Opinion of the Scientific Panel on Animal Health and Welfare on the "Framework for EFSA AHAW Risk Assessments"[1]

(Question N° EFSA-Q-2006-059)

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1. Introduction and the aim of this document

One of EFSA's main missions is to provide scientific opinions and advice regarding risks associated with food and feed, animal health, and animal welfare using an approach referred to as risk assessment (RA). RA can be defined as the process of evaluating the likelihood of a specific hazard causing a particular adverse event and its associate consequences.

The aim of this document is to provide a framework which EFSA's Animal Health and Welfare Panel (AHAW) need to consider, when undertaking RAs involving animals, or the importation of their products, in addition to those 'official' guidelines already in existence.

 The AHAW panel may be asked to produce an opinion on the risks in any one of three distinct situations, these being:
- The risks of introduction and spread of infection and disease from importation of live animals (and their products) to the MS
- The risks of spread of infection and disease to live animals from disease endemic in the EU
- The risks of poor welfare in animals either during importation to the EU or within the EU

This paper focuses specifically on guidelines for RAs in these three situations. However, with respect to producing comprehensive guidelines for animal welfare RAs, further work is required, and this paper gives only some preliminary suggestions, in order to facilitate the next stage. It should be noted that, when applicable (i.e. when required by the mandate), the assessment of risks from infection, disease and to welfare, should be done simultaneously and in an integrated way.

The AHAW Panel reports and opinions on disease and welfare matters are not solely risk assessments. Some factors considered have beneficial effects for the animal in reducing disease and improving welfare in various ways, as explained in Chapter 6.

(Note added at publication: This report was largely completed in January 2007 at which point it represented the state of the art in the development of EFSA animal welfare risk assessments, but was not adopted and published until July 2007. During this period however, developmental work on risk assessment methodology applied to animal welfare continued, and at the time of publication further developments and modifications had been made.)

Specific guidelines have been produced by the World Organization for Animal Health (**OIE**) for the analysis and assessment of risks when importing live animals and their products (http://www.oie.int/eng/publicat/ouvrages/A_IRAvol1.htm, OIE 2004a and 2004b). This includes risks from pathogens, toxins and chemicals (see also MacDiarmid and Pharo, 2003).

With respect to risks from endemic diseases, and risks to animal welfare, no specific international guidelines on RAs exist. Although numbers of endemic disease RAs have been undertaken using the OIE Import RA Guidelines, very few formal RAs have been made for animal welfare by any method.

However, since the principles behind any risk assessment are broadly similar and based on logic chains of events or pathways, guidelines already in existence for specific situations can

be adapted for risk assessments in other situations. For example, in microbiological RAs for food, the framework developed by Codex Alimentarius is often used (Codex Alimentarius guideline on risk assessment in food http://www.codexalimentarius.net/download/standards/357/CXG_030e.pdf and SSC, 2003), and this approach has also been suggested by the OIE for issues involving antibiotic resistance (http://www.oie.int/eng/publicat/rt/2003/a_r20314.htm (Vose *et al.*, 2001). However, challenges in conducting such assessments have been reviewed by Snary *et al.* (2004). Despite some differences in detail, underlying principles are the same and can therefore also be applied e.g. on risks to animal welfare.

The conduct of any RA requires availability of appropriate and adequate data, and this may be difficult to obtain. Also, the process and model production (the model, whether qualitative or quantitative, being the delineation of the series of steps needed, given the defined hazard, for the unwanted outcome to occur), can be very resource-intensive and can become a major challenge. It is therefore considered relevant to complement and use with and alongside the already existing OIE code which is also supported by the EFSA Risk Assessment Colloquium held in December 2004. The creation of an appropriate guidance document has also been recommended in a recent EFSA report regarding quantitative microbiological RA for assessing risks to humans from items intended as human foods (Havelaar, 2005), generally undertaken under the WHO guidelines. As indicated earlier, the current paper does not focus on this type of RA. However, reference is made to aspects which both have in common.

2. Comparison of terminology used in the fields of animal disease and microbiological risk assessment

Whereas risk assessment terminology is well established (OECD, 2003), the terms used in the areas of microbiological food safety and animal disease imports differ somewhat. This has been reviewed by Vose *et al.* (2001), who compares the terminologies used in the two systems. This is itself a summary of a personal communication by Wooldridge (2000) (Annex 1). Table 1, which is based on this personal communication, highlights the main differences, but a full explanation is given in Annex 1.

Although RAs using the WHO (Codex) guidelines are not specifically considered further in this framework this section is included since their alternative terminology is often encountered. This section is therefore included to assist those who come across it.

No specific guidelines, and thus no specific terminology, are yet available for comparison for animal welfare RAs.

Table 1. A comparison of the terminology used in microbial food safety and animal disease import risk analysis and risk assessment

Microbiological food safety (Codex guidelines)	Import of animals and their products (OIE guidelines)
System & model on which the guidelines are based	

US NAS system & model	Covello-Merkhofer system & model
Processes included within Risk Analysis in the guidelines being described	
	Hazard Identification
Risk Assessment	Risk Assessment
Risk Management	Risk Management
Risk Communication	Risk Communication
Processes necessary to undertake a Risk Assessment in the guidelines being described, and their meaning	
	• **Hazard identification** Identifying 'risk agents' (hazards) and the conditions under which they potentially produce adverse consequences
Risk assessment, comprising:	**Risk assessment, comprising:**
• **Hazard identification:** Determining whether a specified chemical causes a particular health effect	• **Risk release assessment:** Assessing the potential of a risk source to introduce 'risk agents' (hazards) to the environment under consideration
• **Dose-Response Assessment (Hazard characterisation):** Determining the relationship between the magnitude of exposure and the probability of health effects	• **Exposure assessment:** Assessing the probability of exposure to 'risk agents' (hazards) resulting from specified release conditions
• **Exposure assessment:** Determining the extent of human exposure before and after regulatory controls	• **Consequence assessment:** Assessing the relationship between exposures to 'risk agents' (hazards) and health and environmental consequences
• **Risk characterisation:** Describing the nature and magnitude of human risk, including uncertainty	• **Risk estimate:** Estimating the timing, likelihood, nature and magnitude of adverse consequences

The hazard characterisation in microbiological food safety and the consequence assessment both deal with the effects of exposure. Hence, whereas there are differences in the terms that are used, ultimately the two approaches include components that are very similar:
- a hazard which must be 'released' e.g. influenza virus in wild birds;
- exposure to that hazard e.g. domestic birds exposed to faeces containing the virus;
- consequences from exposure e.g. infection (initial consequence) and further subsequent consequences e.g. illness, death, spread including other host species, etc.

These elements are then integrated in an overall risk assessment, in both the OIE and Codex systems.

3. General guidelines followed by EFSA AHAW risk assessments

3.1 Outline of steps recommended

Figure 1 gives a general guide to the steps recommended for undertaking RAs in any of the three areas indicated in section 1 above. Further details to assist with these steps are given following Figure 1. Whilst from this diagram this appears to be a linear chain of events it should be appreciated that many of the steps are iterative processes that would be dependent for revision on subsequent steps. It should also be clear that the steps in this figure are all related to one or more of the processes required for a risk analysis as given in Table 1, i.e. all are included in one or more of the processes of risk management, risk communication, hazard identification, and risk assessment.

Initial question(s) posed
by risk manager

Preliminary interaction
between risk manager and risk assessor

Includes:
- **Initial examination of question posed, discussion and agreement with risk manager**
- **Decision on the approach to be taken** *(But these may need revisiting after preliminary information gathering (iterative approach)*
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Next actions by risk assessor
- **Preliminary information gathering**
- **Establishment of 'risk profile'**
- **Assessment of the gaps in knowledge**
- **Determine type of risk assessment, resources required & response timeline**

Conduct a risk assessment
- **Establish risk pathways**
- **Collect and select data; perform any required statistics and formatting on raw data**
- **Assess risk utilizing either qualitative and/or quantitative approach**
- **Assessment of uncertainties**
- **Answer to the risk question(s), in form relevant to risk question and risk managers**

Evaluate and communicate results
- **Peer review of model**
- **Discuss results and address any additional requests (estimate additional resources and new timeline)**
- **Generate report**
- **Obtain feedback on implementation from risk manager**

Figure 1. Stages/phases recommended in this risk assessment guidance document

3.2 Examination of the question posed by the risk manager

In the initial stage of a RA the objectives and the scope of the task at hand are defined. The **risk manager** has a primary responsibility in the construction of the risk question(s). As several agencies may share responsibility for control of the disease(s) or welfare risks under consideration, it is important to identify at the onset all the risk managers and who may have primary roles for the question at hand. For EFSA, this is, or includes, the EU Commission.

The **risk assessor** deals with the RA process. There is a need for the risk assessor who is being requested to carry out a RA to discuss with, and seek a common understanding with, the risk manager for both the question posed and the expectation about the outcome of the RA process. This may be an iterative process, and the specific risk question may need to be amended once the further information becomes available during the RA process. Within EFSA, the risk assessor means the working party undertaking a risk assessment.

To determine the risk question, there is a need to have a clear definition of both the hazard of interest, and the consequence(s) of interest. Is the hazard of interest all species of a bacterial genus? Or all serotypes of a virus? Is it the infection or the disease that is the consequence of interest?

The nature of the hazard merits careful consideration. In the OIE system the hazard is defined as a pathogen (or toxin/chemical); in other systems the definition may be broader to include situations or events, including those which may affect animal welfare. Defining the consequences of interest also require thought. Some micro-organisms are highly infectious and others are much less so. In the latter case disease is often caused by a combination of several factors including, for example inadequate environmental, management and nutritional factors i.e. it is a multifactorial disease and may follow on from an earlier consequence, poor welfare, due to such conditions. Other conditions (consequences), for example metabolic diseases, genetic conditions or diseases caused by chemicals, may be the subject of the mandate, and the relevant hazards will need to be identified.

Whether or not subsequent public health consequences are to be addressed should be clearly stated, with reasons. For example, if the eventual requirement is for an assessment of the impact of salmonella on public health, the prevalence of animals that are shedding the organism in the faeces is much more relevant than the prevalence of animals that are clinically diseased as a result of salmonella infection.

The risk manager has to ensure that the risk question is interpreted similarly by all involved and hence that the risk assessor is addressing the most appropriate question, as posed by the risk manager. The outcome of this interaction between risk assessor and risk manager may be that the question that was initially posed is redefined.

3.3 Preliminary information gathering, plus decision on the approach to be taken

Defining the **scope of the project** usually requires identifying any existing relevant scientific documents which can serve as the basis from which to start. For example, elements of the risk profile, risk pathways (see below), or qualitative risk assessment may have been described in a previous opinion or in a fairly closely related opinion, or elsewhere**.** This helps to identify any novel components of the risk assessment e.g. only the exposure assessment may be new. Based on the findings and following discussion with the risk manager, it may be necessary to revise the proposed scope. Previous RAs may be of use as they avoid 're-inventing the wheel'. While it is recommended that such previous works be considered, they require to be subjected to a critical evaluation to assess their relevance for the purpose of the current RA. The initial scope of the project may be subject to re-evaluation. For example, due to lack of data or the poor quality thereof, the initial decision to initiate a RA may need to be reconsidered. However scientific evidence can still be given using the limited information and data, if it is decided not to proceed and crucial missing data should be identified.

To summarise, these initial steps are useful for the following reasons:
- They help clarify the scope of the project, to gain consensus on timelines, and to identify resources needed which are consistent with the scope and the timelines of the project. For example, whilst it may often be tempting to broaden the scope of a risk assessment this comes at a cost i.e. requires more time and resources. Hence, there may be a need to prioritise various proposed objectives for the RA.
- They serve as a guide during the RA process as they set the scenario in which the RA is to be done.

Specific documentation of the above preliminary findings is not a required step in the OIE guidelines, but is recommended in these EFSA guidelines for all types of RAs, and becomes, effectively, a scoping exercise or preliminary risk profile. It will aid in any further requests for opinions on similar issues in the future.

3.4 Management of the risk assessment process

RA is, by its nature, a **multidisciplinary** activity. The selection of team members needs to consider the various areas of expertise required. The team leader should be sufficiently knowledgeable about the risk assessment process. As well as those experienced in risk assessments, selection of team members may have to address any of the following needs:

- specialists in particular aspects of the type of needed data for the RA, for example microbiologist, animal transport, animal management, animal welfare, bio-security, etc.
- epidemiologists to collate, assess, analyse and interpret the epidemiological data
- mathematicians and statisticians to model the data quantitatively if quantitative approach is used.
- specialists in the control of infection to make sure that the risk mitigation strategies that are evaluated are interpreted correctly
- other specialists and experts as required by the particular RA.

Once the areas of required expertise are identified the actual choice of scientists will depend on the availability of individuals within the required area of expertise. Also, any potential conflicts of interest which could possibly lead to bias or to problems when communicating the RA findings need to be addressed in advance of the appointment.

Thus the issue of the various resources that need to be brought to bear in the conduct of a RA offers an example of the **fitness for purpose principle.** The provision of these resources should be commensurate with the magnitude of the task at hand and the need to complete the RA in a timely manner. In some cases it may be that the RA needs to address an urgent health or welfare question requiring an immediate decision. On the other hand, for detailed research-oriented questions, the timeframe may require and allow for a more in-depth evaluation.

During the RA process findings may emerge which may affect the further conduct of the RA. For example, it may be concluded that the RA as originally planned is not feasible or cannot be carried out within the required timeframe. This is a valid qualitative conclusion of the work undertaken to that point. This is why the **dialogue** between the risk assessor and the risk manager needs to continue after the initiation of the RA. In effect, there is an absolute need for continued dialogue between risk assessor and risk manager throughout the RA process.

Considering the timelines required and resources (i.e. data needs, expertise requirements, and financial requirements) available and required for the various options, an initial choice can be made as to what elements the scientific opinion will include. Specifically, what will be the time-frame and resources required associated with each of: a more detailed risk profile, a qualitative or a quantitative RA; and therefore which, in consultation with the risk manager, will therefore be appropriate and undertaken.

3.5 Recommendations for the performance and content of a Risk Profile

Although no documented risk profile is specifically mentioned or required by the OIE guidelines, it is discussed and recommended in the Codex Guidelines. However, experience with Import and other RAs has indicated that this is a very useful preliminary step for any type of RA and is therefore to be recommended here. Where, due to data deficiencies, a more complete risk assessment cannot be undertaken, a risk profile may be used to represent the current state of knowledge on the risk question. It does not actually attempt to assess the specific risk.

A risk profile will include some or all of the following elements:
- The <u>risk question</u> (specifically here, including the EFSA mandate and terms of reference) is established**.** It summarizes the task at hand as a detailed question and includes the time and geographical components of the question. As an example, the risk question could be: What is the annual probability of foot and mouth disease entering the EU and infecting ruminants, given the measure currently in place, or given alternative measures. This allows the evaluation or comparison of various measures.
- The hazard, i.e. the causative agent/condition of interest, is identified and defined (<u>hazard identification</u>). This may be a pathogen, or other hazard, for example inadequate nutrition, inadequate ventilation etc.
- The range of <u>unwanted consequences</u> (adverse events) which the hazard might cause is identified as fully as possible e.g. injury, 'stress', infection, clinical disease, death,

spread of pathogen within the same species or to other species, and any other relevant consequences. These may also include public health consequences where the hazard is a zoonotic pathogen, or a pathogen carrying antibiotic resistance. Where considered useful or necessary, specific consequences can also be more fully described. (This full description would be the stage described as hazard characterisation in the Codex system but has no specific name in the OIE system).

- The <u>expectations</u> of the RA process. Once the question has been addressed, these are defined. This includes, for example, the time estimate for the work to be undertaken, the resources required, and the format of the output.
- The <u>current understanding</u> of the problem for which the RA is being undertaken, e.g. sources of hazard by country and species, susceptible species, nutrition or space required by the species, import routes, exposure routes, import quantities etc. as appropriate for the risk question, are described. Where the hazard is a pathogen, the epidemiology of the infection should be described in time and space. The time component refers to the incidence over time, while space means the description of the geographical entities of interest with meaningful epidemiological or political boundaries. The latter often determine the disease control policy and options.
- The potential <u>management options</u>, if any, are described. These include those that have been identified which might control or eradicate the risks, current policy etc., that will influence the choices to be made by the risk manager. Their wider impact (e.g. economic, welfare where the primary issue is disease etc.) are also described. The information provided on risk management options and the advantages and disadvantages of the various options should enable an evaluation of each of them, as needed, to be addressed in the RA. Particularly management measures that are considered realistic by the risk manager merit consideration in the RA. Hence, whereas cost-benefit analysis may lie outside the scope of a RA it is essential that the RA team has a clear understanding of the possible mitigation options to control the risks under consideration. This includes their practicality (time and cost), and effectiveness with respect to infection, disease, animal welfare, and public health consequences.
- From the management viewpoint, is there a certain minimum <u>threshold</u> above which the disease is deemed to be a problem?
- The various <u>stakeholders</u> are identified and their involvement is determined.

In straightforward cases, the risk profile may even suffice for a risk management decision to be made.

3.6 Risk pathways

When conducting a RA it is common practice to describe the **risk pathways**. These are also known as risk scenarios. They represent a logic chain (or series of such chains) linking the source of the hazard, the exposure route(s) relevant to that hazard, and its consequence(s).

There is often some degree of uncertainty which pathways to include and the determination of their relative importance is an objective of the risk assessment. Based on whether the pathway assumptions that were made are considered biologically acceptable it is decided to proceed or to revise the pathway i.e. to simplify it or to make it more complex.

It is usually very useful to illustrate such a pathway, or pathways, with a diagram. The pathway description, and diagram, may also indicate enabling or predisposing management factors such as hygiene, environmental factors such as housing, and animal factors such as genetics (e.g. sex, breed) and physiological status (e.g. stage of pregnancy).

The risk pathway model will serve as guidance for data collection, logical deductions, and any quantification required in the subsequent risk assessment.

3.7 Data requirements for a risk assessment

3.7.1 Data collection

Once the risk pathways are established, as a consequence, the initial ideal data requirements have also been identified.

In the interest of time, a risk assessment will generally be addressed using existing data. At the outset, all potentially available data are considered. Frequently, it becomes apparent that the ideal data are not available. Data quality problems often include:

- A variety of biases – including publication bias – where 'negative' results are frequently not published.
- Incompleteness e.g. data may only exist in a limited number of countries or specific conditions
- Lack of uniformity among various relevant studies
- Variability in the outcomes from various studies
- Lack of direct relevance for the intended use

There generally is a lack of standardisation of disease data definitions, definitions of environmental or management conditions, and collection methods. Hence, data generated for a different purpose should be carefully evaluated prior to their use in a RA. An 'intelligent analysis' of the available data may allow one to make the correct inferences for their use in the RA at hand.

Hence, once the studies that are available for possible inclusion have been gathered, it is necessary to evaluate these data and describe their strengths and weaknesses. A qualitative assessment of the uncertainty of each model parameter is recommended. From the inventory of potential studies, some studies may thus need exclusion. These decisions should be based on expert review using evaluation criteria that have been decided upon beforehand by the experts. Thus studies that are included are well characterised and the rationale for exclusion of any others is clear.

If it is decided that a specific data source (given its nature and the form under which it is available) is necessary and useful for the risk assessment, it needs to be collected, entered in a database, cleaned, and checked for errors. This is usually a very time-consuming process. When collecting data that is considered relevant, it is important to understand and characterise the available material:

- The way they have been processed: try to go back to the "rawest" possible data, where relevant
- How they are stored *i.e.* electronically versus paper, databases used, etc.
- Whether their access requires negotiation or special permission
- Their nature e.g. continuous, discrete, nominal, ordinal, interval, or ratio. The numerical nature is a characteristic which may be particularly relevant if a quantitative assessment is being undertaken.

Points where additional data analysis is needed can be identified. In the end, <u>critical data are often missing</u>. Lack of data is not unexpected and the identification of data gaps is in fact a purpose of RA. Frequently 'dose-response' studies have not been carried out. For example, in regard to animal welfare RA, the necessary studies to assess the effects of a specific hazard on animal welfare may be lacking. If no experimental data are available, disease outbreak investigation may sometimes be useful to obtain an indication of the dose-response relationship.

3.7.2 Use of expert opinion

Where data are missing or needs interpretation, <u>expert opinion</u> can be sought. Expert opinion is often the only option for an ex ante prediction of unprecedented events. Expert opinion may also be the only option for the description of complex risk paths or in the presence of endogeneity (e.g., if there is a feedback from prediction to the real system). However, the role of expert opinion goes well beyond that of a placeholder for lacking data. Therefore, it is appropriate to address the issue of subjectivity of expert opinion in a broader context. Guiding principles are that of reproducibility (would independent teams of experts arrive at the same conclusions?) and accuracy (are the conclusions from RA correct with regard to the true but unknown risk?). The entire process of RA has elements of and even critically depends on expert judgement. For example:
- The risk assessment team translates the original risk question posed by the risk manager to operationalise the task
- Risk assessors develop the conceptual model and judge its conceptual validity
- Pathogen, disease, welfare or other specialists judge the validity of the conceptual model with regard to the biological phenomena
- Risk assessors or modellers implement the conceptual model mathematically and judge the correctness and fitness of the model for the intended purpose
- Pathogen, disease, welfare or other specialists deliver information (data and or expert opinion) to calibrate the model,
- Pathogen, disease, welfare or other specialists judge the validity of the information (data and or expert opinion)
- Risk assessors and pathogen, disease, welfare and other relevant specialists together interpret the outcome of the assessment.

None of these expert activities are *per se* free of error. Important quality criteria for the work of experts are that problems are presented in terms of formal concepts, that knowledge is grounded in specific, documented cases, and that problems are solved using known and documented strategies.

Expert responses can be biased in many ways and it is helpful to differentiate individual and group biases to develop remedies for bias reduction. Individual biases include for example:

- Motivational biases, which reflect interests or circumstances of the expert. They should be assessed systematically (declaration of interests). Such biases are typically manageable using incentive measures because they are under rational control (i.e. experts are aware of them).
- Cognitive biases, which emerge from incorrect processing of the information or lack of knowledge. Classical epidemiological fallacies are included here, too. Cognitive biases can only be remedied by means of scientific discussion to make experts aware of them. Cognitive biases include for example:
  - Availability bias: overestimation of the probability of 'prominent' events
  - Anchoring and adjustment: biased assessment towards an initial belief (anchor)
  - Unbounded probability problem: probabilities are assigned to mutually exclusive and jointly exhaustive events ignoring 100% as a restriction
  - Base-rate neglect: Underlying base rate of an event is ignored when judging the impact of additional information
  - Gambler's fallacy: A success is expected after a long series of failures when in fact the data generating process has no memory.

Group biases can arise if the outcome of the group assessment depends on an incorrect or misleading 'initial opinion' by one individual, which represents an anchor in other individual's assessments. Complex sociological interactions within the group of experts may prevent the group from evolving towards a summary opinion which best represents the joint knowledge represented in the group.

Data generated by expert opinion should meet specific quality criteria. The elicitation of expert opinion (on data) from individual experts and from groups of experts should be conducted using well-documented (preferably published) protocols. There is also a need for transparency as to what was sought, how this was acquired and who provided it. In qualitative assessments, care must be taken to ensure that experts agree on the definition and interpretation of terms used. The choice of modelling or other techniques used to summarise expert opinion merits careful consideration. For example, the elicitation and analysis protocols need to describe procedures to work with conflicting opinions. It is often recommended to keep substantial and unresolved differences explicit in the model (sensitivity analysis). In the end, any interpretation can be criticised. The main point, however, is that the process used to make an assessment, e.g. on the prevalence of an exotic infection in various regions of the world, should be well documented so that the process used is transparent.

3.7.3 Parameter estimation for model inputs and analysis of uncertainty and variability

The explorative data analysis may include the following:
- Visualising the data e.g. histogram or other graphical representation
- Summarising the data using descriptive statistical parameters e.g. mean, percentiles, range, and variance.

Parameters assessed from data can be variable (and frequently also uncertain). For example, the prevalence of a certain pathogen or environmental factor may differ between regions and the purpose of the statistical analysis can be to assess the variability of the (uncertain)

variable. Thus, besides a measure of the 'average', a description of the biological variability of the data assessing the sources of variation is needed.

In this regard, variability refers to the natural variation of the data, whereas uncertainty reflects the degree of knowledge used to describe this variability. Hence, while variability is a fact of life, uncertainty can theoretically be reduced through further and better measurement. It should be considered as part of the analysis to assess whether or not new data are required to reduce uncertainty in the light of the robustness of the conclusions from the model. However, this data collection is unlikely to be achievable within the usual timeframe for a RA.

Different statistical methods are available to assess, distinguish, and represent both variability and uncertainty in a variable. Examples include re-sampling techniques (bootstrap, jack-knife) and hierarchical modelling allowing fitting second order random variables. This gives the possibility to distinguish between variability and uncertainty in the subsequent development of a quantitative risk assessment model.

For subsequent more in-depth analysis, exploring the relation between variables, basic rules are to let the problem drive the analysis and use good statistical practice (model fitting, model comparison, and model validation). Two main frameworks for data analysis can be considered. In the frequentist framework, whether parametric or non parametric, parameters are estimated based solely on the available data. In contrast, the Bayesian framework allows for incorporation of prior knowledge in the statistical analysis.

3.8 Conduct of a Risk Assessment

3.8.1 Choice of the model

The backbone of the model is the risk pathways. Model assumptions and data or knowledge gaps are identified. As indicated, where no data is available data gaps can be covered by expert opinion. It can be very difficult to describe the uncertainty that is related to such unknown parameters.

Throughout the RA process fitness for purpose should be considered. This applies for example to the decision regarding the **choice of the model**.

A common modelling approach consists of a logic chain beginning at the source of the hazard and ending with the unwanted consequences of interest. Modelling every step of the full process may be necessary, depending upon the risk question, and the knowledge and resources available. In public health an issue, this approach is often referred to as the '*farm-to-fork*' approach, and here the logic chain (and risk pathway) usually begins with the hazard on the farm, and ends with the 'dose' received by the consumer.

However, alternative approaches requiring fewer resources may be all that is required to answer some risk questions. They may also need to be considered when only fewer resources are actually available. An approach whereby a limited part of the logic chain (risk pathway) is considered and modelled may be adequate under some circumstances, and the possible use of this approach should always be considered.

In some cases (sometimes described as marginal models), the impact of various inputs on the output (the probability of the occurrence of the adverse event) is modelled by establishing their direct relationship or empirical relationship without modelling every single step linking these inputs with the output. These are sometimes referred to as risk assessments, but in fact they are usually, in essence, the results from epidemiological studies. In reality though, it is also the case in almost any RA that not every single step is modelled, as any major step in a RA represents an aggregate of smaller steps which are not individually modelled. However, in marginal models the aim is to reduce the complexity of the model to the minimum appropriate level for the question of interest. For example, the impact of smoking on the risk for lung cancer was demonstrated without a full understanding of the underlying causal relationship. Intervention measures can be proposed, and their effect assessed on the relevant part of the risk pathway, without a full understanding of the disease process. This was also the case with BSE. This approach may also be relevant to describe the link between the farm disease situation and the consumer exposure to e.g. salmonella. While describing the empirical relationship, it is considered essential that the proposed underpinning for this relationship be provided. This helps explain the boundaries within which empirical evidence is available.

Peer-review of the proposed model is recommended. The process should include comprehensive review of the approach and the model. The reviewers should include biologists, welfare experts etc as relevant and also other risk assessors. The latter pertains to checking the model-building approach and, where necessary, remarks can be incorporated. Critiques are better dealt with in this stage rather than later, after the report has gone public. Key message is that a model is NOT the truth but a "mathematical" representation of reality, which needs to serve the given purpose.

3.8.2 Choice of the RA method

The principle of fitness or suitability for purpose also applies to the **choice of the RA method**. Qualitative and quantitative approaches are often contrasted. Also in a qualitative approach explicit empirical quantitative information may be available for some model parameters. If such information is lacking for other model parameters, or if a quantitative assessment is not required, it may sometimes be justified to express such quantitative information using scores (i.e. on a semi-quantitative scale). On the other hand, even uncertain parameters (e.g., expert opinion) can be expressed quantitatively (i.e. using a probability distribution). The choice should be based on their usefulness for the specific assessment. It may mean that one of the two approaches is used, or that both should be used, or that first a qualitative assessment is conducted and after that a decision is made on whether to proceed with a quantitative assessment. In the latter case, the quantitative RA (**QRA**) could be conducted on a part of the RA that was identified to be the most critical in the qualitative RA.

Also, a QRA is sometimes considered too demanding in time and effort because of the perceived modelling complexity and the unavailability of resources to conduct a QRA in a timely manner. However, a qualitative assessment can also be very time-consuming and resource intensive.

In addition, the choice of data inputs and other modelling considerations in any RA, whether qualitative or quantitative, are subjective and this will affect the outcome. Thus no approach is free from subjectivity and each has its advantages and disadvantages.

Regardless of the choice, attention should be paid to the units used to express the results e.g. per animal, per quantity, such as tonnes, imported annually, etc.

Qualitative RAs may offer a lot of detail for every individual step but the expression of the overall probabilities associated with the risks poses a specific challenge. Possible choices include the following:

- Describing the probabilities in 'simple' terms e.g. high, medium, low, negligible etc. These can be considered provided their meaning is clarified. This approach is nevertheless not straightforward as it requires the risk manager to understand the full range of evidence on which this description is based.
- Lengthier blocks of text describing the risk level (model output) in detail, including attendant uncertainty and variability, are often more useful and appropriate. This reduces the likelihood of misinterpretation of, for example, different categories of risk and thus enhances transparency.
- Matrices using combination rules between, for example, the probability of an unwanted event and the impact if it occurs. Matrices can easily lose transparency if inappropriate mathematical combinations of arbitrary scoring systems are used. They are therefore not generally recommended but may on occasion be useful / used.
- Relative risks (higher, lower), *in lieu* of absolute risks, often represent a useful system, for example when there are many possible hazards to compare, and any control system needs to be as robust as necessary to reduce the highest potential risk.

Examples of qualitative risk assessments include EFSA's risk assessments on Cysticercus in low prevalence areas, the Risk of a Rift Valley Fever Incursion (EFSA Opinion EFSA-Q-2004-050) and the Scientific Steering Committee (**SSC**) opinions on residual BSE risk in bovine derived products.

When considering a QRA, firstly, the results of any preceding qualitative RA and the EFSA AHAW mandate may need to be considered to decide whether they justify the conduct of a **quantitative RA** i.e. is the QRA likely to affect the conclusions. The additional precision that needs to be obtained to justify a follow-up QRA should be investigated in the qualitative exercise. In this context, the qualitative exercise would minimally include identifying the risk question, hazard, unwanted outcome, developing the model steps, and identifying the data needed. It may be decided that it is then worthwhile to make part of the following risk assessment quantitative. Next, and considering the timelines involved, the type of quantitative RA (deterministic or stochastic) must be decided (**see** Table 2). The complexity of the question can be such that a full quantitative approach would be too time consuming or even not possible, leading perhaps to a consideration of a semi-quantitative approach.

Examples of RA including both a qualitative and a quantitative approach include EFSA's risk assessments on "Ready to use dairy products" (EFSA Opinion EFSA-Q-2004-161).

Quantitative risk assessment can be either deterministic or stochastic (also referred to as probabilistic). Deterministic modelling is based on the use of probability theory and calculus to work out the probability of an adverse event to occur, using single numbers rather than ranges to represent probabilities. In contrast, the stochastic model will determine not only the probability for an adverse event to occur but also its variability and uncertainty. This is

achieved by expressing variability and uncertainty using probability distributions (Morgan *et al.*, 1990).

In the stochastic approach, using (most often) Monte Carlo simulation, the probability model is calculated repeatedly while, at each iteration, the input values are drawn from their respective input distributions. These distributions can reflect the uncertainty or the variability of the parameter or both. The parameters (including the associated uncertainty and variability) estimated from the epidemiological and statistical data analyses or from expert opinions are the inputs of the quantitative risk assessment model.

Simulation modelling is the standard tool for stochastic risk modelling. The propagation of variances from all variable or uncertain input quantities through the final risk estimate is easy using simulation but becomes almost untraceable using calculus even for simple models. Good modelling practice requires that each simulated outcome (i.e., one iteration of the stochastic model) describes one possible state of nature, which physically can occur (e.g., one animal is either infected or not infected or 12 in 100 000 exposed people become infected). Where a calculation for a particular step in the model is appropriate it may not be necessary to undertake simulation. For example, one could do a simulation to assess the probability that a shipment of a known number of animals coming from a country with certain disease prevalence contains at least one infected animal but this can be also calculated directly.

The actual QRA model is written within the appropriate software environment, there are a number of commercial products although many practitioners write customised software. The problem should, of course, drive the model development.

In contrast to a qualitative RA, in a QRA the overall results may appear to be more revealing, since they are given in a numerical format – either as a number or as a range. However, the very precision of this format can also be misleading. This is especially the case with very low probability consequences and it may be very difficult for the risk manager and others to conceptualise what such a result really means.

As an alternative intermediate approach, <u>semi-quantitative methods</u> are sometimes considered. In this case risks are scored in some way. The semi-quantitative approach differs from a pure qualitative approach in the sense that behind the classification there is a rationale which is fed with the relevant available data. However, there is a risk of differing interpretations of the semi-quantitative descriptions, and especially of inappropriate mathematical manipulations of the scores. These in turn may lead to a lack of transparency, or worse. However, such methods may be useful, for example, for risk prioritisation or ranking.

Table 2. Examples of EFSA semi-quantitative and quantitative risk assessments

Semi-quantitative RA e.g. GBR methodology SSC opinion on the Geographical Risk of Bovine Spongiform Encephalopathy (GBR): 6 July 2000 and its update, 11 January 2002
Quantitative RA Deterministic quantitative e.g. Probability of transmission of Porcine Reproductive and Respiratory Syndrome virus (PRRSv) to naive pigs via fresh meat (EFSA opinion EFSA-Q-2004-100) Stochastic quantitative e.g. Dormont report and opinions on Tallow and Meat and Bone Meal (EFSA opinions EFSA-Q-2003-099)

To aid the risk manager, it is suggested that quantitative results, which are generated to answer a qualitative risk question, should be interpreted ('translated') in qualitative terms, as well as being given numerically. It is also suggested that results should contain a qualitative assessment of the uncertainty for each model parameter, which is not to be confused with measures of dispersion (standard error, variance, distribution/shape). Uncertainty analysis addresses the question of whether the numerical representation of each model parameter is adequate in terms of representativeness and potential biases. Results should also include a list of assumptions regarding the conceptual model and each model parameter. This information should all be included in the RA report, which wherever possible should be subjected to peer-review.

3.9 Evaluation and communication of risk assessment findings

This phase also requires dialogue between risk assessor and risk manager. Communication of the results should be planned and undertaken as a shared responsibility. This approach ensures that the findings of the RA are presented in the report in a way that is clear and meaningful to stakeholders, as well as to a more general audience, i.e. fit for purpose. Guidelines can be found in a document produced by the EFSA Scientific Committee: 'Transparency in risk assessment carried out by EFSA: Guidance document on procedural aspects' (***The EFSA Journal (2006) 353, 1 – 16)*** on the website at:
http://www.efsa.europa.eu/etc/medialib/efsa/science/sc_commitee/sc_documents/1494.Par.00 01.File.dat/sc_guidance_transpaproc_en1.pdf).

The suggestions made in the previous section for the presentation of results and assumptions from a QRA are relevant here. If the format in which the conclusions of the RA are presented are of little or no value for the risk manager an agreement on an alteration of the format of the output can be made. Of course, this does not mean that a change in results should be made to meet any requests for change from the risk manager

Question for clarification and any additional requests of the risk manager are identified. Most of the times, the additional questions require new or other data and it should be discussed as to whether these additional questions fit within the original mandate i.e. within the original deadlines and resources. Also the availability of <u>more current data</u> in this stage of the process is often a problem (when using for example on-line databases new data will be available each day). It is of importance to assess together with the risk manager whether the inclusion of the new data into the model would alter the risk managers decision based on the output of the model (value-of-information analysis). If not, there is no need to include the new data. If there is indication however that the new data would alter the decision then it should be decided, taking into account the extra costs and time it will take, to update the model with the new data, and go through the previous steps again.

A **sensitivity analysis** should be conducted to determine to what extent various uncertainties affect the conclusions and recommendations. Models can be tested for sensitivity to changes in inputs, such as risk reduction measures and estimates, for example based on expert opinion. These can help to prioritise areas for intervention (risk management). It may also help the risk manager decide where to focus resources to reduce uncertainty about the final risk. Equally, key variables for which additional data can reduce the uncertainty of the output can be identified and thus prioritise data needs (research). A question that is sometimes posed is what weight should be attached to a 'worst-case' scenario. The justification for considering reasonable worst-case assumptions should be transparent. One approach is to weigh the likelihood of the various possible outcomes with the magnitude of the consequences that would result from them. For example, the importation of a particular exotic pathogen may be unlikely; however the consequences of this unlikely event may be dramatic.

Validation of findings represents an integral part of the RA. Its aim is to verify whether the model is an adequate representation of the reality. This may relate to outcomes of sub-models or to the final risk estimate (e.g., number of cases per 100 000). Ideally one would like to compare the model outcome with actual observations. While highly desirable, such validation may be difficult or, in the case of rare events, impossible to carry out. Even when experimental or epidemiological data, not available at the time the RA was carried out, can be used it must be remembered that where risk assessment conclusions differ from observed data, this may be because the RA was actually estimating a different quantity. Finally, as discussed above, model validation can best be accomplished via peer review.

Final results and conclusions are communicated to the risk manager through an **opinion**. The reader may have little knowledge and understanding of the methods employed and will often not be familiar with statistics and probabilistic thinking used in QRA. It is the task of the risk assessor to create a report which presents the results and conclusions in an understandable way allowing to the risk manager to make informed decisions. In addition, the risk assessor has a responsibility to clarify parts and give additional explanation when this is requested. As a general guideline, the following elements can be considered for inclusion. Some parts are only relevant for quantitative risk assessment.

The report should include a section which provides a general introduction to the problem that led to the conduct of the risk assessment. It is described together with the decision questions that are addressed and those that are not addressed.

The report should also include an overview of the model structure and describes how the various sections relate to each other. This should allow the reader to understand how the model functions, what the mathematics and assumptions are and where the data (or parameters assessed from this data) is needed and inserted into the model. When discussing the data a (graphical) description and reference of the data is given. This is based on the explorative data analysis conducted previously. The statistical analysis used to derive the necessary parameters from the data is explained, assumptions behind it, and limitations of the methods, are discussed.

The results are presented within the report in a format which is informative and useful for the decision maker. The graphs used should be explained in an intuitive way and the focus should be on graphs giving information on the original questions. Also, the results of the sensitivity analysis showing which inputs have the greatest effect on the outputs are very informative for the decision maker. If validation of the model is possible as discussed in the previous chapter the results should be presented.

A discussion may be included if the relevant points have not been addressed earlier. In fact, in many risk assessment reports, many of the following points are made at an earlier place in the report, where the associated factor is originally presented, so that no 'jumping about' in the report is needed to fully understand the impact of assumptions, choices and methods. Given this, aspects that merit attention at some relevant point in the report in order to achieve transparency include the following:
- The model assumptions that were made
- A description of the quality of the data which identifies data gaps and data weaknesses along with their potential impact on the magnitude of the uncertainty of outcome should be described and explained to the risk manager and, where appropriate, recommendations for improvement in the data collection
- The available data and their relation to model choice together with the inherent assumptions needed in order to reach to the results should also be discussed
- If some major model assumptions are hard to accept, their influence on the outcome should be discussed in case these assumptions were not to hold true in reality
- The results of the sensitivity analysis, along with their implications.

An explanation should be provided on:
- Potential approaches to address the decision questions, given the available information and resources
- Assumptions inherent to the different modelling options
- Why a particular approach was used.

There should be included, either in the discussion or as a separate section (sometimes as an annex):
- Critique on the model from reviewers.

Finally the interpretation of results is discussed along with their impact.

Technical annex
In this annex a more in-depth explanation can be given on the used statistics, mathematics or the derivation of some formulas.

There is also a need for **feedback** from the risk manager about the outcome of the risk assessment. The risk assessment can lead to a change in policy altering the original "system" from which the data originated. This approach allows observations on whether the risk management decision has the predicted effect over time. Actually this is not a true validation of the QRA model but rather a way to look at the usefulness of the approach for a given problem. Also, with regard to safeguards, the evaluation of whether and why proposed management measures worked or did not work as predicted is important information for a future RA.

3.10 Summary comments on the RA process and report

Use of the formal RA process, be it qualitative, semi-quantitative or quantitative, has several benefits:
- first it offers transparency as documentation is provided about the data that were used, the risk pathways that were considered, and the risk assessment model that was chosen;
- a second element is that it can help to prioritise areas for intervention (risk management) and give information on further data needs (research).

Outputs of stochastic QRA are probability distributions. These outputs, if presented in the right way, are far more informative than single-point (deterministic) estimates. Models can be tested for sensitivity to changes in inputs, such as risk reduction measures and estimates which are based on expert opinion.

However, a risk assessment is only as good as the data and the **model** it is based on. Choice of the model structure is subjective and there is no such thing as 'the right model', although some models may be more appropriate than others. In addition, some RAs, for example those involving importation, or micro-organisms, are often based on a pathway that is very long. This is very resource-intensive, time consuming, and requires a substantial amount of data, which may not be available. Thus, important assumptions have to be made, based on expert opinion, which in turn often leads to large uncertainties. Hence, it is critical to focus the question posed as closely as possible when the mandate is examined initially and to maintain this focus during the execution of the project. It may be necessary to break the original question down into several different mandates, RAs and reports.

Critical **data** are often either incomplete e.g. surveillance data or missing e.g. dose-response studies. There generally is a lack of standardisation of disease, welfare or other data definitions and collection methods. Hence, data generated for specific purposes should be carefully evaluated and their suitability assessed prior to their use in a RA.

Risk assessments need, in general, to be carried out in a reasonable and pragmatic timeframe. It is normally not feasible to revise an existing system or set up a new data collection system once it has been decided that a risk assessment should be carried out. Lack of data is not unexpected and the identification of data gaps is in fact frequently a major purpose of RA. The potential impact of data deficiencies on the magnitude of the uncertainty of outcome should be described and explained to the risk manager. In anticipation of future needs, it may be necessary that existing data collection systems be revised to acquire the necessary data. For example, data collection and format for the EFSA zoonosis report, which is based on the data

provided by the 25 EU Member States (prior to January 2007), could be adjusted in anticipation of future risk assessment data needs in the area of zoonoses. Whereas it is not possible to anticipate all precise future needs it may be possible to try and identify future areas of priority and the types of data collection they require. A possible example of such a pro-active approach is the current review of the European Community Animal Health Policy. The strategic choices that are made during this review may reveal future needs that are not covered with existing data acquisition systems.

Risk assessments are conducted as a multidisciplinary team effort. The type of expertise and the magnitude of the **resources** allocated to the RA should be commensurate with the expertise required, the availability of experts, the magnitude of the tasks, and the need to complete a RA in a timely manner.

In addition, as described above, the need for regular communication with the risk manager is obvious. Hence, whereas the roles of risk managers and risk assessors are distinct, a close collaboration between both is essential to guarantee success.

4. Aspects specific to the assessment of risks from importation of live animals (and their products) to the EU

4.1 OIE Import RA Guidelines

As has been indicated in the introduction, guidelines for undertaking risk assessments connected with the importation of live animals have been produced by the OIE. Thus the guidelines given in this paper recommend that the OIE Import RA Guidelines are used (http://www.oie.int/eng/publicat/ouvrages/A_IRAvol1.htm, OIE 2004a and 2004b). These OIE guidelines should be used in conjunction with the further details and recommendations given in the general guidelines outlined above. It should also be noted that the OIE Guidelines are applicable not only to the importation of live animals, but also their products, and where EFSA AHAW Panel need to also consider these products for import (not an uncommon need), the OIE Import RA Guidelines are also appropriate. The OIE Guidelines will not be reproduced in this paper, and nothing discussed in this paper conflicts with OIE Import RA Guidelines. However a number of specific points from that methodology which may be useful to EFSA AHAW RAs will be briefly addressed.

4.2 Risk pathways for import RAs

For an Import RA the risk pathways usually distinguish between two phases. These are the portion of the pathway up to the point of entry to the importing country (release), and the portion following entry of the causative agent into the importing country, which comprises exposure and consequence following introduction (see Figure 2, and examples in OIE 2004a). This is because a country or region (for example the EU) which is considering importing a live animal (or its products), and which doesn't already have the hazard of interest present within its borders, generally wishes to keep it out. Thus the crossing of that border and entry to the country or region of interest is often the most crucial part of the import RA. In fact, it is

often the only part of the import RA actually undertaken, especially for live animals. Figure 2 illustrates this general release pathway for an import RA with reference to any virus (and is taken from EFSA Opinion EFSA-Q-2004-050 on the Risk of a Rift Valley Fever Incursion). However, the import pathway for the release stage for other pathogens would be very similar.

```
┌─────────────────────────────────────────┐
│   Virus present in exporting region     │
└─────────────────────────────────────────┘
                    ↓
┌─────────────────────────────────────────┐
│    Virus present in items for export    │
└─────────────────────────────────────────┘
                    ↓
┌─────────────────────────────────────────┐
│      Pre-export safeguards applied      │
│       (less than 100% effective)        │
└─────────────────────────────────────────┘
                    ↓
┌─────────────────────────────────────────┐
│     Virus present in exported items     │
└─────────────────────────────────────────┘
                    ↓
┌─────────────────────────────────────────┐
│   Virus remains viable during transit   │
└─────────────────────────────────────────┘
                    ↓
┌─────────────────────────────────────────┐
│     Import border safeguards applied    │
│       (less than 100% effective)        │
└─────────────────────────────────────────┘
                    ↓
┌─────────────────────────────────────────┐
│     Virus present in imported items     │
│      (virus 'released' into importing   │
│                 region)                 │
└─────────────────────────────────────────┘
```
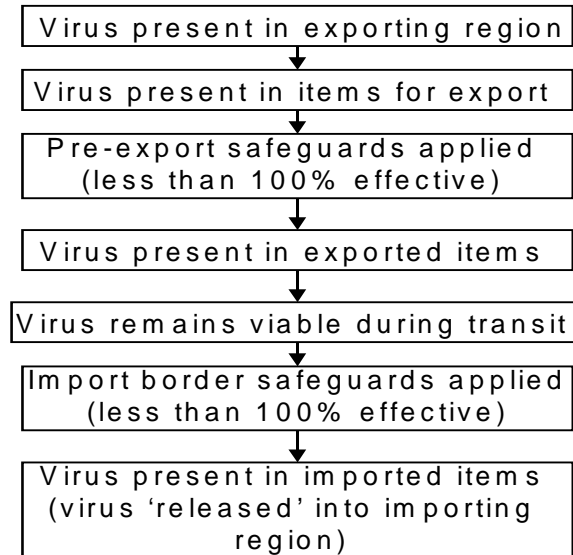
Figure 2. Example of general release pathway for import of any viral pathogen (item for export' refers to any such item, including live animals or their products)

In the context of imports by European Union (EU) - and thus for the EFSA AHAW Panel, import RAs may often focus on imports at the EU level.

4.3 Clarification of some OIE Import RA concepts

For import RA for infection, toxins and chemicals in animals (and their products) the OIE guidelines are most often used as the reference, since they are accepted by the WTO as having legal validity. They cover basic principles for use by all OIE members, i.e. in a broad range of environments. However, it has been suggested that further clarification may be required in a few specific areas. Concerns have been expressed in three related areas, these being the definition of borders, the concept of 'border gradients', and the issue of the presence of hazards, and any differences between them, in the potential trading partners.

As far as borders are concerned, import quarantine facilities physically situated within the importing country are, legally, still pre-border to the importing country. However, physically, they are post-border and if poor bio-security is present, a pathogen may escape directly within the importing country, as from any other animal accommodation. Should this occur, the effect of the escape of live animals, effluent, or animal waste will be the same as if the animals (or products) had crossed the legal border. The risk manager may be interested in how likely this is to occur. Therefore, the way they are considered in the RA will depend upon the risk question and the underlying issue, and will need to be a pragmatically based decision. The recommendation is that there should be no overall rule and that this aspect must be considered on a case-by-case basis to give the risk manager the information they need.

The term border gradients refers here to the situation when the importing country is itself not free of the infection or disease of interest and the question arises whether import poses an additional risk. This additional risk could thus result in an increase in infection and disease prevalence. Currently the OIE guideline does not specifically consider such a scenario although the general methodology remains applicable.

As further discussed in the section on data, related to this is the question about knowledge of occurrence and prevalence of infection and disease in importing and exporting countries. The OIE only requires, from its members, notification of the presence of an infection or disease whereas, for RA purposes, the levels (prevalence) and distribution need to be considered. Knowledge of the surveillance systems present within potential exporting countries is therefore required by the potential importing country or region.

The current understanding of the epidemiology of the infection and, where appropriate, of the disease(s), is essential. This aspect is particularly relevant in an international context. Based on the prevailing epidemiological situation and the control policies in place, regions which group together several countries or parts of countries may be identified as a single epidemiological unit of interest.

4.4 Data required, and data issues specific to, import RA

Data for an import RA generally distinguishes between data required for a release assessment on the one hand, and that for exposure and consequence assessments on the other hand. However, such a distinction is somewhat artificial, as the same database may be used in more than one part of the risk assessment.

Release assessment
Relevant data on the aetiology, pathogenesis, and epidemiology of the hazard is collected. Data is required on the frequency of occurrence of the hazard. This is often expressed either as:
- the prevalence of infection, or toxic/chemical contamination in an animal population; or as
- the prevalence of contamination of animal product along with the distribution of the concentrations of the organism or toxin/chemical that are present i.e. the viral, bacterial or parasitic load, or chemical concentration

The prevalence is the ratio of:
- a numerator representing the number of cases at a given moment in time; and
- a denominator representing the total population that could potentially be infected/contaminated

The numerator can be biased due to underreporting of cases. The total number of animals at risk is also sometimes difficult to obtain, particularly in countries where the veterinary services have limited resources. Classically, prevalence estimates are the outcome of cross sectional (snap shot) studies designed for that specific purpose. When designing and analysing these studies, a decision needs to be made at which level of aggregation the

parameter will be estimated. For example should the data be summarised at the level of a country, or regions within a country, a subcontinent or a continent?

Very often disease <u>incidence</u> rather than disease prevalence data are all that are available. Incidence expresses the number of new cases that have occurred in the population during a certain period of time. It may need converting to prevalence, considering the duration of infection/contamination/disease in a new case, depending on the risk question at hand.

Release data also consists of information on <u>pathogen/toxin/chemical distribution and concentrations</u> in affected live animals and animal products. Whereas pathogen concentrations during infection may be well-known, much less is often known about the decay of virus following slaughter or during and following processing of the animal product. Other elements are storage conditions and packaging materials (their disposal, packaging integrity and cross-contamination) including the persistence (the behaviour of the pathogen over time during storage). Sources of such information are observational studies such as case-control studies and outbreak investigations or experimental studies. Generally there is an absence of standardisation of data definitions as well as a lack of standard methods used to collect data in such studies.

The determination of the status of a biological sample (live animal or animal product) requires a <u>test method</u>. Test here is defined as a measurement process that decreases the uncertainty about the status of interest of a sample, an individual or a group. One level of measurement of the quality of the diagnostic test used is described by its analytical and diagnostic sensitivity and specificity. However, the entire quality assurance environment in which a test is carried out is critical and will affect the overall values for test sensitivity and specificity - and these are the values generally required for use in the RA. For example, how are samples taken, transported, stored and analysed? Clinical examination is also a diagnostic test for which a sensitivity estimate may be required, and will vary with the clinician. Knowledge of characteristics of e.g. the specificity of clinical signs, the nature of the other diagnostic tests used, the number of samples taken, and the sampling frame used, is necessary to be able to address questions such as:

- What is the sensitivity of the total surveillance system used? This sensitivity is the probability to detect at least one case if cases are present at a given prevalence (design prevalence), given the proportion of the population tested and the structure of the surveillance system. These factors therefore influence the sensitivity and specificity of the surveillance system. This is particularly important when demonstration of freedom of infection, contamination or disease is needed. For example, if the prevalence is very low, the number of animals that need testing (and the cost associated with this) may make it impractical to find all new cases. Thus, the biological concept of 'disease freedom' needs to be expressed by the concept of <u>probability of disease freedom</u>. It provides the epidemiological interpretation of 'disease freedom'. Often it can be based on a range of evidences rather than on a single study
- Whether sub-clinical infection will be detectable
- Whether diseases that are thus far exotic can be detected with the diagnostic tests that are used. For example sero-surveillance may be inappropriate to rapidly detect the appearance of such a disease in an area that was thus far free.

In other words, the characteristics of the surveillance system used to generate the prevalence data need to be understood.

The epidemiology of infection or disease is often heavily influenced by human <u>interventions</u> such as disease prevention programmes, control programs and treatments, as well as the structure of the animal production industry and economic incitements. Thus, in order to interpret survey results correctly such aspects need to be considered as well. Finally, it is always useful to have an understanding of the <u>natural history of the infection/disease</u>.

The probability of a pathogen entering a given country in a live animal or its product is also dependant on <u>trade patterns and trade volumes</u> between exporting and importing countries, themselves influenced by official or industry or private based import controls. These are affected by price differences, trade legislation, etc. The magnitude of external trade can be ascertained through official databases such as Eurostat. However, it should be recognised that these do not account for <u>illegal trade</u>. Imports through the latter route could be associated with a higher risk of infection or contamination than in case of legal trade, and where relevant this should be taken into account in the release assessment.

In addition, data on the movements of animals and animal products often resides in <u>databases</u> that are under the responsibility of risk managers. For example, the TRACES database on EU imports and on intra-Community trade of animals and animal products is owned by the competent authorities of the EU member states. Hence, at the onset, when risk assessors and risk managers are defining a RA project, the extent of the risk assessor's access to the relevant data needs to be clarified and agreed upon. The risk assessor needs to provide assistance in this process to the risk manager by indicating precisely what data are needed.

The collection of data on exotic infections is a difficult task as there often is a paucity of such data. For example, world wide disease surveillance networks would be useful but they do not exist at the moment. For key exotic infections the OIE is an obvious starting point as a source of information. This will need to be supplemented with other data, for example from the EU reference laboratories, other laboratories in Europe or elsewhere, from missions carried out by the European Commission and by the EU Member States.

In addition, the quality of the surveillance system is dependent on the resources devoted to it and these may vary considerably. The European Commission's Food and Veterinary Office collects data on these aspects for countries that export to the EU or wish to do so. The assessment of the competence of the governmental authorities responsible for the conduct of surveys is an issue that also merits careful consideration. A decision must therefore be made on a case-by-case basis as to whether the surveillance system gives the assurances required. Such an assessment is another example where interpretation based on expert opinion is needed. In the end, the data on disease occurrence may not be considered to be very reliable. The interpretation may result in a trade dispute.

<u>Exposure and consequences assessments</u>

Data on exposure can include the <u>geographical distribution</u> of susceptible (and potentially infected imported) animal populations illustrated with maps e.g. using Geographical Information Systems (GIS). Animal and animal product movement patterns in the importing country/region are also relevant, for both the imported 'items', and native animals, as they will affect exposure pathways. Epidemiological data on the <u>routes of exposure</u> for susceptible animals are needed. This may require data on movement of animals, animal products,

humans, feed and any other fomites within the importing country or within the region of interest. Again, many of these movements are affected by price differences, trade legislation, etc.

Information on <u>dose-response studies</u> which establish the relationship between exposure (dose) and consequence (response) are ideally required (though rarely available). The dose-response may vary greatly by route of exposure (e.g. inhalation, ingestion etc). For infectious pathogens, data on the probable number of <u>secondary outbreaks</u> following the primary outbreak are also of interest for assessment of the probability of spread. These data may come from infectious disease modelling studies.

5. Aspects specific to risk assessments for diseases endemic to the EU

5.1 Similarities and differences between import RA and endemic disease RA

For the control of animal diseases, epidemiological analyses are classically used to identify risk factors that affect the spread of these diseases. Risk managers use this knowledge about risk factors to lower the risk for spread of endemic diseases. RA is a useful additional tool in this area because it allows the risk manager to assess which of the available options to control or eliminate the disease is most efficient.

In general, the conduct of a RA intended to assess the risk of occurrence of an endemic disease in a given population of live animals, within a particular country or region, can be undertaken in a very similar way to that for an import RA. This is because such occurrence will depend upon relevant 'release', exposure and consequence factors in exactly the same way. Epidemiological factors which govern the spread or occurrence of any infection or contamination will be subject to the same principles for endemic disease as for exotic disease, and the guiding principles of RA will not change. Thus the RA can be approached in a very similar way and, as for import RA; it can be made with or without the effect of additional safeguards.

However, the RA process needs to take some particular factors into account to make it appropriate for use in an endemic disease RA as follows:
- It is generally understood that an <u>endemic disease</u> means one that remains prevalent over time. Some diseases may thus be endemic in one region or herd but absent or have only a sporadic occurrence in other regions or herds. However, <u>sporadic</u> diseases (i.e. non-exotic diseases, caused by endemic pathogens which manifest clinically only under certain conditions) will also need to be considered in this category, as far as RAs are concerned. In addition we also have diseases other than infectious diseases like <u>nutritional and metabolic diseases</u> that also have to be considered.

- The <u>case-definition and prevalence levels</u> may need to include, and be based on, more than a simple 'present-absent' issue e.g. using production records, growth or milk yield records, etc.
- Dependant upon the risk question and the risk managers requirements, <u>control measures</u> included in the RA may include either only those relevant to the control of the disease or infection in the live animals, or also to other risk reduction measures. For example the risk manager may require those that reduce the pathogen load on the carcass and other products to be included (although this is sometimes the case with import RA too). Decisions on control measures weigh the benefits against the costs. In this regard a risk benefit model, weighing advantages and disadvantages of various control measures, may also help the manager.
- Eradication or control of an infection in domestic animals is quite often made more difficult due to its presence in <u>wildlife</u> e.g. avian influenza, brucellosis, rabies, swine fever, trichinellosis, and tuberculosis. The specific interface between farm animals held under commercial conditions and wild animals which can be infected and can have major impact in the disease under investigation should be identified with every RA, where appropriate.
- For these diseases the practical aim is generally not eradication, but instead control - i.e. reduction in prevalence or in severity.

5.2 Data similarities between import RA and endemic disease RA

The data relevant, and required, for any animal pathogen/disease RA are likely to be very similar, whether for an import RA, or for an endemic disease RA. The types of data required, and the issues of concern in collecting that data are therefore also very similar. Details are given in section 4. 4, and except for specific references to international trade, and other international issues, can be applied to this section also.

However, the data collection and assessment process needs to take some particular factors into account to make it appropriate for use in an endemic disease RA as follows:
- Where the disease is a production, or other non-infectious, disease relevant production, genetic, or other appropriate data will need to be collected to assess prevalence and severity
- When required, there should be a thorough evaluation of the data available from wildlife. Instead of authorised surveys of wildlife, hunters may be the main source of such data. The latter data carry a high degree of uncertainty due to incompleteness and biases. To interpret and summarise such data expert opinion may be needed.
- The required data for e.g. prevalence may be held locally, rather than at a national level, or by agencies other than those to which the risk manager is affiliated. This may need to be considered by the risk assessor when discussing data access with the risk managers.

6. Aspects specific to welfare risk assessments

6.1 Background to animal welfare RAs

Animal welfare issues often arise as a result of infections and/or housing and management practices. The RA process has rarely been used in the field of animal welfare. However, it is considered that its introduction may be beneficial to help risk managers identify risk factors as well as risk pathways and also to assess the importance of a specific risk of poor animal welfare, as well as good animal welfare. These two aspects in turn will contribute to an assessment of the overall quality of life of an animal no matter how it is being used. As this is a new and developing area, there may be various potential ways of undertaking a welfare RA.

A further factor is the issue of benefits that may outweigh any harm, but in order to make this assessment a RA has to be made of the potential benefits as well as the harms. This may be particularly important when a claim is made for overall benefit for the animal and its quality of life, the latter being interpreted as a balance of good and poor welfare over the lifetime of an animal.

The following are ideas and suggestions to facilitate further development.

Often in the past, risk managers have asked very general risk questions concerning welfare, for instance regarding the risks of poor welfare for intensively farmed calves. Such a question covers a broad field of calf farming, which needs large resources to cover. However, for methodological reasons, and in order to complete opinions in a reasonable time, it would be better for risk questions in welfare RAs to be limited to more precise individual and specific questions allowing for a reasonable work task.

For an animal welfare RA one starting point is to make a description of the needs of the animal. A clear definition of a need should be presented. A need is a requirement, which is a consequence of the biology of the animal, to obtain a particular resource or respond to a particular environmental or bodily stimulus. Hence needs are associated with all of the major biological functions of the animal. Good welfare depends upon needs being met but there is variation in the importance of the various needs for the welfare of the individual. An animal may have a need which may be based on intrinsic factors such as hormonal changes and which implies that this need may be temporary, whereas other needs may be more continuous over time. Needs may also be absolute or relative and range from resources whose absence results in rapid death to those whose presence improves welfare for a period but whose absence would never result in death. However, a need such as the avoidance of severe pain or the protection of frightened offspring might not lead to death but would lead to poor welfare if not satisfied. The needs of animals, usually affect what the individual wants as indicated by what it will prefer or work for. The amount of space needed by will normally exceed that sufficient for it to stand up, lie down and turn round but include also space for it to carry out other activities or to play. An animal may need the company of other animals, even though this may not necessarily be reflected in its productivity or other output.

The next step in an animal welfare RA might logically be to identify any factor that may prevent the fulfilment of one or several of the animals needs. This can be regarded as a welfare risk factor or hazard. A risk factor, or hazard, is therefore a factor that may cause poor welfare to an individual animal, e.g. inappropriate environment, with excess dust or lacking in space, inadequate nutrition, lack of colostrum etc. These factors or hazards are usually outside

the animal in its environment and often in the management practices that may be applied in the husbandry system. Poor stockmanship can change any husbandry system from one leading to good welfare into one resulting in poor welfare. However, genetic factors may be also regarded as risk factors or hazards if, under certain management conditions, e.g. intensive feeding, they increase the probability that the animal will have poorer welfare. Examples include genetic factors which cause growth rates which are too rapid, or milk production at too high a level. By primarily identifying the needs of the animal, potential factors that may result in these needs not being met, and thus pose a potential risk to the welfare of the animal can then be identified and related to one or several of these needs.

A need can be met to a greater or lesser extent, with consequences for the effects on welfare. In hazard identification and description, the biological importance of the need and the extent of good or poor welfare resulting from that need being partly or wholly met, is important. This is not straightforward because the adverse consequence of a need not being met is the magnitude of poor welfare and not just whether or not death occurs at some point afterwards. As explained below, the magnitude of poor welfare is a function of its severity and duration.

Once these hazards are identified, the potential effects of exposure (including the effects of differing exposure periods) on an individual animal can be identified and described. This is a step in the Codex system known as hazard characterisation, although in the OIE guidelines it has no specific name. For animal welfare hazard characterisation it is considered essential that the key welfare indicator consequences be directly animal based, e.g. lameness. The measurable variables that are proposed as directly relevant relate to health and behaviour.

This raises the question of whether physiological parameters such as immune competence and stress responses can be used routinely as a measure of welfare, or as a welfare indicator. The difficulty with such parameters lies in their interpretation as expressions of welfare. Their use can be recommended *in lieu* of direct observations on health and behaviour when these cannot be measured directly in a particular study and if their relationships with these health or behaviour welfare parameters have been validated in previous studies. Behaviours originate from both intrinsic and extrinsic requirements (needs) that animals seek to satisfy. These needs may be considered to be an ordered hierarchy. For behavioural aspects expression of both 'good' behaviour, e.g. grooming and lack of 'bad' behaviour, e.g. stereotypic behaviour have both to be considered. A list of key welfare indicators can be identified for all species. However, it is necessary to consider indicators that are specific for species, breed, age, physiological state, and production system.
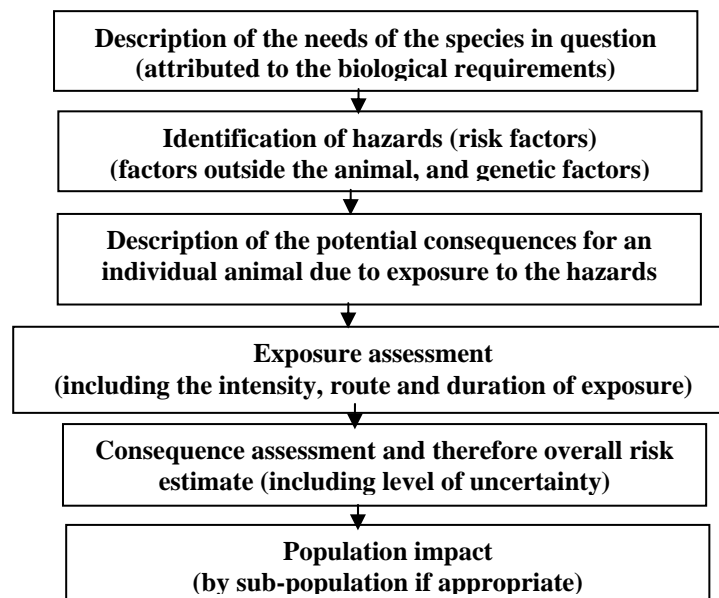
As in other areas of RA, the welfare consequences are the result of the nature of the hazard and the nature of the exposure. The latter includes the frequency (incidence), intensity, and the route and duration of that exposure to the hazard. To assess welfare consequences therefore, an exposure assessment must be carried out taking account of exposure intensity, route, as well as duration. For example, an animal can be exposed to the same electric current, but given as one major shock through the use of an electric prodder the intensity is high and duration short, whereas if exposed to stray voltage intensity may be low, but duration long.

Sometimes there is conflicting evidence as to what extent a potential hazard really influences welfare. Also, evidence may be scarce with a high degree of uncertainty as to what extent an exposure really leads to a poorer state of welfare. In a RA, the scientific evidence is examined and the degree of uncertainty of how the risk factor affects an animal's welfare is addressed and presented. When applicable, a comparison of the wild life/natural situation could be

presented and be used as a help to estimate whether the regime under consideration had in fact "poor welfare" when compared with that; e.g. piglet mortality and prevalence of different diseases in wild boars, as compared with domestic pigs or by comparing two systems of farming management, as mentioned below.

The <u>magnitude of population impact</u> is estimated in a calculation of probable exposure in a relevant population. Sometimes such a population cannot be identified. For example, the target population (which might be the population in the EU) may hold several sub-populations with different characters e.g. sow housing which in some EU countries is approx 100% confined in crates but in some countries 100% kept in loose housing in line with national regulations. In such cases, it might be fruitful to construct several scenarios to illustrate how the animal welfare RA outcome might be in different sub-populations.

The suggested issues listed above, to be considered in an animal welfare RA, are illustrated in Figure 3.

Description of the needs of the species in question **(attributed to the biological requirements)**

↓

Identification of hazards (risk factors) **(factors outside the animal, and genetic factors)**

↓

Description of the potential consequences for an **individual animal due to exposure to the hazards**

↓

Exposure assessment **(including the intensity, route and duration of exposure)**

↓

Consequence assessment and therefore overall risk **estimate (including level of uncertainty)**

↓

Population impact **(by sub-population if appropriate)**

Figure 3. Suggested issues to be considered in an animal welfare RA

A number of issues specific to welfare RAs have already been identified, during these preliminary discussions, which need further consideration, for example:

- Defining the needs of animals in more detail; in particular is there a 'need' to be healthy both physically and mentally.
- Evaluating the role and meaning of stress and stressors, and whether stresses caused by, for example infection, have the same physiological and metabolic consequences as stress caused by the lack of an unsatisfied basic need.
- Balancing advantages and disadvantages caused by the same management with other conditions. For example, giving chickens access to open air may generally reduce the infection pressure from some infections and exposure to gases such as e.g. ammonia and it may reduce stocking density, thus improving the wellbeing of the chickens. On the other hand, it may increase the risk of exposure to infections like Campylobacter and Avian Influenza as well as exposure to predators and climatic uncontrolled

conditions. The approach used in the assessment of the safety and efficacy of veterinary medicines licensing dossiers has to weigh welfare advantages versus disadvantages (EMEA, 2005). It is likely that in areas other than the licensing of veterinary medicines, such as animal welfare, an approach using a risks and benefits assessment, considering pros and cons of various interventions may need to be applied. Thus a balance of all the risks and benefits to both animals and humans has to be undertaken.

- Consequences may alter over time. For example, an animal that has been castrated or docked without any anaesthesia will suffer severe pain at the time, thereafter the pain may be moderate for several days, and then the pain may be mild for several months. Eventually, severe and acute pain may occur only when the site of surgery is knocked in some way.

6.2 A possible approach to Welfare Risk Assessments

Risk assessments involving live animals, for example animal health and import risk assessments generally follow the OIE Animal Health Code (OIE, 2004) methodological guidelines, developed in the context of infectious or toxic poisonings. However, methods for animal welfare risk assessments have no established systems to date. For simplicity, there is therefore a logical argument for live animal welfare risk assessments to follow an adapted and analogous method to that of other live animal risk assessments, if possible, using the steps of hazard identification followed by release/exposure/consequences steps. The following describes such an analogous series of steps and is presented as a potential foundation on which to further develop welfare risk assessment methodology.

The aim of such a welfare risk assessment would be to estimate (in qualitative or quantitative terms) the probability of defined consequences due to the presence of, and exposure to, a defined hazard. Under this system, hazard identification is the step prior to risk assessment. A definition of a welfare hazard analogous to the pathogen or chemical present in other live animal risk assessments, would be the features in existence (e.g. environmental, nutritional, stockmanship, etc.), associated with the animal under consideration, and which could potentially lead to adverse welfare consequences.

The first two stages in an import risk assessment, the release and exposure assessments, describe the steps in the pathway necessary for a particular pathogen or toxin to enter a country or region, followed by the steps necessary for exposure of naive animals to that pathogen or toxin. Each stage also evaluates either qualitatively or quantitatively the probability of each of the steps occurring. This distinction between release and exposure is made because importing countries often need to know the actual probability of importation however in biological terms the combined pathway is, effectively, an exposure pathway. Therefore in the context of welfare, the analogous process is best described by combining the release and exposure stages into a single stage, an exposure pathway, which would allow potential adverse welfare consequences to result from the features in existence (e.g. environmental, nutritional etc.). Again this stage evaluates either quantitatively or qualitatively the probability of that exposure occurring. The exposure pathway itself is likely to be relatively simple, however both frequency and duration of exposure (and where

appropriate, possible adaptation to that exposure) would need to be considered in welfare risk assessments.

The next stage of the risk assessment would, under this system, be similar in both contexts, and this is the recognition, description and estimation of the probability of the consequences which might occur due to the exposure to the hazard. However, whereas with a pathogen, the potential consequences would include such things as infection, local spread, epidemics etc., analogous welfare consequences would include such things as stress, fear, malaise, malnutrition, injury, death etc., depending upon the hazard under consideration. Given a particular hazard, there might be a wide range of potential consequences which would need identifying.

The risk estimate (the final stage) would again be similar in both contexts; that is, the resultant probability of a specific consequence, from all the above stages.
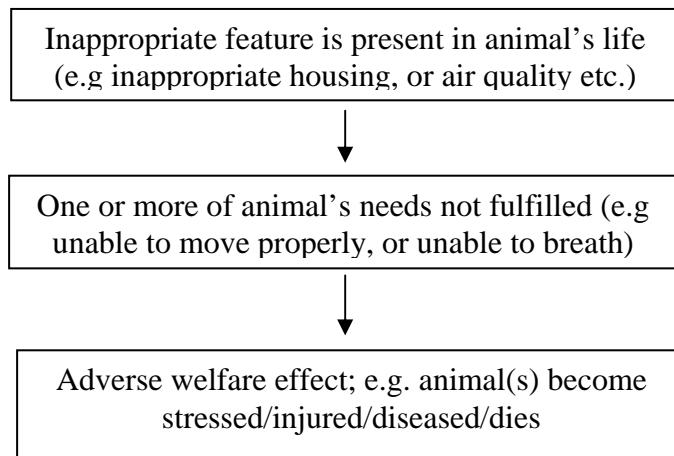
Table 3 summarises the above stages as applied to a welfare risk assessment process, and Table 4 identifies some typical hazards and potential consequences using this system. Figure 4 gives a diagrammatic representation of the risk pathway used in this approach.

Table 3. Summary of the steps described for the process of welfare risk assessment conducted in a manner analogous to other live animal risk assessments

Stage of process in OIE Code	Analogous stage of process in welfare RA
Hazard identification	Identify/describe features of environment, nutrition, husbandry etc. in which animals are kept which are, or are suspected to be, inappropriate for those animals
Release	What is the probability that a specific identified feature results in exposure of the animals to conditions that may result in adverse welfare consequences?
Exposure	
Consequence	What are the probable consequences of exposure (e.g. stress, fear, malaise, malnutrition, death etc.), and what is the probability of each occurring?

Table 4. Some examples of welfare hazards and associated potential consequences

Some examples of features defined as hazards in this system	Examples of possible associated consequences
Inappropriate air quality	Stress, suffocation, disease, death
Inappropriate nutrition	Stress, malnutrition, death
Inappropriate handling	Stress, injury, death
Inappropriate housing design/dimensions	Stress, injury, death

```
┌─────────────────────────────────────────┐
│  Inappropriate feature is present in      │
│  animal's life                            │
│  (e.g inappropriate housing, or air       │
│  quality etc.)                            │
└─────────────────────────────────────────┘
                    │
                    ▼
┌─────────────────────────────────────────┐
│  One or more of animal's needs not        │
│  fulfilled (e.g                           │
│  unable to move properly, or unable to    │
│  breath)                                  │
└─────────────────────────────────────────┘
                    │
                    ▼
┌─────────────────────────────────────────┐
│  Adverse welfare effect; e.g. animal(s)   │
│  become                                   │
│  stressed/injured/diseased/dies           │
└─────────────────────────────────────────┘
```

Figure 4. Example of possible risk pathway for welfare risk assessment

Clearly, this is still only a very overarching outline of how such a risk assessment might be undertaken, and would require considerable work and experience in practice to fully develop the method. However, it could be a suitable starting point, as it is analogous to the current guidelines for live animals.

6.3 Data Aspects specific to animal welfare RAs

To assess animal welfare it is considered that the adverse consequences should be <u>measured directly</u> on the animals e.g. lameness in cows. There usually is a large body of qualitative data (e.g. scores) available for such parameters but very little in the way of quantitative data. Further, the potential consequences of exposure to the hazard (hazard characterisation) might change as the animal grows, or with adaptation due to exposure to the hazard, and in certain states of its reproductive cycle.

For welfare RAs involving the importation of animals and their products, <u>international issues</u> affecting animal welfare, including farming of domesticated and wild animals in various regions of the world, might need to be considered.

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Excerpt of Personal response from Dr M Wooldridge
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1 Two risk analysis terminology systems: description.

1.1 The terminology involved in risk analysis has developed alongside the terminology involved in risk assessment. It may be helpful to look briefly at *risk assessment* terminology first, in particular the two terminology systems used in PH and VPH risk assessment as mentioned above. One system is derived from that first proposed by the National Research Council of the National Academy of Sciences (NAS, 1983) - I will call that the 'NAS model'. The second system is based on that described by Covello and Merkhofer (Covello & Merkhofer, 1993) - I will call that the 'Covello-Merkhofer model'.

1.2 Figure 5 summarises the components of risk assessment in these two models.

NAS model	**Covello-Merkhofer model**
Comprises:	*Comprises:*
Hazard identification	Risk release assessment
Hazard characterisation	Exposure assessment
Exposure assessment	Consequence assessment
Risk characterisation	Risk estimate

Figure 5. *The components of risk assessment: a comparison of the NAS and Covello-Merkhofer models.*

1.3 The meanings of, and relationship between, these components will be described later. However, the major point to note at present is that whilst **hazard identification** is a component of the NAS risk assessment model, it is not a component of the Covello-Merkhofer model. This is because Covello and Merkhofer have identified hazard identification as a completely separate step from risk assessment, a point which will again be considered later.

1.4 The effect of this separation can be seen on the derived terminology relating to risk analysis. In a system based on the NAS model (here called the 'NAS system'), there are only three components of risk analysis, whereas in the system based on the Covello-Merkhofer model (here called the 'Covello-Merkhofer system'), there are necessarily four. Both systems include risk assessment, risk management, and risk communication as components of risk analysis. However, the Covello-Merkhofer system also includes hazard identification as a component of risk analysis, whereas the NAS system - as we have seen - includes hazard identification as a component of risk assessment. These components are summarised in Figure 6.

NAS risk analysis system	Covello-Merkhofer risk analysis system
Risk analysis comprises:	*Risk analysis comprises:*
Risk assessment	Hazard identification
Risk management	Risk assessment
Risk communication	Risk management
	Risk communication

Figure 6. The components of risk analysis; a comparison of the NAS and Covello-Merkhofer systems.

1.5 The terms risk management and risk communications are equivalent under both systems (and reasonably self-explanatory, for the purposes of this document). I shall now look at the meanings of the remaining terms as used in the original NAS and Covello-Merkhofer models, then compare the models and their uses, and then how they have been applied to PH and VPH systems.

2. Two risk analysis terminology systems: meanings

2.1 The NAS model was initially developed to assess the risks to health from exposure to chemicals. The Covello-Merkhofer model was initially developed to assess a wide range of risks from any potential hazard. The specific wording in the explanations in Figure 7 reflects those differences.

NAS system & model	Covello-Merkhofer system & model
	Risk analysis: *Meaning of:* • **Hazard identification** Identifying 'risk agents' (hazards) and the conditions under which they potentially produce adverse consequences.
Risk assessment: *Meaning of:* • **Hazard identification:** Determining whether a specified chemical causes a particular health effect • **Dose-Response Assessment (Hazard characterisation):** Determining the relationship between the magnitude of exposure and the probability of health effects • **Exposure assessment:** Determining the extent of human exposure before and after regulatory controls • **Risk characterisation:** Describing the nature and magnitude of human risk, including uncertainty	**Risk assessment:** *Meaning of:* • **Risk release assessment:** Assessing the potential of a risk source to introduce 'risk agents' (hazards) to the environment under consideration • **Exposure assessment:** Assessing the probability of exposure to 'risk agents' (hazards) resulting from specified release conditions • **Consequence assessment:** Assessing the relationship between exposures to 'risk agents' (hazards) and health and environmental consequences • **Risk estimate:** Estimating the timing, likelihood, nature and magnitude of adverse consequences

Figure 7. The definitions and meanings of terms within risk analysis and assessment where the NAS and Covello-Merkhofer systems and models are different

(based on NAS-RRC, 1983, and Covello & Merkhofer, 1993, Page 28)

3. Comparison of differences between NAS and Covello-Merkhofer models.

3.1 The first difference centres on the place of **hazard identification** in the models. The initial report of the NAS model (NAS 1983), describes hazard identification as a major undertaking. The definition above relates specifically to chemicals, and even there, NAS indicates that it includes weighing the available evidence relevant to cause and effect, as well as evidence relating to magnitude of effect for the specified chemical. It is essentially a qualitative process of considerable magnitude.

3.2 However, largely because of the magnitude of the undertaking of a complete hazard identification, Covello and Merkhofer (1993) consider that: 'treating hazard identification as merely one component of risk assessment underplays its importance'. In their view it: 'provides the essential foundation for and must precede risk assessment'. In addition, in that model hazard identification is an even more extensive process looking for all the potential hazards in a given situation, not just one pre-defined chemical, further increasing the requirement for this separation.

3.3 To put a practical perspective on this, from the definition in Figure 7, we have seen that in the original NAS model the chemical under consideration is already identified and defined. The question is: 'Does this specified chemical cause an adverse health effect?' Thus hazard identification in this system is about 'Is it a hazard?' rather than 'Is it there?' These are very different questions, designed for different situations. In the more general Covello-Merkhofer system, the question asked is 'What potential hazards are present?' This will therefore automatically include, for each possible or potential hazard identified, the supplementary question 'Does this specified potential hazard ('risk agent') cause an adverse health or environmental effect?' That is, it includes the process involved in the NAS model, and more. If a hazard is not identified, the risk cannot be managed.

3.4 The second difference is the presence in the Covello-Merkhofer model of a step called **release assessment**, absent in the NAS model. Covello and Merkhofer argue that this is necessary for describing the probability of a given system (for example an industrial complex, or a meat processing plant or other **risk source**) to release risk agents into the environment of interest. They believe this to be an essential step in obtaining an accurate understanding of risk. From a practical standpoint, this is an essential explicit step if one wishes either to assess the risks due to a particular hazard from a specific source or process, or to undertake a cost-benefit analysis of putting in place release reduction safeguards for that source or process.

3.5 In the real world, after 'release' comes the possibility of exposure. Thus the Covello-Merkhofer model follows release assessment with **exposure assessment** (assessing the probability of exposure by each potential exposure route of interest). Here is the third difference between the models; the NAS model places this step after the dose response (hazard characterisation) step. The precise definitions are also slightly different, here reflecting the fact that the NAS model was developed with an emphasis on assessing the necessity for, and impact of, regulatory controls whereas the Covello-Merkhofer model was developed with the emphasis on assessing the risks actually present in many situations. However, the meanings are similar, and the information and data necessary is likely to be of the same kind.

3.6 The fourth difference is in the place and meaning of consequences in the two models. Exposure can then lead to consequences - unwanted consequences when considering a hazard. Thus the Covello-Merkhofer model places **consequence assessment** after exposure

assessment, and defines it broadly - any consequences which can occur can be considered, and their probability assessed. The NAS model however looks only at the consequences of variation in dose of the chemical being considered - that is, a **dose-response assessment**. It is also sometimes called **hazard characterisation**.

3.7 Both models finish with a step which links all the previous steps. They have different names; **risk estimation** in the Covello-Merkhofer model, and **risk characterisation** in the NAS model. However, and given the specific nature of the risk defined in the NAS model, they do identify the same process; that of putting all the information together to describe the risk in terms appropriate to the situation.

4. Why are the two systems different?

4.1 The NAS risk assessment model was developed in response to a requirement to set maximum limits of, initially, chemical substances in the environment, food, etc. Risk assessments undertaken under this system were initially designed to answer the question:

- 'What is the maximum amount of chemical X to which a person should be allowed to be exposed (per time period Y - acute or chronic) from source S?'

4.2 To summarise: in my opinion the NAS model is a regulatory tool perhaps most useful in setting allowed, acceptable or tolerable levels of contaminants, and is often the system of choice by professional *toxicologists*. Qualitative risk assessments are possible with this model, and whilst numerical outputs (quantitative assessments) are also possible, this model format does not lend itself easily to quantitatively assessing overall risk estimates.

4.3 The Covello-Merkhofer risk assessment model has been designed to assess the actual magnitude of the risk for a specified consequence in a given situation. It can then be used in order to decide whether the risk actually occurring is acceptable as it stands, or whether safeguards are required. It can easily be used for qualitative risk assessments - there is nothing in the model which precludes this. In addition, it is easily used for quantitative modelling as the taxonomy has been designed to mirror the critical links in a chain of events - source, exposure, and effects (consequences). Risk assessments undertaken under this system are designed to answer questions such as:

- 'What is the risk of specific consequence C (the adverse effect of interest) occurring due to exposure to X which came initially from source S (the release-source)?'

4.4 To summarise**:** In my opinion the Covello-Merkhofer system is a very versatile general system for risk questions of all types, and is often the model of choice by professional *risk assessors.* In addition, if the output from an NAS system requires a quantitative overall risk estimate of a specified risk the mathematics required will generally convert it to a form which is essentially equivalent to this model in any event.

5. Application of these models to PH and VPH.

5.1 The older NAS system is the basis of that used currently by the Codex Alimentarius Commission ('Codex'), with various modifications to the definitions to make it applicable to microbiological systems. Being older, and also having been used extensively for chemical risk assessments in the USA, the NAS system was undoubtedly the more familiar system to those adopting it for 'Codex'. This, coupled with the lower profile of quantitative risk assessment in microbiological risk assessment until recently, probably made it the obvious choice.

5.2 There is now an increasing demand for quantitative risk assessments in biological fields of all types. For mathematical and computational reasons processes closely allied to the more recently described Covello-Merkhofer model have generally been used when undertaking these quantitative risk assessments in the animal health field. This already established methodological usage, and the fact that the Covello-Merkhofer model is easily applicable to both qualitative and quantitative risk assessments meant that the opportunity was taken when redrafting the Office Internationale des Epizooties (OIE) Animal Health Code ('OIE-AHC') (from 1997-1999) to base the risk assessment model on this general, versatile model. In addition, given the number of potential pathogen hazards present in animals and their products, this meant that the risk analysis system derived from this, with a separate hazard identification step, was also particularly appropriate.

5.3 Whilst the OIE-AHC model is based very closely on the original Covello-Merkhofer model, a comparison of the two models will show that the 'Codex' based risk assessment model has moved somewhat closer to the OIE-AHC model than were the two original models to each other. In particular, risk characterisation and risk estimate are now very similar in meaning. However, it remains the case that in order to undertake quantitatively the process described in risk characterisation, the mathematical combination of the processes will generally result in a mathematical model with a risk pathway very similar to the Covello-Merkhofer model.