report, assessment of the human BSE risk posed by bovine vertebral column including dorsal root ganglia (adopted on 16 May 2002) (EC, 2002).
- Revised opinion and report on the safety of tallow obtained from ruminant slaughter by-products (adopted on 28-29 June 2001, editorial clarifications introduced at the meeting of 6-7 September 2001) (EC, 2001a).
- Report and Scientific Opinion on mammalian derived meat and bone meal forming a cross-contaminant of animal feedstuffs adopted by the Scientific Steering Committee at its meeting of 24-25 September 1998 (EC, 1998).

c) Advise on how to **interpret the results of the calculation in view of making an estimation of the number of potential BSE and vCJD cases expected per year in a population**.

2.8. Opinion of the Scientific Panel on biological hazards (BIOHAZ) on the on the "Assessment of the human and animal BSE risk posed by tallow with respect to residual BSE risk"

The European Food Safety Authority (EFSA) is invited to:

a) Assess the validity of the outcome of a quantitative assessment of the residual BSE risk in bovine derived products, carried out for gelatine, tallow and dicalcium phosphate from bones, tallow from fat tissues and tallow from rendered mixtures of tissues, and for the presence of small amounts of meat-and-bone meal in feeding stuffs intended for ruminants.

b) If the outcome is considered valid, review the following SSC opinions in the light of the QRA:

- Updated opinion and report on the safety of dicalcium phosphate (DCP) and tricalcium phosphate (TCP) from bovine bones, used as an animal feed additive or as fertiliser (submitted to the SSC at its meeting of 6-7 March 2003) (EC, 2003a).
- Updated opinion on the safety with regard to TSE risks of gelatine derived from ruminant bones or hides (adopted by the SSC at its meeting of 6-7 March 2003) (EC, 2003b).

- Opinion and report, assessment of the human BSE risk posed by bovine vertebral column including dorsal root ganglia (adopted on 16 May 2002) (EC, 2002).

- Revised opinion and report on the safety of tallow obtained from ruminant slaughter by-products (adopted on 28-29 June 2001, editorial clarifications introduced at the meeting of 6-7 September 2001) (EC, 2001a).

- Report and Scientific Opinion on mammalian derived meat and bone meal forming a cross-contaminant of animal feedstuffs adopted by the Scientific Steering Committee at its meeting of 24-25 September 1998 (EC, 1998).

c) Advise on how to **interpret the results of the calculation in view of making an estimation of the number of potential BSE and vCJD cases expected per year in a population**.

B. QUESTIONNAIRE TO THE CHAIRS OF WG

Reflecting the experiences and lessons learnt from modelling/QMRA on biological hazards (EFSA-Q-2011-01174)

Title of the BIOLOGICAL HAZARDS OPINION:

Chair/rapporteur:

Quantitative microbiological risk assessments (QMRAs) are recommended by EFSA whenever feasible and practical to get more precise answers on microbial risks for food safety, and development of models is often an integral part of the quantitative analysis of scientific evidence in QMRA's. The mandates given to EFSA's BIOHAZ Panel by the European Commission increasingly ask for a quantitative evaluation of public health benefits and risks. But the issues of expediency, time pressure, limited resources, and the complexity of the models versus Occam's razor create challenges for all involved.

To help future Biological Hazards working groups in their work please consider following questions based on your experience in chairing the WG and preparing the opinions for adoption.

1. Please list the major strengths and weaknesses of using quantitative analyses and modelling for developing the opinion:

STRENGTHS	WEAKNESSES
1) 2) 3)	1) 2) 3)

2. Please list the major threats and opportunities you experienced when using quantitative analyses and modelling for developing the opinion:

Opportunities	Threats
1) 2) 3)	1) 2) 3)

3. Could you suggest criteria for when quantitative modelling is appropriate for answering a biological hazards question?

4. Could you suggest criteria for when qualitative approach is better suited for answering a biological hazards question?

5. Please, indicate how much you agree on the statement by a number from the scale 1 (fully agree) to 4 (fully disagree). Comments are welcome.

Statement	**Points (1-4)**
A quantitative assessment should be used whenever feasible to get more precise answers on microbial risks for food safety. Comment:	
A qualitative assessment should be used whenever expedient answers on microbial risks for food safety are required Comment:	
Occam's razor (the simple is always preferable to the complex, everything else being equal) should be the guiding principle for BIOHAZ Panel modelling exercises? Comment:	
The state of modelling used for risk assessments on biological hazards is sufficiently well established for producing guidelines Comment:	
Models identify important data gaps or deficits of knowledge and by doing so indicate future research priorities. Comment:	
Launching a modelling task is justifiable only if the resources and time are commensurate with the magnitude and complexity of the task Comment:	
Quantitative models are often novel, complex and not always peer-reviewed before being presented. Comment:	
The period between delivery of the model by the contractors and the adoption deadline for the opinion should be sufficient for a review of a model. Comment:	
The peer-review of a model should be the responsibility of the Panel Comment:	
Only peer-reviewed models should be used Comment:	
The Panel review of a model should be split into a technical part and a biological part Comment:	
Current modelling capacities and skills within EFSA are sufficient. Comments:	
The modelling results and uncertainties are understood by risk managers. Comment:	
Risk managers use the modelling results while making decisions. Comment:	
Communication is the biggest challenge in modelling. Comment:	

6. Which are the critical control points of a modelling exercise when using quantitative analyses and modelling for developing the opinion:

    a. The acceptance of the mandate and its deadline
    b. The design of the modelling exercise (interpretation TOR, TOR for outsourcing, interface, design of WG) after accepting the mandate
    c. Preparatory work (obtaining data, reviewing literature, team assignment...)
    d. Mathematical work (choosing the parameters, distribution curves, algorithms...)
    e. Drafting, reviewing and publishing the results (agreement on the outputs, conclusion...)
    f. Progress reports to the panel
    g. First reading of draft opinion
    h. Other points?

Comment:

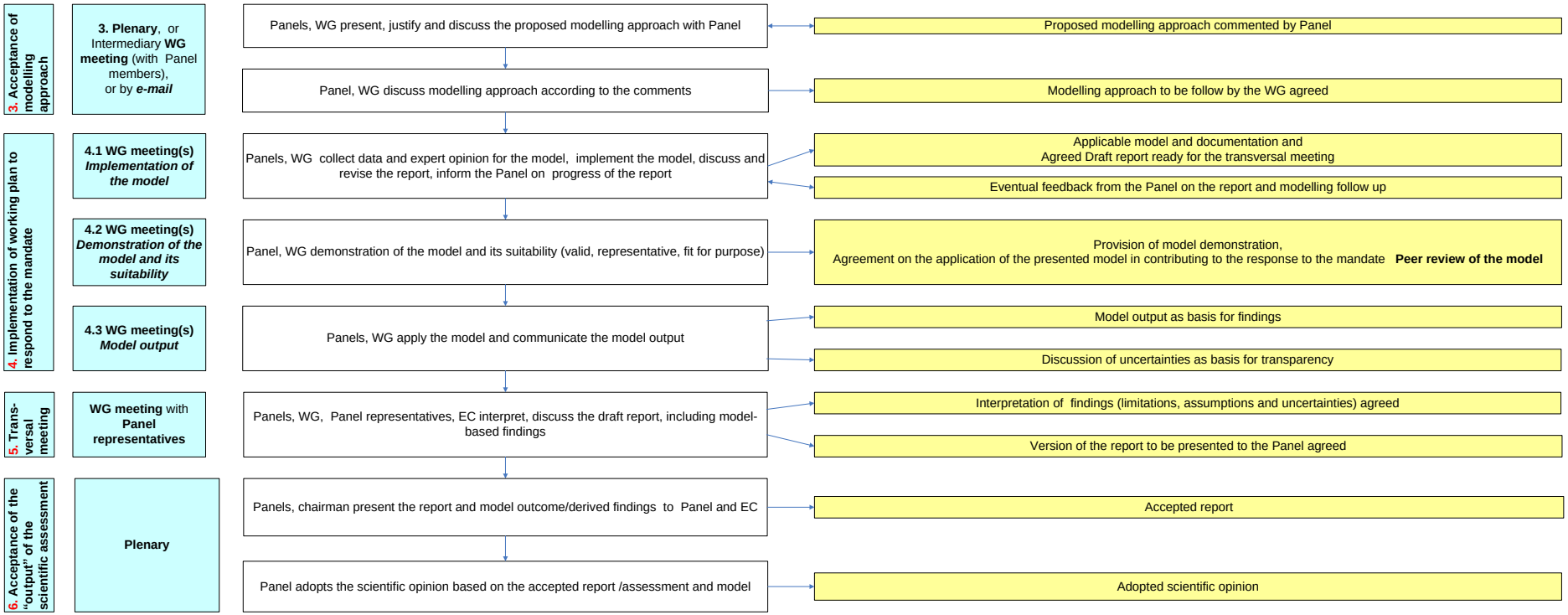
7. Based on your experience, what would be your advice to the new BIOHAZ Panel in order to use modelling in the best way?

Answer:

8. Have you experienced difficulties in understanding or communication quantitative risk assessment? Why? And what would you suggest to improve it?

Thank you very much for answering.

C. MODIFIED FLOWCHART BASED ON EFSA PANEL ON ANIMAL HEALTH AND WELFARE (AHAW), 2009


3. Acceptance of modelling approach
3. Plenary, or Intermediary WG meeting (with Panel members), or by e-mail
Panels, WG present, justify and discuss the proposed modelling approach with Panel
Proposed modelling approach commented by Panel
Panel, WG discuss modelling approach according to the comments
Modelling approach to be follow by the WG agreed
4. Implementation of working plan to respond to the mandate
4.1 WG meeting(s) Implementation of the model
Panels, WG collect data and expert opinion for the model, implement the model, discuss and revise the report, inform the Panel on progress of the report
Applicable model and documentation and Agreed Draft report ready for the transversal meeting
Eventual feedback from the Panel on the report and modelling follow up
4.2 WG meeting(s) Demonstration of the model and its suitability
Panel, WG demonstration of the model and its suitability (valid, representative, fit for purpose)
Provision of model demonstration, Agreement on the application of the presented model in contributing to the response to the mandate Peer review of the model
4.3 WG meeting(s) Model output
Panels, WG apply the model and communicate the model output
Model output as basis for findings
Discussion of uncertainties as basis for transparency
5. Trans-versal meeting
WG meeting with Panel representatives
Panels, WG, Panel representatives, EC interpret, discuss the draft report, including model-based findings
Interpretation of findings (limitations, assumptions and uncertainties) agreed
Version of the report to be presented to the Panel agreed
6. Acceptance of the "output" of the scientific assessment
Plenary
Panels, chairman present the report and model outcome/derived findings to Panel and EC
Accepted report
Panel adopts the scientific opinion based on the accepted report /assessment and model
Adopted scientific opinion

D. THE USE OF MODELLING BY DIFFERENT EFSA SCIENTIFIC PANELS/UNITS

This Chapter discusses the use of modelling by different EFSA Scientific Panels/Units sorted by subjects in the following alphabetical order:

1. Animal health and welfare
2. Biological monitoring
3. Contaminants
4. Dietary & chemical monitoring
5. Emerging risks
6. Feed
7. Food ingredients and packaging
8. GMO
9. Nutrition
10. Pesticides
11. Plant health
12. Scientific assessment support
13. Scientific Committee

All the examples of modelling mentioned in this Chapter have been published as opinions, guidance, scientific reports, external scientific reports, statements or technical reports as EFSA publications and are sorted in chronological order starting with the historically most distanced and finishing with the most recent ones. The criteria for mentioning an example was the search for word "model" on www.efsa.europa.eu/en/publications.htm

Modelling in the field of biological hazards has not been discussed in this Chapter as it has been widely discussed within the other Chapters of this document.

1. Animal Health and Welfare

The AHAW Panel has responded to two thirds of animal health related mandates using some kind of modelling. Every third opinion on animal health was supported by a quantitative model. These models range from simple to complex, employing a combination of scientific, economic, socio-economic, or other types of data.

The AHAW Panel has delivered a scientific opinion on the risk of bluetongue (BT) transmission during animal transit into and out of restricted zones (1) by using a model that suggests that increased treatment efficacy may lead to a reduction of the risk.

Furthermore, the AHAW Panel produced the scientific opinion on control and eradication of Classic Swine Fever in wild boar and animal health safety of fresh meat derived from pigs vaccinated against Classic Swine Fever (2). This opinion was followed by a simulation modelling approach developed to assess the risk of emergency vaccination on the safety of meat compared to the current control of CSF in domestic pigs without vaccination (3).

In this phase, the AHAW Panel developed a guidance document on Good Practice in Conducting Scientific Assessments in animal health using modelling (4). It was found to be necessary to describe and evaluate models that previously were applied in opinions adopted by the AHAW Panel (5). Therefore, a scientific review was undertaken on the past 31 animal health (AH) related opinions passed by the AHAW Panel. To summarise reviewed material, modelling tasks were classified in three categories (assessment of diagnostic test characteristics, disease transmission and end point quantification) and models in four categories (decision tree models, compound probability, meta-analysis and spread models). The review revealed that modelling was frequently applied to substantiate the AHAW Panel's opinions. The main purpose of modelling was to improve understanding.

Recently, the risk of African Swine Fever virus (ASFV) was assessed by using the model that considered factors affecting spread of the disease and assessed the impact of preventive and control measures (6).

A scientific opinion was prepared in order to determine the magnitude, distribution, impact and significance of infection and disease in domestic ruminants and humans, risk factors for the maintenance (in domestic ruminant populations) and spill over (from these populations to humans) of *Coxiella burnetii* (the causative agent of Q fever), and control options in domestic ruminant populations (7).

Lately, an external report was published with the objective to assist a working group (WG) of the AHAW Panel in developing a generic stochastic model of the meat inspection system for swine and to investigate the probability of detection of specific diseases/conditions within that system (8).

1. Risk of Bluetongue Transmission in Animal Transit - Scientific Opinion of the Panel on Animal Health and Welfare
   Scientific Opinion of the AHAW Panel - Published: 18 November 2008
2. Control and eradication of Classic Swine Fever in wild boar
   Scientific Opinion of the AHAW Panel - Published: 30 January 2009
3. Animal health safety of fresh meat derived from pigs vaccinated against Classic Swine Fever
   Scientific Opinion of the AHAW Panel - Published: 3 July 2009
4. Good Practice in Conducting Scientific Assessments in Animal Health using Modelling
   Guidance of the AHAW Panel - Published: 22 December 2009
5. External report reviewing the previous AHAW opinions
   External Scientific Report - Published: 11 March 2010
6. African Swine Fever
   Scientific Opinion of the AHAW Panel - Published: 22 March 2010
7. Q fever
   Scientific Opinion of the AHAW Panel - Published: 12 May 2010
8. Contribution of meat inspection to animal health surveillance - Swine
   External Scientific Report - Published: 3 October 2011

2. Biological monitoring

The report of the Task Force on Zoonoses Data Collection on proposed technical specifications for a coordinated monitoring programme for *Salmonella* and *Campylobacter* in broiler meats at retail in the EU proposed a modelling and simulation approach to be used in the analyses of the results in order to assess the effectiveness of implementation of Community *Salmonella* criteria for broiler meats (1).

For the purposes of estimation of the relative contribution of different food and animal sources to human *Salmonella* infections in the European Union, the microbial sub typing model for source attribution was applied to data from 24 Member States (MSs) and attributed human sporadic salmonellosis to four animal reservoirs: pigs, broilers, layers and turkeys (2).

Several statistical methodologies useful for the evaluation of the *Salmonella* reduction targets in breeding and laying hens of *Gallus gallus* have been assessed using data aggregated at country-level, as well as sample-level data (3). These analyses consisted primarily of logistic regression models incorporating a linear, as well as a quadratic, trend in time.

An extensive examination of the merits of the various methodologies considered is provided in the report dealing with the development of statistical methods for the evaluation of data on antimicrobial resistance in bacterial isolates from animals and food (4). Recommendations for the modelling approaches used here, as well as for the proposed alternative modelling strategies, are given in the recommendations section.

1. Report of Task Force on Zoonoses Data Collection on proposed technical specifications for a coordinated monitoring programme for *Salmonella* and *Campylobacter* in broiler meats at retail in the EU
   Scientific Report of EFSA - Published: 2 September 2008
2. Estimation of the relative contribution of different food and animal sources to human *Salmonella* infections in the European Union
   External Scientific Report - Published: 25 August 2011
3. Statistical Evaluation of the Achievements by Member States of the EU *Salmonella* Reduction Targets in Animal Populations
   External Scientific Report - Published: 5 December 2011
4. Development of statistical methods for the evaluation of antimicrobial resistance data in bacterial isolates from animals and food
   External Scientific Report - Published: 6 December 2011

3. Contaminants

Model calculations on the carry-over of aflatoxins present in feedstuff into milk were used in order to assess Aflatoxin B1 as undesirable substance in animal feed (1).

Tolerable weekly intake for cadmium was assessed by two primary components, a concentration-effect model that relates the concentration of cadmium in urine to that of B2M, and a toxico-kinetic model that relates urinary cadmium concentration to dietary cadmium intake.

1. Opinion of the Scientific Panel on contaminants in the food chain [CONTAM] related to Aflatoxin B1 as undesirable substance in animal feed
   Scientific Opinion of the CONTAM Panel - Published: 19 March 2004
2. Tolerable weekly intake for cadmium
   Statement of the CONTAM Panel - Published: 3 February 2011

4. Dietary & chemical monitoring

The Technical Working Group on Data Collection (TWG-DC) developed a guideline on the standard description of samples and analytical results (Standard Sample Description) (1). This work intended to develop a generalised model to harmonise the collection of a wide range of measurements in the area of food and feed safety assessment.

Long-term dietary exposure to lead (2) and chromium (3) in young children living in different European countries were assessed by using two different models for the calculations: the stochastic beta-binomial-normal (BBN) model and the deterministic observed individual means (OIM) model.

With the assistance of the Technical Working Group on Data Collection, EFSA has developed two guidance documents to facilitate the exchange of data between Member States and EFSA (4). These two guidance documents are intended to provide the basis for a general model to harmonise the collection and transmission of a wide range of measurements in the area of food and feed safety assessment.

Within the EFSA Article 36 project “European Tool Usual Intake” (ETUI) a workshop was organised in May 2010 where the different available models to calculate usual intake were presented and discussed (5). The purpose of the workshop was to evaluate existing statistical methods for estimating usual intake with respect to a number of criteria, so that the performance of each method on each criterion will be well understood after the workshop.

Following the results on acrylamide levels in food from monitoring years 2007-2009 and exposure assessment a mixed effect model was used to evaluate time trend changes in acrylamide levels in defined food groups (6)

.EFSA has prepared a standard data model for the transmission of chemical occurrence data and pesticide residues. This model is referred to as the "Standard Model" (SM) or the "Standard Sample Description" (SSD) (7). As mentioned, building a European database on chemical contaminants in food and feed is a fundamental component of European risk assessment. Implementation of the Standard Sample Description and the XML transformation model is very important in this process (8).

1. Standard sample description for food and feed
   Guidance of EFSA - Published: 29 January 2010
2. Long-term dietary exposure to lead in young children living in different European countries
   External Scientific Report - Published: 10 May 2010
3. Long-term dietary exposure to chromium in children living in Europe
   External Scientific Report - Published: 17 May 2010
4. Guidance on Data Exchange
   Guidance of EFSA - Published: 5 November 2010
5. Statistical modelling of usual intake
   External Scientific Report - Published: 8 December 2010
6. Monitoring of acrylamide levels in food
   Scientific Report of EFSA - Published: 20 April 2011
7. Electronic Transmission of Chemical Occurrence Data
   External Scientific Report - Published: 3 May 2011
8. Electronic Transmission of Chemical Occurrence Data
   External Scientific Report - Published: 11 May 2011

5. Emerging risks

Very recently, an inventory and modelling of the factors influencing the emergence of AFs in maize, wheat and rice crops in EU due to climate change, as well as the production of maps to highlight predicted AF contamination in these crops was requested. Therefore, the aim of the study (1) was to evaluate the scientific literature related to AF contamination in wheat, maize and rice, and to develop predictive models and draw maps of potential AF contamination in these crops in EU.

1. MODMAP-AFLA
   External Scientific Report - Published: 23 January 2012

6. Feed

A tolerance study was designed as a Latin square model in order to evaluate the safety of product 'Yea Sacc' for Leisure horses (1).

The problem of lacking information about used models was stressed by the FEEDAP panel while estimating environmental impact of Astaxanthin-rich Phaffia rhodozyma (Ecotone®) as feed additive (2). As no details are given on the model used and the assumptions made, the FEEDAP Panel (Panel on Additives and Products or Substances used in Animal Feed) was unable to verify whether the calculated value reflects a realistic concentration.

A model calculation with fish meal content in the diet was developed by the FEEDAP panel while estimating the safety and the efficacy of product "KDF Preservative" (3).

The safety of a copper chelate of hydroxy analogue of methionine (Mintrex®Cu) as feed additive for all species was estimated by the FEEDAP Panel by using a model calculation based on SCOOP food consumption data (4).

A complex modelling approach was used for assessing the risks of inputs of Cu and Zn from livestock treatments (5). The assessment utilised the Intermediate Dynamic Model for Metals (IDMM) and soil/agriculture and water chemistry scenarios that were selected to represent the agri-environment conditions that are likely to be experienced across European Member States.

The external report which evaluates the results of bibliographic review on the potential of microorganisms, microbial products and enzymes to induce respiratory sensitization (6) has indicated that there is currently no established model to predict the allergenicity of a molecule. Although *in-silico* models can be useful to predict cross-reactivity between allergens, they do not take into account phenomena like the context of presentation of the antigen to the immune system. There is no reliable, predictive *in-vitro* or *in-vivo* model of allergenicity.

1. Opinion of the Scientific Panel on additives and products or substances used in animal feed (FEEDAP) on a request from the Commission on the safety of product 'Yea Sacc' for Leisure horses.
   Scientific Opinion of the FEEDAP Panel - Published: 3 March 2004
2. Opinion of the Scientific Panel on additives and products or substances used in animal feed (FEEDAP) on environmental impact of Astaxanthin-rich Phaffia rhodozyma (Ecotone®) as feed additive in accordance with Council Directive 70/524/EEC.
   Scientific Opinion of the FEEDAP Panel - Published: 2 April 2004
3. Opinion of the Scientific Panel on additives and products or substances used in animal feed (FEEDAP) on the safety and the efficacy of product "KDF Preservative"
   Scientific Opinion of the FEEDAP Panel - Published: 16 December 2004
4. Mintrex®Cu for all species
   Scientific Opinion of the FEEDAP Panel - Published: 30 November 2009
5. Pre-assessment of environmental impact of copper and zinc
   External Scientific Report - Published: 29 October 2010
6. Enzymes and microorganisms as respiratory sensitizers
   External Scientific Report - Published: 29 October 2010

7. Food ingredients and packaging

The CEF Panel concluded that the SMK-TAMDI and SMK-EPIC methods were suitable for assessing the dietary exposure to smoke flavourings used or intended for use in or on foods (1). Smoke Flavouring EPIC model (SMK-EPIC), makes use of the information on the consumption of smoked foods available from the European Prospective Investigation into Cancer and Nutrition (EPIC) study.

The safety of heme iron (blood peptonates) for the proposed uses as a source of iron added for nutritional purposes to foods for the general population, including food supplements was estimated by using epidemiological and animal model studies which suggested that a high intake of heme iron may be associated with an increased risk of colon cancer (2).

The safety evaluation of allyl isothiocyanate for the proposed uses as a food additive was based on the more refined model, resulting in a two to four-fold exceeding of the ADI in children, and up to eight-fold exceeding in the case of 95th percentile adult consumers (3).

Two different exposure assessment models namely the Smoke Theoretical Added Maximum Daily Intake (SMK-TAMDI) and the smoke flavouring EPIC model (SMK-EPIC) were used by the CEF Panel while evaluating the Safety of smoke flavour Primary Product Zesti Smoke Code 10 (4). These methodologies were developed by the Panel specifically for smoke flavourings and they were applied while estimating the safety of smoke flavour Primary Product Fumokomp, as well (5).

1. Dietary exposure assessment methods for smoke flavouring Primary Products[1]
   Opinion of the Scientific Committee/Scientific Panel - Published: 6 April 2009

2. Safety of heme iron (blood peptonates) as a source of iron added for nutritional purposes to foods for the general population, including food supplements
   Opinion of the Scientific Committee/Scientific Panel - Published: 27 April 2010
3. Safety of allyl isothiocyanate as a food additive
   Opinion of the Scientific Committee/Scientific Panel - Published: 22 December 2010
4. Zesti Smoke Code 10 - 2011 Update
   Opinion of the Scientific Committee/Scientific Panel - Published: 27 July 2011
5. Fumokomp - 2011 Update
   Opinion of the Scientific Committee/Scientific Panel - Published: 27 July 2011

8. GMO

The GMO Panel stressed in the technical report Statistical considerations for the safety evaluation of GMOs: response to the public consultation (1) that there will be even more problems that are linked to the challenge of model fitting. It may be more advisable not to recommend a specific modelling approach, but rather to define what an analysis should demonstrate.

EFSA asked its Panel on GMO to investigate whether more detailed guidance could be provided regarding the performance of field trials and the analysis of data using appropriate statistical models, with the objective of ensuring a more uniform approach and greater transparency in risk assessment of GMOs. In order to carry out this investigation, the GMO Panel has convened a dedicated statistics Working Group who addressed the issue (2).

The mathematical model, developed for maize MON 810, was recalibrated and extended by GMO Panel in order to estimate the efficacy of certain mitigation measures concerning the evaluation of the environmental risk assessment and risk management recommendations on insect resistant genetically modified maize 1507 (3) and maize Bt11 (4) for cultivation.

1. Public Consultation on the statistical considerations for GMOs safety
   Technical report - Published: 31 July 2009
2. Statistical considerations for GMOs safety
   Scientific Opinion of the GMO Panel - Published: 1 February 2010
3. Scientific Opinion updating the evaluation of the environmental risk assessment and risk management recommendations on maize 1507 for cultivation
   Scientific Opinion of the GMO Panel - Published: 18 November 2011
4. Statement supplementing the evaluation of the environmental risk assessment and risk management recommendations on maize Bt11 for cultivation
   Statement of the GMO Panel - Published: 8 December 2011

9. Nutrition

An animal model was used by the Scientific Panel on Dietetic products, nutrition and allergies [NDA] related to the evaluation of goats' milk protein as a protein source for infant formulae and follow-on formulae (1), as well as related to notification from DWV and VINIFLHOR on fish gelatine or isinglass used as fining agents in wine pursuant to Article 6 paragraph 11 of Directive 2000/13/EC - for permanent exemption from labelling (2).

1. Opinion of the Scientific Panel on Dietetic products, nutrition and allergies [NDA] related to the evaluation of goats' milk protein as a protein source for infant formulae and follow-on formulae
   Scientific Opinion of the NDA Panel - Published: 10 March 2004
2. Opinion of the Scientific Panel on Dietetic Products, Nutrition and Allergies related to a notification from DWV and VINIFLHOR on fish gelatine or isinglass used as fining agents in

wine pursuant to Article 6 paragraph 11 of Directive 2000/13/EC - for permanent exemption from labelling

Scientific Opinion of the NDA Panel - Published: 23 August 2007

10. Pesticides

While developing a Guidance Document on Pesticide Exposure Assessment for Workers, Operators, Bystanders and Residents, the Panel on Plant Protection products and their Residues stressed that the current method of risk assessment is not completely satisfactory (1). For some exposure scenarios, the empirical data underpinning exposure estimates are sparse, making the estimates less reliable statistically. For others, more than one model may be available with which to estimate exposures, and where this occurs, there can be inconsistency between the approaches adopted by regulatory authorities.

Within the process of selection of scenarios for exposure of soil organisms to plant protection products, a simplified model was selected to generate maps of the concentration in total soil and the concentration in the liquid phase over the entire area of annual crops in the three zones (2).

The FOCUS PEARL model was parameterized to perform simulations for Plant Protection Product (PPP) emissions from greenhouses to surface water, after application to a tomato crop (3).

As part of the revision of the Guidance Document on Persistence in Soil (9188/VI/97 rev 8 published in 2000), the PPR-panel was asked to start the development of tiered exposure-assessment approaches for soil organisms in which European exposure scenarios play an important role. The Panel therefore contributed to this revision by developing a systematic approach to the selection of realistic worst-case scenarios for exposure of soil organisms to substances in soil. The scenarios are part of a tiered approach. Tier 1 is proposed to be based on a simple analytical model. Tier 2 is to be based on simulations with the numerical fate models PEARL and PELMO (4).

The PPR Panel carried out a public consultation on its draft Guidance Document (GD) for evaluating and using results of field persistence and soil accumulation experiments for exposure assessment of soil organisms to substances in soil (5). The half-life was stressed as an important input parameter in model simulations of the exposure of organisms in soil and therefore this guidance is an important part of this revised methodology.

Current numerical models used for simulating behaviour of plant protection products in soil in the context of the EU regulatory exposure assessment are unable to describe satisfactorily the daily fluctuations of the soil temperature and of the volume fraction of water in the top millimetres of soil (6). The Panel recommends research is conducted to further improve the reliability of mechanistic models for simulating loss processes at the soil surface especially for photo degradation and volatilisation.

Within the estimation/calculation of emissions of plant protection products from protected crops greenhouses and cultivations grown under cover) to support the Development of risk assessment methodology under Council Directive 91/414/EEC and EU regulation 1107/2009 (EC) it was stressed that the uncertainties and limitations inherent in the assessment must be considered and additional model simulations are needed to test the validity of the conclusions drawn here for a wider range of conditions (7).

The parameterisation of realistic worst-case scenarios for Tier-1 and Tier-2A simulations was described which are part of a tiered approach (8). In order to have a sufficient overview on the differences between simulations performed with the analytical Tier-1 model and the numerical Tier-2A models, PEARL and PELMO test runs were performed covering all relevant substance properties and all evaluation depths.

1. Preparation of a Guidance Document on Pesticide Exposure Assessment for Workers, Operators, Bystanders and Residents
   Scientific Opinion of the PPR Panel - Published: 18 February 2010
2. Selection of scenarios for exposure of soil organisms
   Scientific Report of EFSA - Published: 16 June 2010
3. PPP emissions from greenhouses
   Scientific Report of EFSA - Published: 31 August 2010
4. Request for scientific information for the revision of the Guidance Document on Persistence in Soil under Council Directive 91/414/EEC(Sanco/9188VI/1997 of 12 July 2000)
   External Scientific Report - Published: 25 November 2010
5. Outcome of the Public Consultation on the DRAFT Guidance for evaluating and using results of field persistence and soil accumulation experiments
   Technical report - Published: 16 December 2010
6. Guidance to obtain DegT50 values in soil
   Guidance of the PPR Panel - Published: 16 December 2010
7. Emissions of PPP from protected crops
   External Scientific Report - Published: 2 May 2011
8. Parameterisation of scenarios for exposure of soil organisms
   Scientific Report of EFSA - Published: 13 January 2012

11. Plant health

The Panel on Plant Health reviewed pathway scenarios; model and parameters used for a quantitative pathway analysis of the likelihood of *Tilletia indica* M. introduction into EU with importation of US wheat and found several shortcomings regarding model equations and parameter values, particularly a lack of scientific evidence for the infection threshold (1).

The scientific opinion of the Panel on Plant Health on the technical file submitted by the US Authorities to support a request to list a new option among the EU import requirements for wood of *Agrilus planipennis* host plants was based on a Probit regression model (2).

1. *Tilletia indica* quantitative pathway analysis
   Scientific Opinion of the PLH Panel - Published: 18 June 2010
2. Evaluation of *Agrilus planipennis* heat treatment proposal from USA
   Scientific Opinion of the PLH Panel - Published: 8 July 2011

12. Scientific assessment support

Bayesian meta-analysis and hierarchical modelling was used to build an overall dose-effect relationship accounting for inter-study heterogeneity and for inter-individual variability of dose and effect within the meta-analysis of Dose-Effect Relationship of Cadmium for Benchmark Dose Evaluation (1).

The technical report on Data Collection of Existing Data on Protected Crop Systems in the European Member States - Coding Manual stressed that in order to establish a common inventory; a harmonized data model has to be defined (2).

Within the quantitative risk assessment of *Salmonella* Enteritidis in shell eggs in Europe and in order to assess the impact on public health of various *Salmonella* flock prevalence (i.e. observed and targets), a quantitative model was developed (3).

The main purpose of the Model-based comparative assessment of the Australian and European hygiene monitoring programmes for meat production was to quantitatively compare the efficiency of

the microbiological monitoring programmes at process level of Australia and Europe, using a model-based approach (4).

Within the Statistical re-analysis of the Biel maze data of the Stump et al (2010) study: "Developmental neurotoxicity study of dietary bisphenol A in Sprague-Dawley rats" the time to escape was analysed using 4 time to event models, namely, the semi-parametric frailty model (main model), the parametric frailty model, the semi-parametric marginal model and the parametric marginal model (5).

For the purposes of Comparison of the Approaches Taken by EFSA and JECFA to Establish a HBGV for Cadmium modelling was done using summary measures (geometric mean and standard deviations) (6).

The Assessment Methodology Unit was asked to contribute to the analysis of the results of the EU baseline survey on the prevalence of *Salmonella spp*. in broiler carcasses at slaughterhouse level, after chilling but before further processing, by building, developing and validating a model to assess the impact of *Salmonella spp*. on the probability of meeting the Microbiological Process Hygiene Criteria (7).

1. Meta-analysis of Dose-Effect Relationship of Cadmium for Benchmark Dose Evaluation [1]
   Scientific Report of EFSA - Published: 31 March 2009
2. Data Collection on Protected Crop Systems – Coding Manual
   Technical report - Published: 30 March 2010
3. Quantitative risk assessment of *Salmonella* Enteritidis in shell eggs
   Scientific Report of EFSA - Published: 20 April 2010
4. Model-based comparative assessment of the AU and EU monitoring programmes
   Scientific Report of EFSA - Published: 7 June 2010
5. Statistical re-analysis of the Biel maze data of the Stump et al (2010) study: "Developmental neurotoxicity study of dietary bisphenol A in Sprague-Dawley rats"
   Scientific Report of EFSA - Published: 30 September 2010
6. Comparison of the Approaches Taken by EFSA and JECFA to Establish a HBGV for Cadmium
   Scientific Report of EFSA - Published: 8 February 2011
7. Simulation-based assessment on Microbiological Process Hygiene Criteria
   Scientific Report of EFSA - Published: 18 February 2011

13. Scientific Committee

The aim of the project Applicability of physicochemical data, QSARs and read-across in Threshold of Toxicological Concern assessment (1) was to investigate how the applicability of TTC schemes could be improved by incorporating physicochemical data (both experimental and predicted), as well as toxicity data generated by non-testing methods such as Quantitative Structure-Activity Relationships (QSARs), experts systems and read-across within structurally related chemical groups. One oft he main objectives was investigation of the possible use of physicochemical data and predicted toxicity data generated by QSARs by refinement of the Cramer classification scheme by statistically based methods, e.g. identification of structural subclasses within Cramer class I and III and development of a ranking classification model.

1. Applicability of physicochemical data, QSARs and read-across in TTC assessment
   External Scientific Report - Published: 23 June 2011