DISSERTATION

EPIDEMIOLOGY AND VETERINARY PUBLIC POLICY

Submitted by
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WE HEREBY RECOMMEND THAT THE DISSERTATION PREPARED UNDER OUR SUPERVISION BY CRISTOBAL ANDRES ZEPEDA SEIN ENTITLED EPIDEMIOLOGY AND VETERINARY PUBLIC POLICY BE ACCEPTED AS FULFILLING IN PART REQUIREMENTS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY.

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ABSTRACT OF DISSERTATION

EPIDEMIOLOGY AND VETERINARY PUBLIC POLICY

Official Veterinary Services are increasingly required to base veterinary public policy decisions on scientific grounds, epidemiology and risk analysis play an important role in shaping these decisions. A formal, in-depth analysis of the multiple interactions between epidemiology, risk analysis and veterinary public policy was conducted to enable decision-makers to direct resources more efficiently and facilitate compliance with international agreements, in particular the Agreement on the Application of Sanitary and Phytosanitary Measures (SPS) of the World Trade Organization. The SPS Agreement recognizes the World Organization for Animal Health (OIE) as the international organization responsible for developing animal health standards. The OIE's Terrestrial Animal Health Code contains scientifically based recommendations for international trade in animals and animal products. However, to date, these recommendations have not been assessed from a risk-based perspective.

The study is divided in two major sections: 1) the role of epidemiology in veterinary public policy and 2) the application of risk-based approaches to the assessment of international animal health standards. The first section addresses the international framework, risk analysis and its use worldwide, and the development of international standards. The second section focuses on quantitative risk assessment approaches for the international movement of animals and products, as well as the application of compartmentalization to aquaculture production systems emphasizing the use of a HACCP approach to biosecurity.

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TABLE OF CONTENTS

Chapter 1

The role of epidemiology in veterinary public policy

Introduction

The Uruguay Round of Multilateral Trade Negotiations of the General Agreement on Tariffs and Trade (GATT) concluded, after seven and a half years of negotiations, with the signature of the Final Act, in Marrakesh on April 15, 1994. This became known as "the GATT of 1994". The GATT of 1994 led to the creation of the World Trade Organization (WTO) on January 1, 1995. Among the agreements that were included in the treaty that established the WTO is the Agreement on the Application of Sanitary and Phytosanitary Measures (SPS Agreement), which sets out the basic rules for food safety and animal and plant health standards.

The SPS Agreement's main intent is to avoid the use of sanitary and phytosanitary measures as unjustified barriers to trade. While recognizing the right of countries to protect both human and agricultural health, the agreement dictates that all measures must be scientifically based and not unnecessarily restrictive. The SPS agreement has truly changed the way in

which decisions related to veterinary public policy are made, in particular decisions related to trade in agricultural products.

The SPS Agreement introduced several key concepts including regionalization, equivalence, harmonization, transparency and risk analysis. In the animal health arena, veterinary epidemiology is the central pillar providing the scientific basis for the application of these concepts and thus is essential to achieve compliance with the SPS Agreement.

The text of the agreement considered a delay of two years for full implementation, the grace period expired on January 1, 1997; however, least-developed countries could elect to extend this period up to five years (i.e. up to 2000). A review of the operation and implementation of the agreement recognizes that although the SPS agreement has contributed to improved international trading relationships and has led to increased transparency on the application of SPS measures, several developing countries still have implementation problems (WTO, 1999). To date (early 2008), this situation persists as the WTO counts new member countries and several countries that adhered to the WTO from its creation still face implementation issues.

Conceptual hypotheses

1. As Official Veterinary Services are increasingly required to base veterinary public policy decisions on scientific grounds, epidemiology and risk analysis play an important role in shaping these decisions. A

formal, in-depth analysis of the multiple interactions between epidemiology, risk analysis and veterinary public policy will enable decision-makers to direct resources more efficiently and facilitate compliance with international agreements, in particular the Agreement on the Application of Sanitary and Phytosanitary Measures of the World Trade Organization.

2. The SPS Agreement recognizes the World Organization for Animal Health (OIE) as the international organization responsible for developing animal health standards. The OIE's Terrestrial Animal Health Code contains scientifically based recommendations for international trade in animals and animal products. However, to date, these recommendations have not been assessed from a risk-based perspective. The development of probabilistic, risk-based approaches to assess current OIE standards will constitute a useful tool and provide a framework for the development of future standards and recommendations.

General objectives

1. To explore the interrelationships of epidemiology with animal health research, animal disease surveillance and risk analysis and the overall influence in veterinary public policy decisions, both at the national and the international levels. Appropriate characterization of these interrelationships will enable the identification of areas requiring further epidemiological input, leading to the development of new

approaches and methods. The overall findings will help determine priorities and optimize resources to develop scientifically based veterinary public policy decisions.

2. Develop and apply probabilistic, risk-based approaches to assess existing animal health standards for international trade and provide a framework for international standard setting in animal health.

Specific objectives

The study will be divided in two major sections: 1) the role of epidemiology in veterinary public policy; and 2) the application of risk-based approaches to the assessment of international animal health standards.

The overall objective for the first section of the study is to identify the role of epidemiology in different areas of interaction, focus on current constraints and propose possible solutions. Three areas of interaction have been identified: international framework, risk analysis and development of international standards. Case studies and examples will be provided for each area. Specific objectives for each topic are outlined below.

The objective of the second section is to propose approaches to assess the probability of introducing selected disease agents through international trade, under current OIE Code recommendations. Risk assessment methods based on stochastic simulation modeling will be applied to the recommendations of

the OIE International Animal Health Code for selected economically important diseases.

Section 1. The role of epidemiology in veterinary public policy

A. International framework - Analyze the international framework for the development of veterinary public policy; identify the main problems faced by WTO member countries to implement the SPS Agreement.

- Historical perspective
- The role of the OIE
- Epidemiology and the SPS Agreement
- Compliance issues
- Case studies

B. Risk analysis - Identify methodological issues and data requirements for the risk analysis process.

- Description of the process
- The role of epidemiology in risk analysis
- Survey on the use of risk analysis internationally

C. Development of international standards

- The OIE process for development and adoption of international standards
- The role of the OIE Ad hoc group on epidemiology
- Compartmentalization as an example of the process

Section 2. The application of a risk-based approach to the assessment of international animal health standards

The OIE Code contains recommendations for international trade in animals and animal products for the most economically important animal diseases. The Code also contains recommendations on the application of disease management and control strategies that allow trade even while disease has not been completely eradicated in a country. For selected OIE listed diseases, probabilistic models will be developed to assess the risk of introduction through international movement of animals and products. An approach to the application of the recently developed concept of compartmentalization will also be developed.

This section will contain targeted examples on the use of a risk-based approach to decision making.

A. Live animals – Development of probabilistic approaches to quantify the probability of disease introduction due to the movement of live animals from infected countries or zones.

- Foot-and-mouth disease
- Bovine brucellosis
- Other selected economically important diseases

B. Products - Assessment of the risk of introducing low pathogenic avian influenza virus through the importation of poultry meat.

- Assessing the probability of the presence of low pathogenicity avian influenza virus in exported chicken meat
- Methodological issues in quantitative risk assessment

C. Disease management strategies - A risk-based approach for the application of compartmentalization.

- Compartmentalization in aquaculture productions systems

Methodology

Section 1

An in depth discussion of each area will be based on a comprehensive literature review, as well as discussion with experts in the field and where relevant, demonstrations of application.

Section 2

For each disease a thorough literature review focusing on the significant factors involved in disease transmission and survival of the agent in animals or animal products will be conducted. The risk analysis methodology that will be applied is described in the OIE International Animal Health Code (OIE 2007).

The study will assess recommended mitigation measures in the OIE Code; therefore, only the release assessment component of the risk assessment will be treated quantitatively. Exposure and consequence assessments are dependent on each importing country's pathways of introduction and local mechanisms for disease spread. Similarly, the economic impact of disease

introduction will vary from country to country. These steps of the risk assessment process will not be addressed in this study.

Expected results

Section 1

Section 1 will identify constraints for the implementation of the SPS Agreement, through an analysis of the interactions between epidemiology and veterinary public policy. The analysis of these constraints will lead to recommendations and suggested alternatives for compliance with the SPS Agreement and increased access to export markets, in particular for developing countries.

Section 2

The results from this section are two-fold. On one hand, the probability of introduction of the selected disease agents will be estimated for each type of commodity susceptible of harboring these agents. The risk assessment models will allow for the measurement of the effect of each mitigation measure, and on this basis, specific suggestions for modification of the OIE Code will be made if appropriate. Suggestions for modifications may range from the recommended length of quarantine periods and the use of diagnostic tests to specific treatments for animal products.

The application of probabilistic, risk-based approaches will provide a framework for the assessment of current OIE standards and will improve the process by which OIE Code standards are developed.

Limitations of the study

This study will only address selected diseases listed by the OIE. Further, only the release assessment step of the risk analysis process will be addressed quantitatively. However, the choice of diseases will allow for the development of approaches that are applicable for most situations: animal imports as well as meat, dairy products, semen and embryos imports. These approaches may be used as guidelines or templates for assessment of other OIE Code chapters. This dissertation outlines principles, methods and approaches that contribute to the development of international standards that comply with the requirements outlined in the SPS agreement (Chapter 2) ensuring the application of epidemiologic principles and careful consideration of the needs of all OIE member countries.

References

OIE (2007) International Animal Health Code. Office International des Epizooties, www.oie.int

WTO (1995) Agreement on the Application of Sanitary and Phytosanitary Measures. World Trade Organization, www.wto.org

WTO (1999) Review of the operation and implementation of the Agreement on the Application of Sanitary and Phytosanitary Issues. World Trade Organization, www.wto.org

Chapter 2

The role of veterinary epidemiology and veterinary services in complying with the World Trade Organization SPS Agreement[1]

Introduction

The Uruguay Round of Multilateral Trade Negotiations of the General Agreement on Tariffs and Trade concluded in 1994, after seven and a half years of negotiations, with the signature of the Final Act, in Marrakesh on 15 April 1994. This became known as "the GATT of 1994" and led to the creation of the World Trade Organization (WTO) on January 1, 1995 (WTO, 1998a). Among the agreements that were included in the treaty that established the WTO is the Agreement on the Application of Sanitary and Phytosanitary Measures (SPS Agreement) which sets out the basic rules for the protection of public, animal and plant health during international trade (WTO, 1995).

[1] Published paper. Zepeda C., Salman M., Thiermann A., Kellar J., Rojas H and Willeberg P. (2005). The role of veterinary epidemiology and veterinary services in complying with the World Trade Organization SPS agreement. Preventive Veterinary Medicine 67:125-140.

The SPS Agreement has truly changed the way in which trade decisions related to agricultural products are made. Its main intent is to avoid the use of sanitary and phytosanitary measures as unjustified barriers to trade. While recognizing the right of countries to protect human, animal or plant life or health, the Agreement dictates that all measures must be scientifically based and not unnecessarily restrictive.

The challenge

Official veterinary services worldwide, particularly those in developing countries, are faced with an enormous challenge. On one hand, the general tendency over the past two decades has been to reduce the size of government. Often, veterinary services have not been considered as a high priority and have suffered severe budget cuts, resulting in a loss of operational capability and presence in the field.

On the other hand, most countries have become members of WTO and have also signed bilateral or regional agreements that demand greater responsibility and capacity of these limited infrastructures. Specifically, the SPS Agreement has placed an increased emphasis on the importance of sanitary and phytosanitary measures, requiring improved surveillance and monitoring systems, adequate laboratory diagnosis, risk analysis capabilities and quality assurance (Vallat and Wilson 2003).

The text of the Agreement considers a delay of two years for full implementation (the deadline expired in 1997); least-developed countries could elect to extend this period up to five years (i.e. up to 2000). A recent

review of the operation and implementation of the Agreement recognizes that although it has contributed to improve international trading relationships and has lead to increased transparency on the application of SPS measures, several developing countries still have implementation problems (WTO, 1999).

The SPS Agreement demands that all sanitary and phytosanitary measures should be science-based, non-discriminatory and encourages the application of international standards, if they exist. In the field of animal health the World Organization for Animal Health (Office International des Epizooties, OIE) is the organization responsible for setting international standards. These standards are laid out in the Terrestrial Animal Health Code (the OIE Code), the Aquatic Animal health Code and their corresponding Manuals for Diagnostic Tests and Vaccines. (OIE; 2003a, b, c, d)

This paper discusses the impact of the SPS Agreement on official veterinary services, identifies issues in achieving compliance and suggests areas where veterinary epidemiology can contribute to the development of possible solutions.

The implications of the SPS Agreement

The SPS Agreement is a relatively short document consisting of 14 articles and three annexes. Nevertheless, despite its concise nature, it has had profound consequences for veterinary services worldwide. This section analyzes the text of the Agreement highlighting its implications and effects

and emphasizes the role of epidemiology in implementing the key provisions of the Agreement.

Art. 1. General provisions

The Agreement applies to all sanitary and phytosanitary measures that affect international trade. Sanitary and phytosanitary measures are legitimate arguments that can be applied to regulate international trade as long as they are scientifically based.

The Agreement has placed SPS measures at the forefront of negotiations for international trade in agricultural products. Veterinary services and plant health services have acquired an extremely important role in international trade. However, to successfully participate in international trade, veterinary services need to clearly understand the implications of the SPS Agreement and adjust their organizational structures and activities to comply with their obligations under the SPS Agreement (Zepeda, 1998; Marabelli, 2003).

Art. 2. Basic rights and obligations

Countries have the right to protect human, animal or plant health as long as the applied measures are scientifically based and non-discriminatory. Countries can request sanitary measures for diseases that are exotic in their territory or for diseases under an official control program and in the latter case, only if the requested measures are also applied internally. In order to apply SPS measures, countries are expected to determine their animal health status based on accurate disease reporting and surveillance to establish a

scientifically based list of the country's foreign animal diseases and declare which diseases are under an official control program.

The demonstration of disease status has become increasingly important, veterinary epidemiology has contributed in the development of methods and approaches to declare disease freedom; a more detailed discussion is presented under Article 6. The OIE has recently drafted guidelines for recognition of historical freedom from disease, establishing basic criteria by which countries can declare disease freedom from diseases that have never occurred or that ceased to occur, without having to apply extensive, active surveillance. Similarly, the OIE Code contains guidelines for the recognition of disease freedom for a few selected diseases (OIE, 2003b). However, guidelines to recognize disease freedom after eradication are still lacking for most diseases.

Countries are expected to have clear rules and regulations governing the application of SPS measures. This implication has had a positive impact and has promoted the development of standards and regulations. It also has led to formalize disease control efforts into official programs at the national and regional levels. However, several countries still need to develop a formal process of regulation drafting that is transparent and open to public comment.

Art. 3. Harmonization

Harmonization is the establishment, recognition and application of common sanitary and phytosanitary measures. The article encourages countries to base their SPS measures on international standards developed by the

relevant international organizations: the Codex Alimentarius for food safety, the International Plant Protection Convention (IPPC) for plant health and the World Organization for Animal Health (OIE) for animal health. Countries may apply SPS measures that are more stringent than the international standards as long as they are scientifically justified and based on a risk assessment.

Although membership of the reference international organizations is not mandatory, the SPS Agreement has led to an increase in the number of countries belonging to and actively participating in these organizations. In the particular case of OIE, this has meant a steady increase in its membership, now numbering 166 countries (OIE, 2003a) (the WTO has 143 member countries).

Not all WTO member countries are members of OIE (and *vice versa*). Although OIE membership fees are reasonable, for some smaller developing countries membership fees constitute a sizeable part of the veterinary services budget and therefore are not able to participate in the process of developing standards that they will have to follow. Some countries have financed their membership through international or regional organizations.

The development of international standards increasingly requires significant input from veterinary epidemiologists. To draft these standards, the OIE convenes experts from its member countries including specialists on the specific topic as well as epidemiologists. Examples include the Code chapters on risk analysis, evaluation of diagnostic tests and surveillance guidelines. Recently, the OIE created a group on epidemiology in support of

the Scientific Commission. The development of revised guidelines for surveillance and recognition of disease freedom are among the first tasks of this group.

Art. 4. Equivalence

The concept of equivalence implies the consideration of different methods as long as they achieve similar results. Exporting countries have to justify the scientific basis of the procedures used and objectively demonstrate that they achieve the level of protection required by the importing country.

Member countries are encouraged to develop bilateral or multilateral equivalence agreements. Major trading partners, such as the European Union and the United States, have negotiated or are in the process of negotiating equivalence agreements. They key of equivalence is that it focuses on the results rather than on the methods, this allows for flexibility in the organization of official veterinary services and allows for countries to direct their efforts on key areas, according to resources and priorities.

The OIE Code contains a chapter on equivalence of sanitary measures (Chapter 1.3.7) (OIE, 2003) that discusses principles and outlines a step-wise process to be used in determining equivalence. Furthermore, the chapter emphasizes that equivalence may apply to specific measures (e.g. comparison of different diagnostic procedures) or on a system-wide basis (e.g. equivalence of surveillance systems). There is a need to develop and establish methods to recognize equivalency. Epidemiologists have a role in

developing scientific procedures enabling an unbiased comparison of different approaches.

Art. 5. Assessment of risk and determination of the appropriate level of sanitary or phytosanitary protection

The SPS Agreement defines risk assessment as the "evaluation of the likelihood of entry, establishment or spread of a pest or disease within the territory of an importing member according to the sanitary or phytosanitary measures which might be applied, and of the associated potential biological and economic consequences; or the evaluation of the potential for adverse effects on human or animal health arising from the presence of additives, contaminants, toxins or disease-causing organisms in food, beverages or feedstuffs." (WTO, 1995)

The article on harmonization states that in the event that an international standard does not exist or does not meet the level of protection required, a country has the right to establish SPS measures based on a scientifically sound risk assessment. The OIE Code contains a section on import risk analysis (Section 1.3) (OIE, 2003b). It is interesting to note that the SPS Agreement refers to risk assessment, while the OIE talks about risk analysis, of which risk assessment is one of the components of the process.

A common perception is that if an importing country applies the risk-mitigation recommendations of the OIE Code, a risk analysis is not necessary. While it is true that an in-depth risk analysis may not be necessary, the establishment of import requirements involves at least a partial application of the risk

analysis process. Part of the complexity in developing import requirements is that multiple hazards can be identified for each commodity; however, the Code provides recommendations on an individual disease basis. The question then becomes how to merge the Code recommendations with the hazards that were identified? Risk analysis in its simplest form provides a framework to establish a link between the hazards identified for the specific commodity, the sanitary status of the exporting and importing countries and the recommendations of the Code.

A recent survey conducted among OIE member countries showed that the majority of countries still require training in risk analysis methods despite the fact that the same survey found that most countries had already received some type of training in this area (Zepeda, 2002). The OIE Collaborating Center for Animal Disease Surveillance Systems and Risk Analysis developed a series of short training courses on epidemiology and risk analysis and has organized and conducted several training sessions internationally. Similarly, other institutions worldwide are offering short courses on risk analysis. However, there is a lack of formal training opportunities in animal health risk analysis within universities at the graduate or postgraduate levels.

There is a need to promote a better understanding among decision-makers of the concept of risk analysis, its application and limitations. Although each risk assessment is different, there are common methods, tools and techniques that can be used. Currently, efforts are underway to harmonize the approach to risk assessment internationally.

The OIE has published two volumes of the Scientific and Technical Review dedicated to risk analysis (Vol. 12 (3), 1993 and Vol. 16 (1), 1997). Several comprehensive guidelines on animal health risk analysis have also been published (OIRSA, 2000; CFIA, 2002; Murray, 2002; AFFA, 2003).

The OIE Code (Chapter 1.3.2.) describes the risk analysis process consisting of four steps (OIE, 2003b):

- Hazard identification
- Risk Assessment
    - Release assessment
    - Exposure assessment
    - Consequence assessment
- Risk estimation
- Risk Management
- Risk Communication

Risk is defined as the probability of occurrence and the magnitude of the consequences (Ahl et al., 1993). Although a complete risk assessment should include all the relevant steps, the OIE Code chapter on risk analysis states that when the results of the release or exposure assessments demonstrate no significant risk the risk assessment may conclude at this step. However, under the dispute settlement process of the WTO a complete risk assessment is required. The Appellate Body report reviewing the Canadian salmon dispute established three conditions to assess if a risk

analysis can be considered valid. These include (1) identifying the diseases that may be introduced and their associated consequences, (2) evaluation of the likelihood of entry, establishment and spread of the diseases identified as hazards as well as the biologic and economic consequences and (3) evaluation of the likelihood of entry, establishment and spread of the diseases according to the SPS measures that might be applied (WTO, 1998b). The Canadian salmon dispute was the first animal health case to go through the WTO dispute settlement process. A more thorough description of the findings of the Panel is given under the dispute settlement section of this paper.

For a risk assessment to withstand legal scrutiny, the implication is that all the steps of the process need to be properly addressed. However, within the risk assessment process, most of the emphasis has been placed on the release assessment portion, the exposure and consequence assessment steps have not been addressed as thoroughly.

Risk management requires comparing the results of the risk assessment with the country's acceptable level of protection (ALOP). The SPS Agreement recognizes that establishing the ALOP is a prerogative of the importing country (WTO, 1995; WTO, 1998b). However, it does not define how to establish the ALOP, although the process by which it is established must be transparent and applied in a non-discriminatory fashion. Currently, there is considerable interest in developing approaches to define this level, also called acceptable level of risk (WTO, 1995). The difficulty in defining the

ALOP resides not only on developing good quality risk assessments, but also needs to consider economic implications and societal values.

Risk analysis calls for several epidemiologic inputs, most of which are dependent on a well structured surveillance system (OIRSA, 2000; Zepeda et al., 2001; Murray, 2002; AFFA, 2003; MacDiarmid and Pharo 2003; OIE 2003b), underscoring the importance of developing surveillance systems that are well designed and monitored for quality (Stärk, 2003; Zepeda and Salman, 2003).

The application of the risk analysis process requires expertise and a multidisciplinary approach. In some developing countries, this expertise does not exist, emphasizing the need for training and ensuring access to relevant scientific information.

Art. 6. Adaptation of regional conditions, including pest- or disease-free areas

Zoning and regionalization

In the past when a disease agent existed in a country, the entire territory was considered as infected. The SPS Agreement recognizes that it is possible to consider regions (i.e. groups of countries), countries or zones within countries free from disease/infection based on the epidemiology of the disease and other criteria. This provision is generally known as zoning or regionalization and is reflected in the OIE Code (Chapter 1.3.5) (OIE, 2003b).

Zoning and regionalization require an effective surveillance system and good quality veterinary services both at the national and regional level. When determining the animal health status of a country or zone consideration of several factors has been suggested (USDA, 2003):

1. Authority, organization, and infrastructure of the veterinary services organization in the region
2. Disease status of the region
3. Status of adjacent regions with respect to the agent
4. Extent of an active disease control program
5. Vaccination status of the region
6. Degree to which the region is separated from adjacent regions of higher risk through physical or other barriers
7. Extent to which movement of animals and animal products is controlled from regions of higher risk and the level of biosecurity regarding such movements
8. Livestock demographics and marketing practices in the region
9. Type and extent of disease surveillance in the region
10. Diagnostic laboratory capabilities
11. Policies and infrastructure for animal disease control in the region, i.e., emergency response capacity

The quality of the veterinary service both at the national and at the regional level plays a crucial role in preventing the re-introduction of disease. Surveillance systems are essential in providing information for the recognition of disease-free zones and to conduct scientifically valid risk assessments. The assessment of the quality of veterinary services has received great

attention in the past few years. The OIE Code initially developed guidelines for the assessment of veterinary services (Chapters 1.3.3 and 1.3.4) (OIE, 2003). However, the emphasis was placed more on the inputs rather than the outputs of the service. More recently, several efforts have been directed towards developing criteria that will allow a more objective evaluation of veterinary services (Dunn, 2003; Correa, 2003; Templeman et al., 2003), that focus on results and allow for different organizational structures according to the priorities and production systems in each country.

Different approaches to zoning and regionalization have been adopted:

- Zoning to contain disease outbreaks
- Zoning of disease-free areas

Although the same principles are applied, the emphasis is different. The ways of defining a region or zone have important differences. From a risk point of view, the application of zoning as a reaction to disease incursion is not the same as the application of zoning as a measure of progress of a disease eradication program. In the first instance, a zone is a way to separate a diseased area in an otherwise disease-free country; in the second, the zone is a way to secure a free area in an otherwise infected country.

A zone that is defined on grounds of infection is less stable. Movement controls, although strict, may not be efficient; there may be incentives for producers to circumvent them. The disease may spread and the zone's boundaries may need to be modified accordingly. A certain amount of time is needed to achieve stability.

A zone that achieves disease eradication and claims freedom is much more stable, it reached that status through a structured disease control program, animal movement controls, active surveillance and producer participation. Furthermore, usually the rest of the country is also under a disease control and eradication program.

Compartmentalization

A new concept for the management of animal health is compartmentalization, which is a procedure to define animal populations of different animal health status based on management and biosecurity. Regionalization consists of establishing zones of different animal health status on the basis of either geographical features or production systems.

During the process of defining compartments the focus should be on the disease-free compartment, this is the compartment primarily interested in reaching and maintaining its status. Once again, the stability of the compartment is the key concept, the disease-free compartment being much more stable than the diseased compartment.

Compartmentalization can be applied in situations where different production systems co-exist such as commercial and subsistence farming. In general, commercial farms are in a better position to control and eradicate disease and maintain their status. Having reached this status it is possible through appropriate biosecurity measures to effectively avoid the reintroduction of disease from the affected compartment.

As is the case with regionalization credibility is the basis for recognition of the status of the compartment. Credibility can only be achieved by effective surveillance, movement controls, producer participation and most importantly, transparency.

Regionalization has allowed resources to be directed more efficiently by allowing access to export markets from disease-free areas without the need to achieve eradication in the entire territory of a country (Zepeda, 1998). From a scientific perspective, disease freedom cannot be conclusively demonstrated. There is a need for the development of methods to substantiate disease freedom claims that include evidence from structured random surveys as well as non-random data sources, such as information from passive surveillance systems. Quantification of the joint probability of detection of all the components of a surveillance system allows reaching a high level of confidence of the absence of disease (Cannon 2002, Cameron 2003), higher than any of the components individually. There is also a need to include economic considerations in defining the intensity of surveillance and deciding upon the optimal combination of surveillance components of a system.

Art. 7. Transparency

Notification of SPS measures

Under Article 7 and Annex B of the SPS Agreement, countries must notify the WTO about changes in SPS measures that have an impact in international trade. SPS measures must be published and accessible through an official

enquiry point. The transparency provision also includes control and inspection procedures as well as risk assessment. Throughout the process confidentiality of commercial information is maintained (WTO, 1995).

The transparency provision has led in many countries to review the process of regulation drafting, resulting in more open processes that allow input from all interested parties.

Notification of disease status

Transparency is the basis for trust. Under the OIE, the concept has been interpreted as transparency in reporting the animal health status by member countries. In this respect, surveillance systems are an essential component guaranteeing the quality of the information. International disease reporting guidelines are currently being restructured. OIE list A and B diseases will be merged into a single list, this will allow different diseases to 'gravitate' according to their relative importance (since publication of this paper the OIE created a single list of notifiable diseases). Countries will need to report on an emergency basis 'significant epidemiological events' i.e. events that have an impact on the animal health status of a country including (OIE 2003e):

- Occurrence of a disease or strain of a pathogen that is considered exotic to the country or zone
- Reintroduction of a previously eradicated disease
- Emerging diseases
- Significant changes in the epidemiology of an existing disease

Countries will also be required to notify periodically the occurrence of all OIE listed diseases.

Art. 8. Control, inspection and approval procedures

The requirements for procedures for sampling, testing and certification are described in detail in Annex C of the SPS Agreement. In general, the intent is that control, inspection and approval procedures should be transparent, non-discriminatory, timely and scientifically based.

This creates the need to revise the adequacy of current procedures including sampling protocols with a view to optimize cost, efficiency and practicality. Epidemiologists can contribute in designing sampling strategies that are scientifically based and statistically sound.

Art. 9. Technical assistance

A report by the SPS committee (WTO, 1999) noted that although the SPS Agreement had contributed to improving international trading relationships with respect to sanitary and phytosanitary measures, there were several issues regarding the operation and implementation of the Agreement that still needed to be resolved. In particular, the report stressed the need to provide assistance in areas such as human resource development, national capacity building and the transfer of technology and information. Technical assistance can be delivered either bilaterally or through the relevant international organizations.

Many developing countries feel that SPS measures are becoming more stringent and are being used as new barriers to trade. International and regional organizations have played and continue to play a crucial role in assisting developing countries to develop the adequate infrastructure to satisfy the demands of the international market.

The WTO and several international organizations have carried out numerous workshops to increase the understanding of the Agreement. However, in order to achieve compliance several countries require assistance and access to funding sources. In response to this, in September 2002, the WTO developed in partnership with the World Health Organization, the World Bank, the OIE and the Food and Agriculture Organization, the Standards and Trade Development Facility (STDF). Its objective is to fund projects with the purpose of enhancing the capacity of developing countries to meet SPS standards (STDF, 2003; WTO, 2003a). One of the first projects funded by the STDF is a project to develop a tool to assess and evaluate national veterinary services capacity to benefit from the SPS Agreement (WTO, 2003a). Technical assistance has been provided trough the OIE Collaborating Centers in areas of epidemiology, risk analysis, evaluation of veterinary services as well as diagnostic capability. Other international and regional organizations have been actively involved in providing technical assistance.

Art. 10. Special and differential treatment

The SPS Agreement recognizes that some countries may require longer time-frames for compliance with new SPS measures, as long as the appropriate level of protection is not compromised. Countries may solicit

time-limited exceptions to any obligation under the Agreement taking into account their financial, trade and development needs. The Doha Ministerial declaration specifically stated that this time frame should be at least 6 months (WTO, 2001).

Apparently, the provisions under article 10 have had limited use. The review conducted by the SPS Committee on operation and implementation noted that it had no information on the extent to which the special and differential treatment had been granted to developing countries. During the period covered by the review no specific requests for special and differential treatment had had been submitted to the Committee (WTO, 1999).

It is likely that many countries lack a clear understanding of the SPS Agreement and have not interpreted Article 10 as a means to obtain additional time for implementation than what is established in Article 14.

Art. 11. Consultations and dispute settlement

Dispute settlement

WTO member countries have the right to invoke the dispute settlement procedure; however, bilateral settlements are always encouraged. The OIE has set up a procedure for 'in house' dispute settlement under the good offices of the Director General (Chapter 1.3.1, OIE Code) (OIE, 2003; Vallat and Wilson, 2003). Countries using the dispute settlement procedure must be ready to defend their positions with scientifically valid arguments.

The WTO dispute settlement procedure is a lengthy procedure that can be very costly (WTO 2003b). It often requires legal advice and a continuous presence at WTO's headquarters. Therefore, it is a procedure best suited for issues that imply large amounts of trade. It is possible that developing countries may not be willing to elevate a dispute to this level due to financial constraints, leading to an inequitable application of the rights embedded in the SPS Agreement.

Article 12 establishes the creation of the SPS Committee to provide a forum for regular consultations. Further, the article encourages the Committee to facilitate negotiations and discussions between parties involved. The SPS Committee acts as the first forum in which SPS-related disagreements can be discussed once bilateral talks have been exhausted. Often, the fact of raising an issue at the SPS Committee level leads to renewed bilateral discussions resulting in very few disputes needing to go through the entire dispute settlement process. In fact, only three cases related to SPS issues had been through the complete formal WTO dispute settlement procedures.

In all formal disputes risk assessment has been the central part of the technical and scientific evidence submitted to the expert panel. The Appellate Body reviewing the Canadian/Australian salmon case underscored the importance of submitting complete risk assessments and further defined a three-pronged test to assess if a study can qualify as a risk assessment under Article 5 and the definition in annex B. According to the panel, an import risk assessment needs to (WTO, 1998b):

1. "*identify* the diseases whose entry, establishment or spread a Member wants to prevent within its territory, as well as the potential biological and economic consequences associated with the entry, establishment or spread of these diseases;
2. *evaluate the likelihood* of entry, establishment or spread of these diseases, as well as the associated potential biological and economic consequences; and
3. evaluate the likelihood of entry, establishment or spread of these diseases *according to the SPS measures which might be applied.*"

The Appellate Body report emphasized the importance of a solid scientific basis and the coherence between the risk assessment and the resulting SPS measures that are applied. Evidently, good epidemiology is the basis to satisfy this requirement. The report also distinguished between *possibility* -- instead of *likelihood* or *probability* -- of disease entry, stressing that the second test requires the evaluation of the likelihood (not mere possibility), without there being a need for this evaluation to be done necessarily in a quantitative way.

Art. 12. Administration

As mentioned above the Agreement envisages the creation of the SPS Committee as a forum for consultations between WTO member countries. The Committee has the task of maintaining close contact with the international standard setting organizations (OIE, IPPC and Codex

Alimentarius) as well as promoting and monitoring harmonization and the use of international standards, guidelines and recommendations.

The text of the SPS Agreement establishes a review three years after its adoption and on an as needed basis thereafter. The Doha Ministerial declaration set the schedule for these reviews on operation and implementation at least once every four years (WTO, 2001).

Art. 13. Implementation

Signatory countries are responsible to comply with all obligations of the Agreement and have the responsibility to implement all the provisions. Furthermore, countries should ensure that non-centralized government bodies, non-governmental entities and regional bodies comply and act in a manner consistent with the provisions of the Agreement.

Industry and consumer organizations should participate actively in the implementation process by providing a significant input in the rule-making process. To ensure this, countries should establish open working relationships with industry and consumer groups to promote the understanding of the SPS Agreement and its implications.

When drafting regulations that require significant scientific input, academia and researchers should be considered in addition to these groups. Clearly, the implementation of the SPS Agreement in the animal health arena requires significant epidemiological input. Internationally, there are several research groups working in issues related to specific topics of the Agreement.

However, to avoid duplication of efforts and maximize the benefits of research, a certain degree of coordination is required. Veterinary services are the main means for the application of epidemiologic methods and techniques. Researchers in veterinary epidemiology and animal health economics should consider the challenges in the application of the international rules by national veterinary services. This challenge, however, would require full understanding and appreciation about the role of veterinary epidemiology by animal health decision makers and implementers of animal health programs. The International Society on Veterinary Epidemiology and Economics (ISVEE) could serve as a forum for communication and coordination for such efforts. The ISVEE forum can be expanded to include application of epidemiologic methods and engagement of staff members of veterinary services.

Art. 14. Final provisions

Time frame for implementation

Countries agreed to comply with the Agreement within two years after its inception; however upon request to WTO, countries could have up to five years for implementation. The delays applied to all provisions of the Agreement with the exception of the transparency provision (Article 7) and the right of a country to request an explanation if a measure, not based on an international standard, is perceived as a barrier to trade (Article 5.8). These periods expired on January 1st 1997 and 2000 respectively, therefore all WTO Member countries have the obligation to comply with the Agreement. It is important to recall that countries may request additional time for the implementation of the Agreement under Art. 10.3.

Alternatives and solutions

In summary, a veterinary service wishing to comply with the SPS Agreement is required to have a fairly significant infrastructure able to:

- Demonstrate their animal health status by means of scientifically based surveillance efforts
- Draft regulations based on international standards and develop transparent means to divulge them to the public and the international community
- Develop risk analysis capabilities
- Apply and be willing to recognize the concept of regionalization
- Develop control, inspection and approval methods that are transparent, non-discriminatory and scientifically based

Complying with the SPS Agreement demands the strengthening of veterinary services in several areas of competence. The question then is how to enhance the delivery of official veterinary services under severe budget constraints? Several successful alternatives have been applied; all of them include one or more of the following elements (Zepeda, 1998):

- Accreditation of private professionals to carry out official actions;
- Privatization of services under the regulation and supervision of the state;

- Schemes of mixed financial participation with specific objectives such as disease eradication campaigns

The active participation of private professionals is crucial to restore the delivery of veterinary services to a satisfactory level. However, a minimum official infrastructure is required, which is efficient and sufficiently well organized to coordinate the activities to be carried out by the private sector, to issue norms and to supervise their fulfillment.

Conclusions

The SPS Agreement lays out rights, obligations and disciplines that have led to a risk-based approach to trade allowing countries access to export markets that were previously inaccessible due to the presence of specific diseases. The hope is that this in turn will improve transparency, as countries will not get excessively penalized for not achieving complete eradication of disease agents. It must be recognized however, that although science has become increasingly important in the process of decision-making, other factors such as politics and economics will continue to play a role in the process. A common misconception is that countries that are not planning to export are not impacted by the SPS Agreement. This is false. All countries need to be able to justify their SPS measures to their trading partners and to their own consumers, producers and industry groups.

In the field of animal health, veterinary epidemiology is the cornerstone for successful implementation of the SPS Agreement. Through the use of objective risk assessments, veterinary services should be able to establish

priorities and direct efforts according to risk, including the down-scaling of certain activities, minimizing ill-founded political prioritization.

National animal health authorities must establish a closer working relationship with the international scientific community and vice versa. This link should be established through the epidemiologists working in the veterinary services. In service training on basic epidemiologic methods, such as the series of short courses offered by the OIE Collaborating Centers and other institutions, is essential to ensure that veterinary services have adequately trained personnel in the appropriate positions able to understand the broad international context and incorporate methods and approaches developed by academia. It is important to emphasize that some issues may simply require the application or adaptation of existing methods, while others will require the development of new methods and approaches.

Although there are successful examples of implementation of the SPS Agreement, many countries are still struggling to adjust to the new world trade environment. A significant effort is required by governments and international organizations to achieve compliance with the SPS Agreement. International funding organizations need to adjust their policies and be willing to support the development of sustainable infrastructures that will allow developing countries access to the world marketplace. Successful compliance requires strong veterinary services that develop and apply science based veterinary public policies. Unfortunately, many governments (and society in general) do not fully understand the importance of the role of official veterinarians. Producers and veterinary professionals in public

service, academia and private practice have an important part to play in convincing higher government levels of the significance of supporting their official veterinary services. Sadly, often a crisis is the impetus to elicit this support.

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Chapter 3

Compartmentalization as a model of the development of international standards

Introduction

The primary responsibility of veterinarians, particularly those in public service, is to promote and safeguard human health. Schwabe (1984) used the term 'one medicine' to describe the intricate relationship between human and veterinary medicine and even stated that *"veterinary medicine is a human health profession."* Veterinary medicine's role in public health is accomplished primarily by two means: avoiding the direct spread of zoonotic diseases and ensuring food security.

The World Food Summit declaration (FAO, 1996) stated that "*Food security exists when all people, at all times, have physical and economic access to* ***sufficient, safe and nutritious*** *food to meet their dietary needs and food preferences for an active and healthy life.*" The contribution of the veterinarian to food security is therefore, the implementation of measures aimed at guaranteeing food safety from the farm to the first point of

transformation, as well as ensuring a sufficient food supply by limiting the impact of animal diseases on production.

Developing animal health regulations requires finding the balance between science, economics, politics and public perception. Decision-makers are often faced with difficult choices as many decisions benefit certain interest groups but affect others. Veterinary public policy is both a science and an art, "*...the art lies in an ability to orchestrate the application of knowledge in a manner acceptable to many specialized interest groups*" (Schnurrenberger, 1987). The science side of this combination, however, is provided by the discipline of epidemiology.

The task of developing regulations that prioritize the public good versus the individual benefit is ensured when decision-makers in animal health recognize the role of the veterinarian in the promotion public health. At a broader level, international animal health standards need to abide by these principles and at the same time ensure their applicability in a wide-ranging set of conditions throughout the world. This can only be achieved successfully by applying sound epidemiological principles and having a clear understanding of 'the big picture', including economic, social, cultural, political and religious factors that may play a role in animal and human health.

The World Organization for Animal Health (OIE) and the development of international standards

The OIE was created in 1924 as a response from the international community to the reintroduction of rinderpest into Europe, with the primary responsibility

to control the international spread of diseases. Since then, the mandate of the OIE has been expanded to improve animal health worldwide (Vallat, 2007). This revised mandate includes the responsibility to:

- Ensure transparency in the global animal disease situation
- Collect, analyze and disseminate veterinary scientific information
- Encourage international solidarity in the control of animal diseases
- Safeguard world trade by publishing health standards for international trade in animals and animal products
- Improve the legal framework and resources of national Veterinary Services
- Provide a better guarantee of food of animal origin and to promote animal welfare through a science-based approach

One of the main roles of the OIE continues to be the development of international standards to ensure safe trade of animals and animal products. These standards, officially called recommendations, are contained in the Terrestrial Animal Health Code (OIE, 2007a) and the Aquatic Animal Health Code (OIE, 2007b).

The OIE Codes are dynamic documents that are under a process of permanent updating. Suggested modifications or additions to the Code may come from the International Committee (the main decision-making body), the different OIE commissions or from the permanent delegate of a member country. The request then goes to the appropriate commissions. The OIE has four specialist commissions (OIE, 2007c):

- Terrestrial Animal Health Standards Commission (Code Commission)
- Scientific Commission for Animal Diseases (Scientific Commission)
- Biological Standards Commission (Laboratories Commission)
- Aquatic Animal Health Standards Commission (Aquatic Animals Commission)

The commissions consider the request and may create an *ad hoc* group of experts to consider the issue and may also seek the opinion of the other commissions as appropriate. A draft proposal is prepared and circulated to member countries for comment. All comments are reviewed and relevant changes made to the original text. This revised proposal is then submitted for adoption by the International Committee during the OIE General session that is held once a year in May (Figure 3.1).

The OIE does not claim to have scientific expertise in all topics of animal health. One of the strengths of the OIE resides in its ability to access the best expertise in the world through its network of reference laboratories and collaborating centers and convene *ad hoc* groups to develop new chapters or propose modifications to existing ones.

One such group is the OIE *ad hoc* group on epidemiology which provides advice to the Scientific Commission for Animal Diseases (SCAD). The group, created in 2003, is composed of epidemiologists from different member countries and is chaired by the president of the SCAD (OIE, 2003).

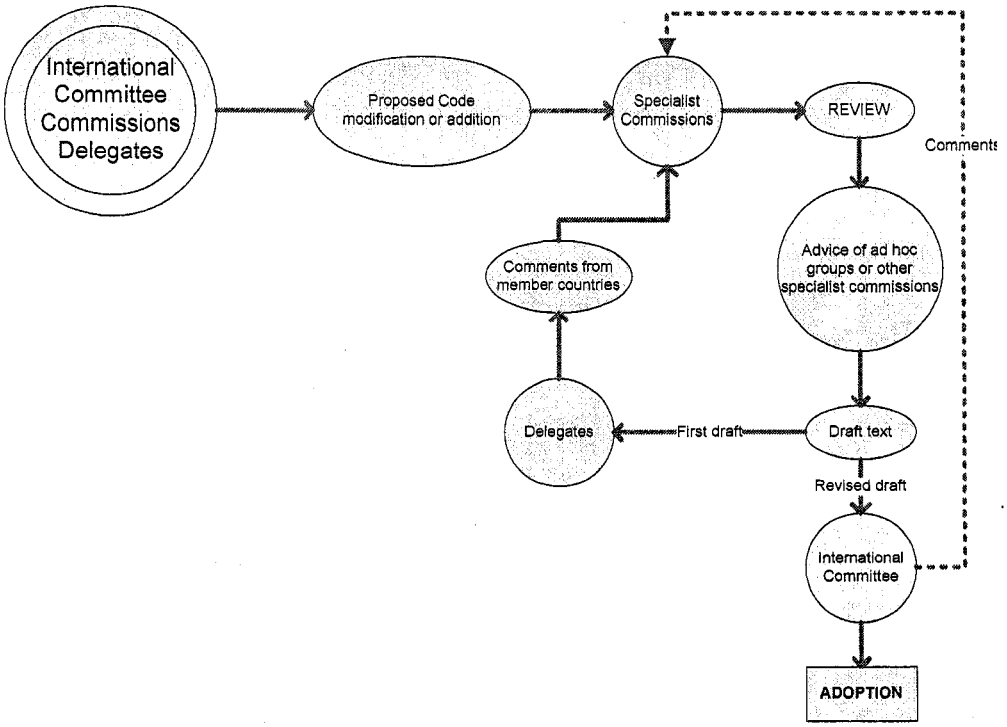

Figure 3.1 –Adoption process for international standards of the World Organization for Animal Health (OIE)

Since its creation, the group (of which the author is a member) has provided scientific and technical input and drafted or reviewed several chapters and appendices for the Terrestrial Animal Health Code including the following appendices (OIE, 2007a):

- Appendix 3.8.1. General guidelines for animal health surveillance
- Appendix 3.8.2. Guidelines for the surveillance of rinderpest
- Appendix 3.8.5. Factors to consider in conducting the bovine spongiform encephalopathy risk assessment recommended in Chapter 2.3.13.
- Appendix 3.8.7. Guidelines for the surveillance of foot and mouth disease

- Appendix 3.8.8. Guidelines for the surveillance of classical swine fever
- Appendix 3.8.9. Guidelines for the surveillance of avian influenza
- Appendix 3.8.10. Guidelines for the surveillance of bluetongue

Additionally, the group has reviewed and amended the chapters on several animal diseases including foot-and-mouth disease, avian influenza, classical swine fever, African swine fever, to bring them in line with the development of new approaches for disease management, such as compartmentalization and containment zones.

Compartmentalization a new tool for disease management and international trade

The application of the concept of compartmentalization is a good example of the use of epidemiology in the development of international standards. Compartmentalization was introduced into the OIE code a few years ago as an alternative to recognize animal populations of a distinct health status based primarily on management and biosecurity measures in a premise or a group of epidemiologically linked premises (OIE, 2007a). Chapter 1.3.5 of the OIE Code is devoted to zoning and compartmentalization. However, it only describes the concept in very broad terms and focuses primarily on the bilateral process that trading countries should follow to recognize compartments within their territories.

In 2004, the SCAD requested the USDA-APHIS Centers for Epidemiology and Animal Health (CEAH), an OIE Collaborating Center, to develop a concept paper on the application of compartmentalization to support chapter

1.3.5 on zoning and compartmentalization and provide the basis to develop specific guidelines to be included in the Terrestrial Code.

A group of CEAH epidemiologists led this effort that included representatives from industry as well as researchers. The result was a concept paper on the practical application of compartmentalization; this paper was submitted to the SCAD and reviewed by the OIE *ad hoc* group on epidemiology. Finally, a paper was published in the OIE Review, reflecting the joint work of the group led by CEAH and the OIE *ad hoc* group on epidemiology (Scott et al., 2006).

Simultaneously, the OIE *ad hoc* group on epidemiology began drafting proposed guidelines for the application of compartmentalization for inclusion in the OIE Code, based on the CEAH concept paper. The final version of the guidelines, taking into consideration comments from member countries, were submitted for adoption and approved during the OIE general session in May 2008.

In addition, at the request of the Aquatic Animal Health Standards Commission, the author was requested to write a paper on the application of compartmentalization in aquaculture production systems that will be published in a special number of the OIE Scientific and Technical Review. This paper is presented in Chapter 8. The expectation is that this paper along with the guidelines on compartmentalization in the Terrestrial Code will be the basis for the development of guidelines for the Aquatic Code.

Conclusions

The process of adoption of international standards can be lengthy. Nevertheless, the process ensures that the OIE Code recommendations are based on scientific principles by accessing the best experts in the field, it also allows transparency and a democratic approach as all member countries have an opportunity to comment on proposed modifications to the OIE Codes.

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Chapter 4

Risk analysis as a decision support tool for the control and prevention of animal diseases

A survey of OIE member countries[2]

Introduction

International trade in live animals and animal products has occasionally lead to the spread of disease between countries resulting in severe consequences for the agricultural economy of a country. Several examples of trans-boundary spread of diseases have been documented. The spread of rinderpest to Belgium from cattle originating in India destined for Brazil and transiting in the port of Antwerp in 1920 reintroduced the cattle plague to Europe (OIE, 1999a). Foot-and-mouth disease was introduced to Mexico from Brazil in the 1950's and led to the destruction of one million head of cattle, sheep and goats and to a severe socio-economic crisis (Machado, 1968). In 1978, an African swine fever epidemic broke out in the island of

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[2] Zepeda C. (2002). Risk analysis: a decision support tool for the control and prevention of animal diseases. Compendium of technical items presented to the International Committee and Regional Commissions 2002-2001. World Organization for Animal Health. Paris, France.
The core of this Chapter was presented as a technical item during the 69th General Session of the OIE. Paris, May, 2002.

Hispaniola and could only be controlled by the destruction of the entire swine population on the island. In Haiti in particular, this had a dramatic effect on the already precarious livelihood of the rural population (Zepeda, 1988). More recently, in 1997 classical swine fever was introduced to the Netherlands and forced the destruction of roughly 11 million pigs (Dijkhuizen, 1999); that same year FMD caused the destruction of Taiwan's swine industry (OIE, 1999b), the disease spread throughout Asia and was introduced into the United Kingdom in 2001 with devastating consequences (OIE 2007b, c). Finally, during the past few years, we have seen the spread of highly pathogenic avian influenza H5N1 in South East Asia, Europe and Africa (OIE, 2007b). The introduction of rinderpest to Belgium in 1920 highlighted the need to have an international body to help coordinate disease control efforts and, in particular, to regulate international trade in animals and animal products. In 1924, the Office International des Epizooties (OIE), now known as the World Organization for Animal Health, was established by an international agreement signed by 28 countries. Its main purpose is to inform governments of the occurrence and course of animal diseases throughout the world and of ways to control these diseases, to coordinate, at the international level, studies devoted to the surveillance and control of animal diseases and to harmonize regulations for trade in animals and animal products among member countries (OIE, 2000).

The Agreement on the Application of Sanitary and Phytosanitary Measures (SPS Agreement) of the World Trade Organization (WTO) recognizes the OIE as the standard setting body for animal health (WTO, 1995). The key principles included in the SPS agreement are risk analysis, regionalization,

harmonization, equivalence and transparency. Both risk analysis and regionalization depend on data generated by animal disease surveillance systems. Epidemiology, therefore, is a key element in providing the scientific basis to satisfy international trade requirements. Harmonization, equivalence and transparency are the basis for mutual trust between veterinary services, an essential requirement to ensure safe trade (Zepeda et al., 2001).

The intent of this chapter is to provide a general background on risk analysis and explore how risk analysis is being used among the OIE member countries. For this purpose a survey was developed and sent to the 158 OIE member countries (number of OIE member countries in 2001). Ninety-seven countries (61%) responded:

Algeria, Andorra, Angola, Argentina, Armenia, Australia, Austria, Azerbaijan, Bangladesh, Belgium, Bolivia, Bosnia and Herzegovina, Botswana, Brazil, Bulgaria, Burkina Faso, Burundi, Buthan, Canada, Colombia, Congo, Costa Rica, Côte-d'Ivoire, Croatia, Cyprus, Czech Republic, Denmark, Dominicana (Rep.), Ecuador, Egypt, El Salvador, Eritrea, Estonia, Finland, Former Yug. Rep. of Macedonia, France, Germany, Ghana, Greece, Guatemala, Honduras, Hungary, Iceland, Iraq, Iran, Ireland, Israel, Italy, Jamaica, Japan, Jordan, Kenya, Kuwait, Laos, Latvia, Lithuania, Luxembourg, Malaysia, Malta, Mauritius, Mexico, Morocco, Myanmar, Nepal, New Caledonia, New Zealand, Nicaragua, Norway, Oman, Paraguay, Peru, Poland, Qatar, Romania, Saudi Arabia, Singapore, Slovakia, Slovenia, South Africa, Spain, Sudan, Sweden, Switzerland, Syria, Taipei China, Tanzania, Thailand, Togo, Tunisia, Turkey, Ukraine, United Kingdom, United States of America, Vanuatu, Venezuela, Vietnam and Zimbabwe.

The role of the OIE in the implementation of risk analysis

The OIE has a role in helping member countries in the implementation of risk analysis capabilities within the official veterinary services. The SPS Agreement specifically designates the OIE as the organization responsible to develop international standards for animal health and zoonoses. In the case of risk analysis, both the OIE *International Animal Health Code* (OIE *Code*) and *International Aquatic Animal Health Code* each contain an entire section dealing with import risk analysis including the evaluation of Veterinary Services, zoning and regionalization and surveillance and monitoring of animal health (OIE, 2001).

The OIE has published two volumes of the *Scientific and Technical Review* dedicated to this topic (Vol. 12 (3), 1993 and Vol. 16 (1), 1997) in order to expand on the concepts and methods of risk analysis. In addition, the OIE Director General convened an Ad hoc group to draft an "Import Risk Analysis Handbook" published in 2002 (OIE, 2004a; OIE 2004b), largely based on previous work by Vose (2000) and Murray (2002).

In 1998, recognizing the importance of risk analysis and the need to implement effective surveillance systems to detect animal diseases, the OIE International Committee approved the USDA-APHIS-VS Centers for Epidemiology and Animal Health (CEAH) as the OIE Collaborating Center in Animal Disease Surveillance Systems and Risk Analysis. The Collaborating Center has four primary objectives: (1) Review, evaluate and adapt methodologies and approaches to enhance animal disease surveillance

systems and the risk analysis process, (2) Promote the harmonization of methods applied in disease surveillance and risk analysis, (3) Provide technical cooperation to OIE Member countries on an Ad hoc basis in areas related to animal disease surveillance systems and risk analysis, and (4) Establish a critical mass of trained individuals in OIE member countries to improve the quality of animal disease surveillance and risk analysis. The OIE Collaborating Center in Animal Disease Surveillance Systems and Risk Analysis has conducted several training sessions on risk analysis in Latin America, Asia, Africa and Eastern Europe in cooperation with the OIE Regional Representations, other Collaborating Centers and other organizations.

In 1999, the OIE Regional Commission for the Americas created an Ad hoc Group with the mandate to interpret the Risk Analysis Chapter in the OIE *Code*, provide training in risk analysis methods, develop practical guidelines for risk analysis, provide methodological guidance for risk analysis studies and offer methodological reviews of risk analyses submitted for consideration. This group met several times and has created a website containing information related to its work (http://www.aphis.usda.gov/oieamericas/oieindex.htm).

Risk analysis – general principles

Countries involved in international trade have always assessed the risk involved in allowing imports of animals and animal products. However, the decision-making process often has not been documented and the rationale used to arrive at a conclusion has not always been shared among the

interested parties (the "black box" approach).

The SPS agreement states that the methodology used to conduct risk analysis and sanitary and phytosanitary measures and risk assessments should be based on international standards that, in the case of animal health, are contained in OIE's Terrestrial Animal Health Code (OIE, 2007a). The contribution of the OIE Code is to provide a structured approach to conduct scientifically valid risk analysis.

According to the OIE Code, risk analysis is a process comprising various phases (OIE, 2007a):

- Hazard identification
- Risk assessment
    - Release assessment
    - Exposure assessment
    - Consequence assessment
    - Risk estimation
- Risk management
- Risk communication

Risk analyses can be quantitative, providing a numeric estimate of the probability and the magnitude of the consequences, or qualitative – using a descriptive approach. Although quantitative assessments provide more detailed information, both types of assessments are equally valid and can withstand scrutiny if challenged, provided they are based on data of good quality and address all the defined stages of the process.

A common perception is that, if an importing country applies the risk-mitigation recommendations of the OIE Code, a risk analysis is not necessary. While it is true that an in-depth risk analysis may not be necessary, the establishment of import requirements involves at least a partial application of the risk analysis process. Part of the complexity in developing import requirements is that multiple hazards can be identified for each commodity, while the Code provides recommendations on an individual disease basis. Risk analysis in its simplest form provides a framework to establish a link between the hazards identified for the specific commodity, the sanitary status of the exporting and importing countries and the recommendations of the Code. Several countries have developed conceptual frameworks for the application of risk analysis based on the OIE's guidelines (AFFA, 2003; Anon, 1995; CFIA, 1994; CFIA, 2000; CFIA, 2002).

Hazard identification

The first step of the process is to perform a thorough identification of all the pathogens that could be associated with the commodity that are present in the exporting country. The OIE is the main source for official information on disease occurrence in its member countries. Updated information can be obtained through the OIE's World Animal Health Information Database (OIE, 2007b) and the Weekly Disease Information Reports. Excellent reviews on the hazards associated with meat products, poultry and most domestic species have been produced (MAF, 1991; MAF, 1999; CFIA 2000).

Epidemiological information and disease surveillance data will help in

determining whether diseases may be present in the exporting country but do not affect the species of interest, or whether diseases may affect the species but the agents are not present in the export product.

Hazard identification may be initiated by a request from the exporting country to be recognized as free from a specific disease. In this situation, the methods used to document the absence of disease and the measures taken to avoid its introduction or reintroduction need to be assessed.

The SPS agreement allows the application of sanitary measures only if measures achieving a similar level of protection are applied internally under an official program in the importing country or if the disease is exotic. Therefore, once a list of hazards is established it has to be contrasted with the diseases that are exotic or are under official control programs in the country to determine the validity of the application of sanitary measures (Figure 4.1).

The next step of the process is to verify that the recommended measures in the OIE Code satisfy the importing country's appropriate level of protection. Although the application of the measures contained in the Code is the preferred option, the SPS agreement recognizes the right for countries to adopt more stringent measures provided they are based on a scientifically valid risk assessment (WTO, 1994).

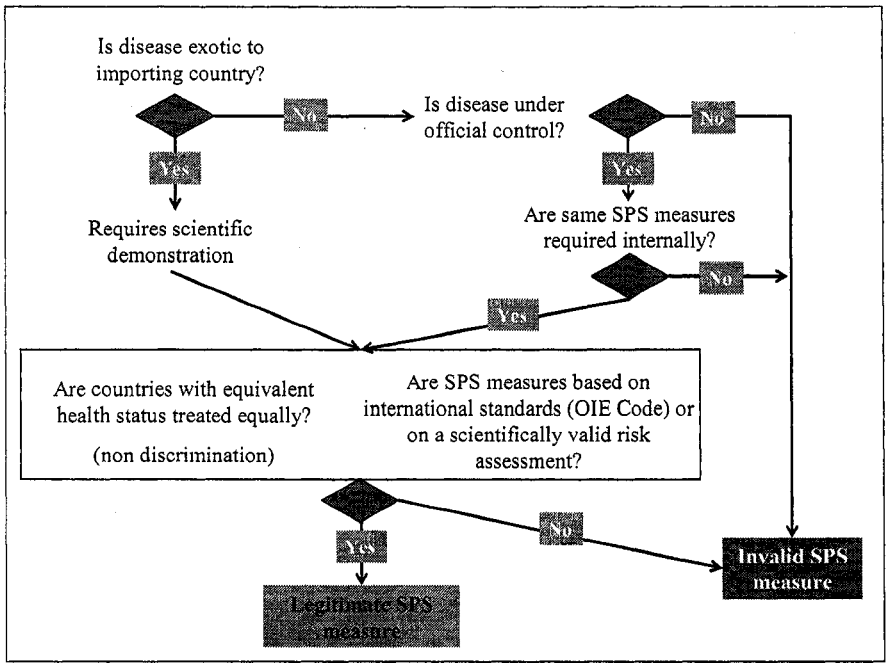


Figure 4.1 – Determination of the validity of sanitary measures (Zepeda et al., 2001)

The pathogens identified during hazard identification are arranged by importance of the disease(s), usually according to OIE criteria for the categorization of diseases. However, diseases (hazards) other than those listed by the OIE may be included in the list.

Risk assessment

In theory, a risk assessment should be conducted for each hazard. In practice, however, a risk assessment is conducted initially for the most important hazard, if the risk is deemed to be acceptable, then the remaining hazards are assessed. Alternatively, all hazards can be assessed qualitatively; and a more thorough, quantitative assessment is performed only on those hazards for which the risk (i.e. likelihood and consequences) (Ahl et al., 1993) is perceived to be high.

Risk assessment consists of four interrelated components: release assessment, exposure assessment, consequence assessment and risk estimation. Each of these steps requires a thorough epidemiological knowledge of the disease in question. In the case of quantitative risk assessments, an understanding of probabilistic and statistical methods also is needed. The application of quantitative methods in animal health has been reviewed by several authors (McDiarmid, 1993; Miller et al., 1993; Morley, 1993a; Morley 1993b; Murray 2002; Osborne et al., 1995 and Vose, 2000).

Release assessment

Release assessment describes the biological pathways leading to the introduction ("release") of the hazard into the importing country and estimates the associated probabilities. One asks whether the disease is present (or potentially present) in the country of origin. To answer this question, one must analyze available survey and surveillance findings, the survey methods, characteristics of the diagnostic systems used and the relationship between different production systems. Most importantly, the epidemiologic characteristics of the disease and the agent must be taken into account (e.g. the length of the incubation period, the range of susceptible species, transmission mechanisms and agent inactivation procedures).

Exposure assessment

The fact of introducing a product contaminated with a disease agent does not necessarily mean that it will cause an outbreak. The next component in the process is the exposure assessment; it describes the pathways that could

lead to infection of human or animal populations in the importing country and estimates the associated probabilities. This requires information on the demographics of the susceptible populations, immune status, geographic distribution of herds, types of production systems, presence and distribution of vectors and seasonality. Exposure pathways often are shaped by economic forces that regulate the volume of trade and the potential for distribution of the commodity within an importing country. It is important to understand the factors influencing trade to analyze the potential consequences of disease introduction.

Consequence assessment

Risk is the combination of the likelihood of occurrence of an adverse event and the magnitude of the consequences (Ahl et al., 1993; OIE, 2007d). Once the probability of occurrence (release and exposure) has been determined, the next step in the risk assessment is the consequence assessment, which deals with both the biologic and economic impacts following a disease introduction. The expected number of affected herds, mortality and morbidity rates, contact rates and wildlife susceptibility, as well as direct and indirect economic costs, must be assessed to estimate the magnitude of the impact of the adverse event. Thus, epidemiological information about the disease and agent under investigation is of prime importance at each of the three steps of the risk assessment process.

Table 4.1 summarizes the main epidemiological components and data requirements for each part of the risk analysis process.

Table 4.1 – Epidemiological components in risk analysis (Zepeda et al., 2001)

Risk-assessment steps	Epidemiological components	Data/knowledge requirements
Hazard identification	List of pathogenic agents that could be associated with the commodity.	• Existing control programs • Exotic diseases • Emerging diseases • Epidemiology of each disease in relation to the commodity
	Knowledge on the presence or absence of disease in a country or zone	• Methods to demonstrate absence of disease
Release assessment	Prevalence of disease in the importing country / Risk of introduction of disease from neighboring countries or zones or from trade with other countries	• Survey and surveillance results • Survey methodology • Confidence level, precision, expected prevalence • True prevalence • Herd-level sensitivity and specificity • Animal-level sensitivity and specificity • Role of commercial and backyard operations • Regionalization
	Epidemiological characteristics of the disease and the agent	• Incubation period • Carriers • Role of wildlife • Morbidity • Mortality • Method of spread • Pathogenesis • Target organs • Susceptible species • Agent inactivation procedures
	Diagnostic tests	• Test Se and Sp • Cut-off values • Testing strategies

Risk-assessment steps	Epidemiological components	Data/knowledge requirements
Exposure assessment	Characteristics of the susceptible populations and environmental factors in the importing country	• Pathways for exposure • Herd and animal densities • Immune status • Vectors • Seasonality • Cultural practices • Volume • Intended use of the commodity
Consequence assessment	Biologic and economic consequences	• Susceptible species • Method of spread • Contact rates • Morbidity • Mortality • Number of affected herds/animals • Direct economic impact (mortality, impact on production) • Cost of control and eradication • Indirect economic impact: interrupted trade, loss of international markets

Risk estimation

Risk estimation is the integration of the results of the release, exposure and consequence assessments. A two-step process has been proposed; the model was originally developed by Australia (AFFA, 2003) and subsequently adopted by others. The first step is to obtain a qualitative estimate of the or likelihood of the occurrence of the event by combining the results of the release and exposure assessments as indicated in Figure 4.2.

		Exposure probability						
		Insignifi-cant	Extre-mely low	Very low	Low	Slight	Modera te	High
Release probability	High	I	EL	VL	L	S	M	H
	Moderate	I	EL	VL	L	S	M	M
	Slight	I	I	EL	VL	L	S	S
	Low	I	I	I	EL	VL	L	L
	Very low	I	I	I	I	EL	VL	VL
	Extremely low	I	I	I	I	I	EL	EL
	Insignificant	I	I	I	I	I	I	I

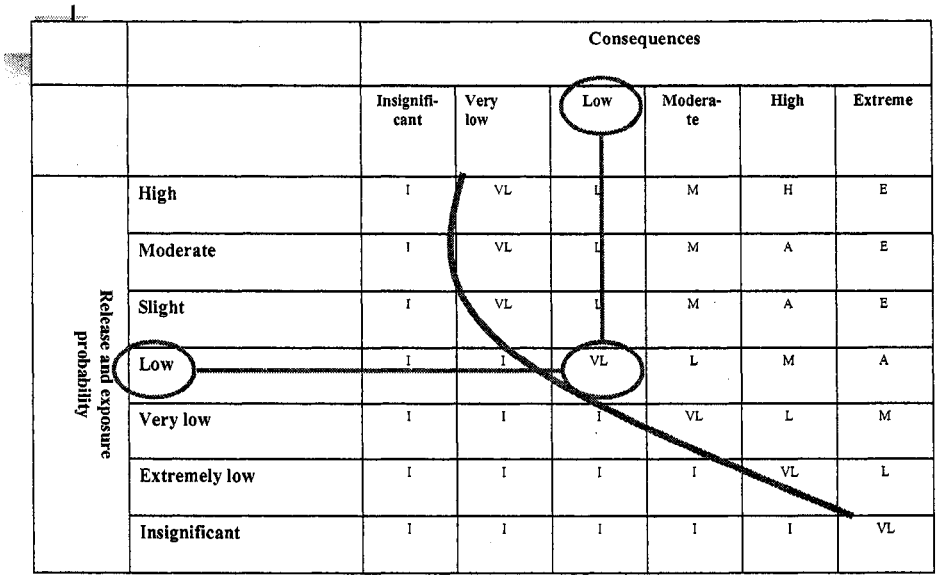
Figure 4.2 – Combining the results of release and exposure assessments

The second step is to combine the overall result obtained in step 1 with the results from the consequence assessment as depicted in Figure 4.3.

Risk management

Risk management begins by contrasting the results of the risk assessment with the acceptable level of risk a country is willing to take. The notion of "acceptable risk" has been debated for a long time. The SPS Agreement does not indicate how to determine the acceptable level of risk (also termed the appropriate level of protection (ALOP)). A current line of thought is to include economics in the determination of the appropriate level of protection by taking into consideration the benefits of trade and the potential costs of

disease introduction and its associated probability of occurrence. However, this is an idea that has not yet gained wide acceptance, particularly at political levels. Regardless of the method used to determine the ALOP, a country must be consistent in its application and should try to minimize the negative effects on international trade.



Release and exposure probability	Consequences					
	Insignifi-cant	Very low	Low	Modera-te	High	Extreme
High	I	VL	L	M	H	E
Moderate	I	VL	L	M	A	E
Slight	I	VL	L	M	A	E
Low	I	I	VL	L	M	A
Very low	I	I	I	VL	L	M
Extremely low	I	I	I	I	VL	L
Insignificant	I	I	I	I	I	VL

Figure 4.3 – Integration of risk assessment results

In the proposed decision matrices a country may chose to define its ALOP by only accepting those assessments yielding an insignificant risk (I). Therefore, in the example presented in figure 4.3, the "very low risk" result would be unacceptable. Additional mitigation measures would be needed to reduce the risk to an insignificant level.

One of the objectives of risk analysis is to determine the most-appropriate

methods to achieve the desired level of protection. Risk assessment identifies the points along the pathway of introduction that have the greatest effect on risk (an appropriate selection of mitigating measures applied to the most sensitive points in the process usually allows for substantial reductions in risk). The decision to use mitigation measures should be based on their efficacy, feasibility of application and cost.

Evaluating the efficacy of the selected options is an iterative process that involves their incorporation into the risk assessment and the comparison of the resulting level of risk to that considered acceptable. Generally speaking, mitigation measures can be grouped as follows (Pharo, 2002):

Diagnostic tests – taking into consideration the sensitivity, specificity, predictive values, herd-level sensitivity, herd-level specificity and the prevalence of the disease.

Quarantines – considering efficacy of inspection, duration of viremia, carriers, clinical signs, duration of quarantine.

Processing – with the specific objective of achieving inactivation of the agent. Time and temperature combinations, maturation of the product and the related pH changes are some of the factors that should be reviewed.

Risk communication

Risk communication is an integral part of the risk analysis process and has been defined as an interactive process for exchanging information

and opinions between risk evaluators, risk managers and other interested parties,. According to Chapters 1.3.1 and 1.3.2 of the Terrestrial Animal Health Code, risk communication is the process by which information and opinions regarding hazards and risks are gathered from potentially affected and interested parties, and by which the results of the risk assessment and proposed risk management measures are communicated to the decision-makers and interested parties in the importing and exporting countries. Risk communication is a multidimensional and iterative process that should ideally begin at the start of the risk analysis and continue throughout.

Survey results

The survey was designed to obtain information on how risk analysis is being used among OIE member countries focusing on four broad areas:

- Use of risk analysis
- Training
- Risk analysis capabilities
- Communication

Use of risk analysis

Eighty percent of reporting countries indicated the regular use of risk analysis for decision-making. Import-export decisions and in-country decision-making were the most frequent uses of risk analysis (79% and 66%, respectively). Nineteen countries (20%) indicated that they do not use risk analysis or perform an incomplete non-methodological risk assessment; the main reason

cited was lack of knowledge and training.

The overwhelming majority of countries (75%) which conduct risk analyses utilize a qualitative/descriptive approach. Three factors affect the choice of a qualitative/descriptive approach over a quantitative approach; in order of importance these are: the type and quality of data, the time required to conduct more detailed assessments and lack of training.

A complete risk assessment consists of the following sequential steps: hazard identification, release, exposure and consequence assessments and risk estimation. The survey shows that most countries (64%) carry out the entire process up to the consequence assessment level, while 16% only carry out hazard identification, 10% arrive at the release assessment level and 10% carry out the process up to the exposure assessment level. While most countries (82%) reported that risk analysis was a very useful tool for decision-making, lack of training and resources were the two main reasons for not conducting risk analyses on a regular basis.

Training

Most countries (74%) have received training in risk analysis. Universities, private consultants, OIE Collaborating Centers and other organizations have provided training. Most of the training received (59%) covered both qualitative and quantitative risk analysis methods. The main reasons cited for not having received training were lack of funding (44%), lack of awareness (24%) and lack of availability (23%).

The type of participants in training sessions were mostly field personnel (52%), decision-makers (14%), risk analysts (17%) and participants with other backgrounds and responsibilities (17%). When asked about the effectiveness of training, the majority of respondents (57%) felt that, although the training provided was a good introduction to general concepts, more in-depth training was needed. Only 18 countries (19%) felt that participants were able to conduct risk analysis after training. Ninety-six percent of respondents thought that the OIE should play a more active role in training through its Collaborating Centers.

Risk analysis capabilities

Only 20 countries (21%) reported having a dedicated risk analysis unit. In the countries that did not have a specific risk analysis unit, the responsibilities were generally allocated in the epidemiology and disease surveillance unit (47%) and the import-export unit (31%). An interesting finding of the survey was that over half of the countries (51%) hired external consultants to perform risk assessments.

Risk analysis is a multidisciplinary effort; according to the survey, the professionals involved in risk analysis were veterinary epidemiologists (37%), veterinarians (35%), statisticians (15%), agricultural economists (6%) and professionals with other backgrounds (7%).

Communication

Risk communication is an essential part of the risk analysis process. However, only thirty countries (25%) indicated they routinely publish risk

assessments while an overwhelming seventy-five percent of countries did not. The official gazette or its equivalent was the most frequent means of dissemination (47%), followed by electronic means through a website (28%) and other means (25%).

Risk analyses cannot be conducted in isolation; with this in mind, studies should ideally be subjected to an independent peer review. The results of the survey showed that most countries (56%) submit their analyses to peer review which is conducted mostly internally within the veterinary service (75%) and only occasionally submitted to external reviewers (25%). Ninety-three percent of respondents believe that the OIE should develop a role in making the results of risk analyses available.

Conclusions

The survey results show that risk analysis is considered as a very important tool in decision-making within veterinary services. Although quantitative risk assessments provide more in-depth information, the fact that most countries choose a qualitative approach to risk analysis shows that the process is not required to be quantitative or overly complex; this view is shared by most countries even those that have pioneered the use of quantitative risk assessments.

Reliable risk assessments, either qualitative or quantitative, depend on data of good quality. The choice of a qualitative approach over a quantitative one due to the scarcity and the limited quality of data will not provide a sound basis for decision-making. Veterinary services must be able to provide

accurate information on the occurrence of animal diseases within their territories and other factors that play a role in risk assessment.

Complete risk analyses have to be thorough, scientifically based and address all the steps of the process. An area that has not been addressed as thoroughly as the other areas of the process is consequence assessment. Recognizing this, the OIE Collaborating Center for Animal Disease Surveillance Systems and Risk Analysis convened in 2001 an international meeting to delineate the minimum scope that should be addressed in consequence assessments and to agree on the basic approach that should be followed. Consequences should consider both biological and economic considerations including losses in international trade.

To ensure proper application of risk analysis decision-makers, risk analysts and field personnel need to be trained. However, risk analysis training must be adjusted to cover the expectations and needs of different audiences. The OIE Collaborating Center in Animal Disease Surveillance Systems and Risk Analysis has developed a training strategy with several courses and seminars specifically designed for each level.

Dedicated risk analysis units are not a requirement within a veterinary service. The finding that close to eighty percent of countries do not have a specific unit to deal with risk analysis supports this statement. Satisfactory risk analysis capabilities can be developed within the epidemiology and disease surveillance unit and the import-export unit. Furthermore, many countries contract-out the development of risk analysis studies with external

consultants. This approach can yield acceptable results as long as proper guidance is given on the context of the study and the epidemiological coherence of the process.

Risk communication is a multidirectional effort involving all interested parties in the decision-making process; it is the cornerstone to achieve the transparency required by the SPS Agreement. However, this is the area of the risk analysis process that has received the least attention. The survey suggests that the OIE should take a more active role in disseminating the results of risk analyses. Recognizing that the OIE should remain neutral, an option for consideration could be to publish risk analyses to demonstrate approaches and methods and eliminate all references to individual countries and any other information that may be considered sensitive.

Animal health risk analysis is a continuously evolving field. As such, peer review of methods and approaches will help improve the quality of risk analysis internationally. At present, risk analysis studies are mostly reviewed internally within the veterinary services; there is an opportunity to broaden the scope of reviewers recognizing the multidisciplinary nature of the process.

Veterinary Services worldwide have always assessed risk even though these assessments have not always followed a structured methodology. The increase in trade worldwide implies a potential increase in the risk of introduction of diseases. It is therefore essential to establish mechanisms that allow commercial exchanges and at the same time safeguard the animal health status of the countries involved. Risk analysis is a tool for decision-

making that provides, by means of a logically structured and consistent process, information on the risk of introduction of animal diseases through trade in animals and animal products.

Many countries have taken significant steps in the development and application of risk analysis. Others, however, still require assistance to strengthen their risk analysis capabilities. Article 9 of the SPS Agreement considers the provision of technical assistance through the appropriate international organizations. It is therefore the role of the OIE to provide such technical assistance through its Collaborating Centers and member countries willing to share their expertise in the field.

Risk analysis provides a structured framework to analyze different animal health-related problems and is a very useful tool to reduce subjectivity in the decision-making process. Although risk analysis has been used mostly in the context of international trade decisions, it can be used in many other situations, such as the introduction of animals into a herd, assessing the effectiveness of biosecurity measures or declaring disease-free herds, zones or countries. The risk communication component of the process ensures transparency and allows a better understanding of how decisions are made, leading to increased trust.

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Chapter 5

Assessment of the probability of introducing infected live animals into a country, zone or compartment following international trade regulations

Introduction

The movement of live animals either domestically or internationally may lead to the introduction of disease agents into susceptible animal populations. The World Organization for Animal Health's (OIE) Terrestrial Animal Health Code provides recommendations for the international trade of live animals. These recommendations include the use of diagnostic tests prior to allowing the movement of animals (OIE, 2005). When conducting risk assessments, veterinary services in the importing countries are interested in quantifying the probability of disease introduction. This section will provide guidance on the quantification of the probability of introducing at least one infected animal under different conditions.

The purpose of this chapter is to provide a methodological "toolbox" to assess OIE Code recommendations for trade of live animals and provide decision

makers with an objective means to justify their decision to accept the OIE recommendations or stipulate import requirements that frequently will be more stringent. The latter is explicitly allowed under the Agreement for the Application of Sanitary and Phytosanitary Measures (WTO, 1995) as long as there is a scientific justification to depart from the recommendations by the relevant standard setting organizations.

No test

In general, the probability of interest is that one or more infected animals are present, as a single infected animal in a shipment will introduce the disease.

The probability of at least one success ("success" is a diseased animal) in "n" trials (the number of animals) with a probability (p) can be calculated using the binomial expression:

$$P(x \geq 1) = 1 - (1 - p)^n \qquad \text{Eq. 1}$$

where "x" is the number of infected animals and "P" is the probability that any animal is infected, in other words, the prevalence. The binomial distribution assumes that every trial is independent and the probability of success is constant (Samuels and Witmer, 1999). In reality, when selecting animals to be tested, the selection process is done without replacement, therefore the probability of success is not constant and a hypergeometric distribution is the correct approach to use. However, when "n" is small in relation to the population size the binomial distribution approximates the hypergeometric and since it is computationally simpler, it is usually the preferred approach.

Table 5.1 shows the probability of introducing at least one infected animal into an importing country at different prevalence levels and sizes of shipments.

Table 5.1 – Probability of introducing at least one infected animal from an infected country or zone.

	Number of animals in shipment				
Prevalence	**10**	**50**	**100**	**500**	**1000**
0.1%	0.0099	0.048	0.095	0.04	0.63
0.5%	0.05	0.22	0.39	0.92	0.99
1%	0.10	0.39	0.63	0.99	0.999
2%	0.18	0.64	0.87	0.999	1.00
5%	0.40	0.92	0.99	1.00	1.00
10%	0.65	0.99	0.999	1.00	1.00

Given that the probability of introducing an infected animal is relatively large even at low disease prevalence (table 5.1), animals are not usually moved internationally without a negative test result.

Single negative test

The use of a diagnostic test reduces the probability of introducing an infected animal in a shipment. Unfortunately, tests are not perfect and may yield false positive (FP) and false negative (FN) results (Figure 5.1).

The probability of interest is that of at least one test-negative but infected animal, i.e. a false negative animal. The probability of a single animal being false negative is calculated as:

$$P(D+ \mid T-) = \frac{FN}{FN + TN} \qquad \text{Eq. 2}$$

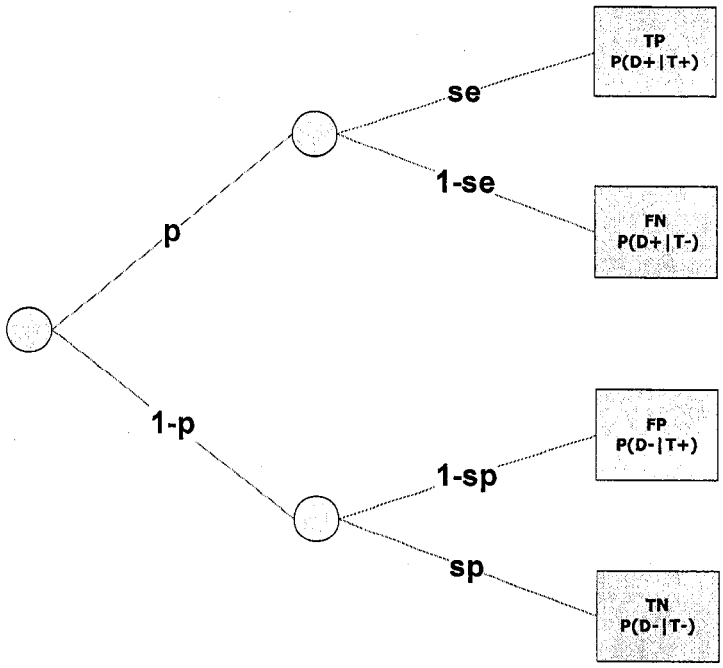

Figure 5.1 – Probability tree for the different outcomes of the application of a diagnostic test. P (prevalence), Se (sensitivity of the test), Sp (specificity of the test), TP (true positive), FN (false negative), FP (false positive), TN (true negative).

Therefore, the probability that one or more of the animals in a group will be false negative is:

$$P(x \geq 1) = 1 - \left(1 - \frac{FN}{FN + TN}\right)^n \qquad \text{Eq. 3}$$

where 'x' is the number of false negative animals.

Figure 1 shows a probability tree leading to all the possible outcomes of a diagnostic test. If the values for the prevalence (p) and the sensitivity (se) and specificity (sp) of the test are known, the probability of any of the outcomes can be calculated using the multiplicative rule of probability (Samuels and Witmer, 1999). Thus, equation 3 can be rewritten as:

$$P(x \geq 1) = 1 - \left(1 - \frac{p \times (1 - se)}{(q \times sp) + (p \times (1 - se))}\right)^n \qquad \text{Eq. 4}$$

Alternatively, equation 4 can be expressed in terms of the negative predictive value (NPV) (the probability of a test-negative individual being truly negative) of the test:

$$P(x \geq 1) = 1 - \left(\frac{q \times sp}{(q \times sp) + (p \times (1 - se))} \right)^n = 1 - NPV^n \quad \text{Eq. 5}$$

Table 5.2 shows the probability of introducing at least one infected animal into an importing country at different prevalence levels and sizes of shipments, given that all the animals in the group had a negative test result for a test with 95% sensitivity and 99% specificity. It is clear from this example with relatively high sensitivity and specificity, that as the size of the shipment and the prevalence increases, the probability of including one or more animals with false negative results increases significantly, to the point where it may not be sensible to import the group of animals.

Table 5.2 – Probability of introducing at least one test-negative but infected animal from an infected country or zone (se = 0.95 and sp = 0.99).

	Number of animals in shipment				
Prevalence	**10**	**50**	**100**	**500**	**1000**
0.1%	0.0005	0.0025	0.005	0.025	0.049
0.5%	0.003	0.013	0.025	0.119	0.224
1%	0.005	0.025	0.050	0.225	0.400
2%	0.010	0.050	0.098	0.403	0.643
5%	0.026	0.124	0.233	0.735	0.930
10%	0.054	0.244	0.429	0.939	0.996

Two consecutive negative tests

As seen above, depending on the circumstances, the probability of introducing one or more false negative animals in a shipment using a single test can be considered unacceptable, i.e. above the acceptable level of risk.

A risk management alternative is to apply an additional test using parallel test interpretation (Equation 6). The use of tests in parallel increases the overall sensitivity of the process and the negative predictive value (Dohoo et al., 2003). Table 5.3 shows the probability of introducing at least one infected animal into an importing country at different prevalence levels and sizes of shipments, given that all the animals in the group had two consecutive negative tests, for the same 95% sensitivity and 99% specificity of the test.

$$P(x \geq 1) = 1 - \left(1 - \frac{p \times (1 - se_1) \times (1 - se_2)}{(q \times sp_1 \times sp_2) + p \times (1 - se_1) \times (1 - se_2)}\right)^n \quad \text{Eq. 6}$$

Table 5.3 – Probability of introducing at least one test-negative but infected animal from an infected country or zone in a group of animals with two consecutive negative tests. (se_1 = .98, se_2 = .95, sp_1 and sp_2 = .99).

	Number of animals in shipment				
Prevalence	**10**	**50**	**100**	**500**	**1000**
0.1%	0.00001	0.00005	0.0001	0.0005	0.001
0.5%	0.00005	0.0003	0.0005	0.0026	0.005
1%	0.0001	0.0005	0.001	0.0051	0.01
2%	0.0002	0.001	0.0021	0.0104	0.021
5%	0.0005	0.003	0.0054	0.026	0.052
10%	0.0011	0.006	0.011	0.055	0.107

When testing in parallel, the overall sensitivity and specificity of the process can be calculated as:

$$se\,process = se_1 \times se_2 \quad \text{Eq. 7}$$

$$sp\,process = 1 - [(1 - sp_1) \times (1 - sp_2)] \quad \text{Eq. 8}$$

It is important to note that both tests need to be biologically independent, for example a screening test that measures antibodies, and a confirmatory test searching to isolate the agent. If the results of the tests are dependent, the covariance for the sensitivities and specificities of the tests should be used to obtain the corrected overall sensitivity and specificity of the process (Gardner et al. 2000).

Testing and quarantine

Often, quarantines are used as a risk mitigation measure. During this period, animals are examined clinically and may be subjected to a diagnostic test. As in the previous examples, the event of interest is the probability of importing at least one test-negative but infected animal. This probability is calculated as:

$$P(x \geq 1) = 1 - \left(1 - \left(\frac{p \times (1 - se)}{p \times (1 - se) + (1 - p) \times sp} \times (1 - p_{quarantine})\right)\right)^{n} \quad \text{Eq. 9}$$

where:

p – probability of an animal being infected (prevalence)

$p_{quarantine}$ - probability of animal being detected during quarantine

se – Sensitivity of the test

sp – Specificity of the test

n – number of animals imported

Occasionally, import requirements demand a specific quarantine period and two negative tests, one performed at the beginning of the quarantine period followed by a repetition of the same test at the end of the quarantine period. Obviously, the results of both tests are highly correlated, as an infected

animal that tests negative with the first round of testing, is very likely to have a second negative test. The only advantage of such a policy is to reduce the cost of quarantine by ensuring that only seronegative animals are quarantined. The probability of detection is increased by allowing infected but seronegative animals to seroconvert during the quarantine period. However, the gain in sensitivity will not be as great as if two biologically independent tests were used.

Application examples

Foot-and-Mouth disease

The OIE Code sets recommendations for the importation of live animals. The Code chapter on foot-and-mouth disease recommends two biologically independent tests and a quarantine period (OIE 2006):

[Animals] "*were kept in a quarantine station for the 30 days prior to shipment, all animals in quarantine were subjected to diagnostic tests (probang and serology) for evidence of FMDV infection with negative results at the end of that period, and that FMD did not occur within a ten-kilometre radius of the quarantine station during that period*".

The probability of at least one infected animal after the fulfillment of this requirement can be calculated by combining equations 6 and 9:

$$p(x \geq 1) = 1 - \left(1 - \left(\frac{p \times (1-se_1) \times (1-se_2)}{(q \times sp_1 \times sp_2) + p \times (1-se_1) \times (1-se_2)} \times (1 - p_{quarantine})\right)\right)^n \quad \text{Eq. 10}$$

The prescribed serological test for FMD is a solid phase competition ELISA (SPCE) (OIE, 2006a,b). Sensitivity and specificity values for cattle were estimated using data from Paiba et al. (2004) using a beta distribution with

parameters s+1 and n-s+1, where "s" is the number of successes and "n" the number of trials. Figure 5.2 shows the resulting distributions obtained.

According to the OIE (OIE 2006b), probang samples can be tested by virus isolation or reverse-transcription polymerase chain reaction (RT-PCR). The sensitivity of virus isolation using the plaque test with probang samples has been estimated to be approximately 60% while RT-PCR has a higher sensitivity (Moss and Haas, 1999). For calculations the sensitivity of virus isolation was modeled using a uniform distribution with 0.6 and 0.85 as minimum and maximum values respectively.

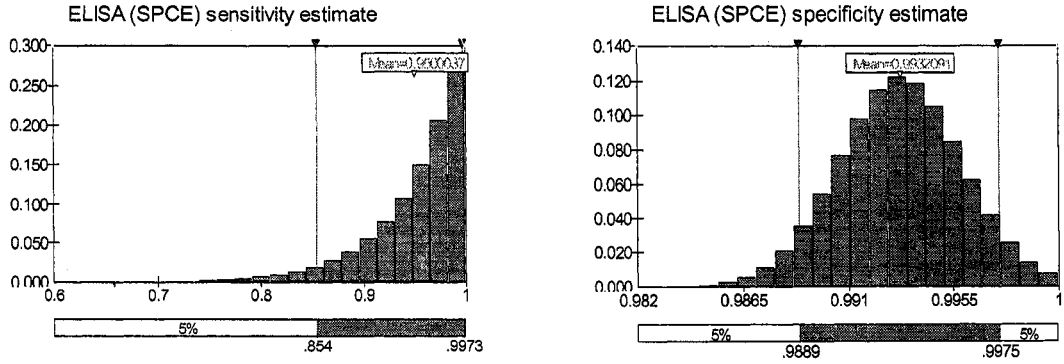

Figure 5.2 – Distribution of sensitivity and specificity estimates for the solid phase competitive ELISA (SPCE) test for FMD based on a simulation with 5000 iterations using @Risk (Palisade Corporation, Newfield NY, USA) and Excel (Microsoft Corporation).

The probability of detection of clinically affected animals during quarantine was assumed to be 80%. Table 5.4 shows the expected values (mean) for the probability of at least one infected animal escaping detection under these requirements.

Table 5.4 – Mean probability of at least one FMD-infected animal escaping detection with two consecutive negative tests (SPCE and probang) and a quarantine period.

	Number of animals in shipment				
Prevalence	**10**	**50**	**100**	**500**	**1000**
0.1%	0.00003	0.0001	0.0003	0.0014	0.0028
0.5%	0.00014	0.0007	0.0014	0.0069	0.0138
1%	0.00028	0.0014	0.0028	0.0139	0.0276
2%	0.00056	0.0028	0.0056	0.0279	0.0549
5%	0.00146	0.0073	0.0145	0.0702	0.1355
10%	0.00307	0.0152	0.0303	0.1424	0.2645

As an illustration, figure 5.3 shows the effectiveness of the application of different testing regimes as risk reduction measures. Figure 5.4 shows the effect of increasing shipment sizes on the probability of at least one animal escaping detection following the OIE recommendations above.

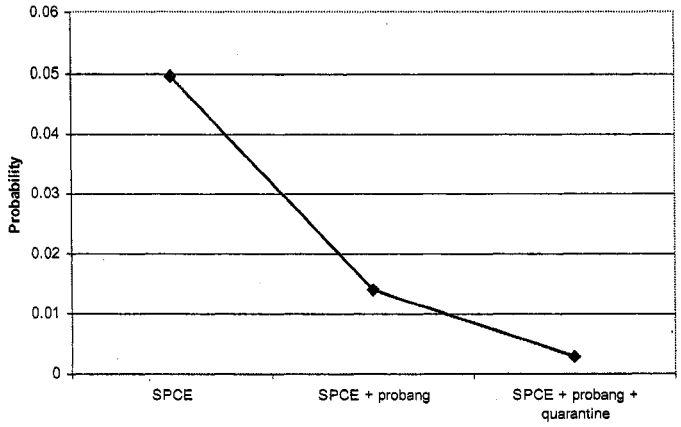

Figure 5.3 – Mean probability of at least one FMD-infected animal with different testing regimes for a shipment of 100 animals and a prevalence of 1%.

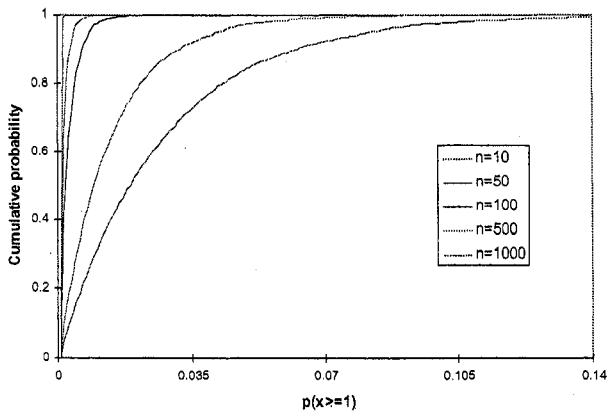

Figure 5.4 – Effect of different shipment sizes (n=10 to 1000) on the probability of at least one infected animal escaping detection. Cumulative distribution after 5000 iterations for a prevalence of 1%.

Bovine Brucellosis

Serological tests for bovine brucellosis are difficult to interpret, particularly when trying to determine the status of individual animals (OIE, 2006b). Most brucellosis control programs use a screening test, usually an agglutination test, followed by a confirmatory test (SENASICA, 1996; USDA, 2003; FAO, 2003; OIE 2006b). The OIE Manual of Standards and Diagnostic Tests and Vaccines (OIE, 2006b) does not recommend the use of the serum agglutination test (SAT) for the purpose of international trade, but it advocates the use of buffered *Brucella* antigen tests (BBATs), i.e. the rose bengal test (RBT) and the buffered plate agglutination test (BPAT), as well as the ELISA and the fluorescence polarization assay (FPA), as suitable screening tests in national control programs.

The diagnostic sensitivity and specificity of several diagnostic tests for brucellosis have been determined. Gall and Nielsen (2004) conducted a comprehensive review of tests for bovine brucellosis comparing their cost and

accuracy. When diagnostic tests are used in series or in parallel it is important to estimate the sensitivity and specificity of the process. By testing in series the specificity of the process is increased, while testing in parallel increases the sensitivity of the process. However, when the tests used are correlated, the degree of the correlation needs to be taken into account to adjust the estimates, as dependence between test results may change significantly sensitivity and specificity estimates of diagnostic processes (Gardner et al., 2000; Dohoo et al., 2003) (Equations 11-14).

Testing in series with correlated tests:

$$se_{series} = se_1 \times se_2 + \text{cov}(+) \quad \text{Eq. 11}$$

$$sp_{series} = 1 - (1 - sp_1) \times (1 - sp_2) - \text{cov}(-) \quad \text{Eq. 12}$$

Testing in parallel with correlated tests:

$$se_{parallel} = 1 - (1 - se_1) \times (1 - se_2) - \text{cov}(+) \quad \text{Eq. 13}$$

$$sp_{parallel} = sp_1 \times sp_2 + \text{cov}(-) \quad \text{Eq. 14}$$

where:

$$\text{cov}(+) = p_{111} - se_1 \times se_2$$

$$\text{cov}(-) = p_{000} - sp_1 \times sp_2$$

p_{111} - the probability of being positive to both diagnostic tests and the gold standard in the infected group.

p_{000} - the probability of being negative to both tests and the gold standard in the non-infected group.

To illustrate the effect of using conditionally dependent tests, a dataset of 188 animals with complete results for a battery of brucellosis tests including bacterial culture as a gold standard (B. Corso and J. Rhyan, unpublished data) was used to determine the degree of correlation between selected combinations of tests with the objective to assess the optimal combination for series and parallel testing. Table 5.5 is an example on the classification of test results in order to be able to compute the covariances and the series and parallel sensitivity and specificity. The process was repeated for each test combination shown in table 5.6.

Table 5.5 – Data requirements to calculate the sensitivity and specificity of series and parallel testing using correlated diagnostic tests. An example using the card test as screening test and rivanol as a confirmatory test.

	Number of animals by test-result combination				Total	Se	Sp
Card	+	+	-	-		0.974	0.460
Rivanol	+	-	+	-		1.000	0.613
Culture (+)	37	0	1	0	38		
Culture (-)	58	23	0	69	150		
Total	95	23	1	69	188		
p111	0.974						
p000	0.460						
p001	0.000						
p110	0.387						
Covar(+)	0.000						
Covar(-)	0.178						

Table 5.6 – Sensitivity and specificity estimates of different brucellosis test combinations accounting for correlation

	Card test / Rivanol		Card test / CF		BAPA / CF		BAPA / Rivanol	
	Series	**Parallel**	**Series**	**Parallel**	**Series**	**Parallel**	**Series**	**Parallel**
Se	0.974	1.0	0.895	1.0	0.921	1.0	1.0	1.0
Sp	0.613	0.460	0.537	0.309	0.477	0.302	0.627	0.38

Based on the results from table 6, the most efficient combination of screening/confirmatory tests for series interpretation would be the buffered antigen plate agglutination (BAPA) and rivanol. This test strategy maximizes sensitivity and specificity, therefore allowing a very efficient detection of infected animals while at the same time minimizing the proportion of false positives. For parallel testing the most efficient test combination was the card test/rivanol.

The calculated specificity for all binary combinations of tests interpreted in parallel was 1.0. In reality, this is unlikely to be true; however, based on the limited number of observations this result is correct. For the purpose of estimating the probability of introducing one or more false negative animals into a population, once the overall parallel sensitivity and specificity of the process have been calculated, their values can be used directly in equations 5 or 9.

The method to account for dependency of diagnostic tests proposed by Gardner et al. (2000) is difficult to apply in practice as it requires positive and negative results of all tests for all animals, as well as confirmation by a gold standard. Commonly, when testing in series the confirmatory test is applied only to those individuals having a positive test result to the first test, the test-negative animals on the first test are not re-tested with the second test. A similar situation occurs with parallel testing, where only the test-negative animals are tested with the second test. Finally, very rarely are individual animals tested in addition by a gold standard.

In the case of the dataset analyzed, the gold standard was considered to be bacterial culture. A positive culture result has a predictive value of one (or 100%), barring potential contamination of the sample. However, a negative bacterial culture result is not conclusive as many factors can lead to an inability to culture the agent. This results in low relative specificity estimates for the tests used, which in turn inflates the negative covariance (cov -) and reduces the expected gain in specificity when testing in series.

Nevertheless, despite the inherent difficulties of obtaining the necessary data to perform the calculations, it may be worthwhile to establish *a priori* these parameters by running a battery of tests, including the gold standard, on a group of animals that are representative of the population to determine the most efficient test strategy for the purpose of control or eradication programs.

Other applications

Most requirements in the OIE code for international trade of live animals from infected countries include quarantine and testing. There is some latitude on how these requirements are structured, different alternatives include:

- Quarantine, no testing
- Test, no quarantine
- Quarantine and a single serological test
- Quarantine and the same serological test applied twice
- Quarantine and two biologically independent tests
- Quarantine and two correlated tests

Table 5.7 provides a guide for quantification of the probability of introduction of infected animals for selected diseases from the OIE list. The diseases were chosen due to their economic significance and trade impact and also because the OIE Code recommendations cover most relevant test situations.

Conclusions

Diagnostic tests are imperfect, no single test or test combination is able to achieve a 100% sensitivity and specificity. While the OIE Code recommends trading of animals with different diagnostic strategies, in reality, the probability of introducing one or more infected but test negative animals into a population is not negligible, even when the prevalence is low. Most importing countries intuitively recognize this (although few have attempted to quantify the probability of the event) and decide to trade only with countries or zones that do not have the disease.

A common problem for an epidemiologist is to find reliable estimates of diagnostic test sensitivity and specificity in the scientific literature. Validation studies are difficult to perform. Although studies to estimate the specificity of a test are, in principle, relatively simple to perform, obtaining samples from known non-infected animals may prove difficult. Determining sensitivity values is more complex, samples from known infected animals are required and laboratory conditions to conduct such studies are limited and expensive. This frequently means that very few animals are used in these studies, leading to very wide confidence intervals around sensitivity estimates.

Table 5.7 – OIE Code recommendations for international trade of animals fro selected diseases and suggested analytical approach

Disease	OIE Code recommendations for the importation of live animals from infected countries or zones	Prescribed tests	Type of situation	Suggested approach
Rinderpest	[Animals] *have not been vaccinated against rinderpest, were isolated in a quarantine station for the 30 days prior to shipment, and were subjected to a diagnostic test for rinderpest on two occasions with negative results, at an interval of not less than 21 days*	• Competitive ELISA	Quarantine and same serologic test twice	Little or no gain in sensitivity by applying the same test twice. Equation 9 can be used ignoring the effect of testing twice.
Foot and Mouth disease	[Animals] *were kept in a quarantine station for the 30 days prior to shipment, all animals in quarantine were subjected to diagnostic tests (probang and serology) for evidence of FMDV infection with negative results at the end of that period, and that FMD did not occur within a ten-kilometer radius of the quarantine station during that period*	• Solid phase competition ELISA • Virus isolation • RT-PCR	Quarantine and two independent tests	Equation 10
Classical swine fever	Domestic pigs only allowed from free countries, zones or compartments. No testing requirements. Wild pigs from free countries or zones: *if the zone where the animal has been captured is adjacent to a zone with infection in wild pigs:* • *were kept in a quarantine station for*	• Neutralizing peroxidase-linked assay (NPLA) • Fluorescent antibody virus neutralization (FAVN) • ELISA	Quarantine and two independent tests	Equation 10

Disease	OIE Code recommendations for the importation of live animals from infected countries or zones	Prescribed tests	Type of situation	Suggested approach
	40 days prior to shipment, and were subjected to a virological test and a serological test performed at least 21 days after entry into the quarantine station, with negative results.			
Avian influenza	Birds other than poultry regardless of the NAI status of the country: • *the birds were kept in isolation approved by the Veterinary Services since they were hatched or for at least the 21 days prior to shipment and showed no clinical sign of infection with a virus which would be considered NAI in poultry during the isolation period;* • *the birds were subjected to a diagnostic test 7 to 14 days prior to shipment to demonstrate freedom from infection with a virus which would be considered NAI in poultry*	• Agar gel immunodiffusion (AGID) • Hemagglutination inhibition (HI)	Quarantine and single diagnostic test	Equation 9
Dourine	• *[Animals] were kept for the 6 months prior to shipment in an establishment where no case of dourine was officially reported during that period;* • *[Animals] were subjected to a diagnostic*	• Complement fixation	Quarantine and single diagnostic test	Equation 9

Disease	OIE Code recommendations for the importation of live animals from infected countries or zones	Prescribed tests	Type of situation	Suggested approach
	test for dourine with negative results during the 15 days prior to shipment.			
Bovine brucellosis	• *[Animals] were isolated prior to shipment and were subjected to a serological test for bovine brucellosis with negative results on two occasions, with an interval of not less than 30 days between each test, the second test being performed during the 15 days prior to shipment. These tests are not considered valid in female animals which have calved during the past 14 days.*	• Buffered Brucella Antigen Test (BBAT) • Complement fixation • ELISA • Fluorescence polarization assay (FPA)	Quarantine and same test twice	Little or no gain in sensitivity by applying the same test twice. Equation 9 can be used If a screening and a confirmatory test are used The Se and Sp of the process should be estimated considering the dependence between tests. These values can be used in equation 9.
Bluetongue	• *Option 1- [Animals] were protected from attack from Culicoides likely to be competent BTV vectors for at least 60 days prior to shipment; or* • *Option 2 – [Animals] were protected from attack from Culicoides likely to be competent BTV vectors for at least 28 days prior to shipment, and were subjected during that period to a serological test according to the Terrestrial Manual to detect antibody to*	• Agent id., AGID, ELISA, PCR	Option 1 – Quarantine only, no test Option 2 – Quarantine, single serological test Option 3 – Quarantine, single antigen detection test	Option 1 – Equation 1 can be used, where (p) is the probability of an animal being infected and viremic after the quarantine period Options 2 and 3– Equation 9

Disease	OIE Code recommendations for the importation of live animals from infected countries or zones	Prescribed tests	Type of situation	Suggested approach
	the BTV group, with negative results, carried out at least 28 days after introduction into the quarantine station; or • *Option 3 – [Animals] were protected from attack from Culicoides likely to be competent BTV vectors for at least 14 days prior to shipment, and were subjected during that period to an agent identification test according to the Terrestrial Manual, with negative results, carried out at least 14 days after introduction into the quarantine station*			
Heartwater	• [Animals] were subjected to a diagnostic test for heartwater with negative results during the 15 days prior to shipment	• ELISA • Indirect fluorescent antibody test	Single serological test, no quarantine	Equation 4

An additional problem is that new tests are frequently validated against a gold standard that, in turn, has not been properly validated in terms of its sensitivity and specificity and, in which case it is not possible to determine accurately these parameters for the new test.

In recognition of these problems, a special issue of Preventive Veterinary Medicine (Gardner and Greiner, 2000a) was devoted to the validation of diagnostic tests. Some of the issues addressed in that issue include (Gardner and Greiner, 2000b):

- Sensitivity and specificity estimates when the gold standard is imperfect
- Sensitivity and specificity estimates when there is no gold standard
- Pooled interpretation of test results
- Series or parallel interpretation of correlated tests
- Herd level sensitivity and specificity estimates
- Declaration of disease free zones and compartments

The OIE, through its network of Reference Laboratories and Collaborating Centers, should promote studies that provide more accurate estimates for the diagnostic sensitivity and specificity of the prescribed tests for international trade. This will allow epidemiologists and decision-makers to reduce the uncertainty in decisions related to the recognition of disease freedom and import risk assessments.

Diagnostic processes should not be conducted in isolation; they need to respond to the epidemiologic reality in the field. Therefore, a close and permanent communication between epidemiologists and scientists working in diagnostic laboratories, as well as those involved in the development of new tests and vaccines, should be maintained. This interaction should occur at the international level between OIE reference laboratories and collaborating centers, in particular those dealing with epidemiology, as well as at the national level between the national laboratories and the disease surveillance system (Zepeda, 2007). Ideally, sensitivity and specificity estimates should be determined at the national level as local production conditions such as breed, nutrition and concomitant infections might lead to changes in the performance of the test.

The application of the approaches outlined in this chapter should allow importing countries to make more informed decisions when deciding to import live animals. In addition, quantification of the probability of disease introduction should lead to a revision of the recommendations for trade in live animals presented in the OIE Code.

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Chapter 6

Assessing the probability of the presence of low pathogenicity avian influenza virus in exported chicken meat[3]

Introduction

Avian influenza (AI) is a disease of great importance for the poultry industry. Highly pathogenic AI viruses (HPAIV) have caused devastating outbreaks in many countries, killing and prompting the destruction of large numbers of birds (OIE, 2006). Recently, some strains of AIV have been able to infect humans causing great concern among public and animal health authorities worldwide. Low pathogenic AIV (LPAIV), on the other hand, produce localized respiratory and gastrointestinal infections with mild or no clinical signs. To date, all available scientific evidence indicates that chicken meat is not a vehicle for LPAIV. The recently adopted chapter on AI in the OIE Terrestrial Animal Health Code recognizes this fact and allows trade of poultry meat from countries affected by LPAIV (OIE, 2005a). Despite the OIE

[3] Published paper. Zepeda C. and Salman M.D. (2007). Assessing the probability of the presence of low pathogenicity avian influenza virus in exported chicken meat. Avian Diseases 51: 344-351

recommendations, several countries still place restrictions on trade of poultry meat from LPAIV-infected countries. These restrictions are extremely trade disruptive and entail significant losses to the poultry industry. The purpose of this risk assessment is to quantify the probability of the presence of LPAIV in exported chicken meat, thus providing further support to the consensus of the scientific community.

Basic scenario

In 2004, world-wide exports of chicken meat reached nearly 8.3 million metric tons. While many countries participate in international trade of chicken meat, three exporting countries or regions cover 95 percent of the world's chicken meat exports: the European Union, Brazil, and the United States (GTA, 2005). The scenario under which this assessment is conducted is based on the export of 46,000 metric tons per year, which represent the median of the top twenty importers from the United States. Most of the data on surveillance, flock size, number of flocks, and number of production cycles are based on the commercial system of production prevalent in the United States, but can be adapted to reflect the situation of any given country.

Risk assessment outline

Risk assessment is the evaluation of the likelihood and the biological and economic consequences of entry, establishment, or spread of a pathogenic agent within the territory of an importing country (OIE, 2005b). Risk assessment consists of several interrelated steps: release, exposure, and consequence assessments. Table 6.1 describes the events leading to

infection of poultry in an importing country and the information required to document each step.

Table 6.1 – Pathway of events leading to the introduction of LPAIV through poultry meat

	Event	Data requirements
	Release assessment	
A	Flock is infected by an H5 or H7 LPAIV.	- Flock prevalence - Number of LPAIV infected flocks prior to detection - Number or broiler flocks.
B	Birds within a flock are infected with LPAIV.	- Within-flock prevalence.
C	Infected flock is not detected during routine surveillance prior to slaughter or during ante or post-mortem inspection.	- Probability of detecting an infected bird/flock prior to slaughter or either ante or post-mortem inspection.
D	Virus survives in the carcass.	- Probability of virus presence in muscle.
E	Infected carcasses are exported.	- Exported volume. - Number of flocks involved in export. - Number of flocks exported during the risk period. - Average flock size. - Average weight per bird.
	Exposure assessment	
F	Poultry in the importing country consumes uncooked, infected meat scraps and becomes infected.	- Proportion of the total imported volume that would be discarded uncooked and be fed to poultry. - Amount of meat that would contain an infectious dose. - Virus titer in muscle, bone, blood vessels ID50/g of tissue - Oral infectious dose for chickens. - Can LPAIV be transmitted to chickens through uncooked meat scraps?

Consequence assessment		
G	Impact of LPAIV strains to poultry.	- What is the effect of LPAIV infection in poultry? - Biological consequences - Economic consequences

The proposed model assesses the probability that at least one LPAIV-infected chicken carcass is exported, i.e. the release assessment. Currently, the model does not address the probability that poultry would consume an infectious dose, an infection would be established, and the potential of transmission of LPAIV to flocks in the importing country (exposure assessment). Each of the steps in the exposure pathway should further reduce the probability of LPAIV occurrence.

Description of the model

The probability of interest is the probability of exporting at least one infected poultry carcass with LPAIV in muscle tissue (T). The probability estimates were calculated using the following binomial expression:

$$P(x \geq 1) = T = 1 - [1 - (A \times C \times (1 - (1 - BD)^n))^E]$$

where:

x – Infected poultry carcass with LPAIV in muscle

A – Flock prevalence

B – Within-flock prevalence

C – Probability of not detecting an infected flock through passive surveillance

D – Probability of LPAIV presence in muscle

n – Number of birds per flock

E – Number of flocks exported prior to detection

The derivation of the probabilistic approach can be found in Appendix 1.

Methods

A stochastic simulation model was developed using a spreadsheet (Excel, Microsoft Corp.) and simulation software (@Risk, Palisade Corp.). Results are based on a simulation with 10,000 latin hypercube iterations and presented as probability density function (PDF) graphs, as well as tables with key descriptors of the distribution of results. The spreadsheet model can be found in Appendix 2.

Hazard identification

AI is caused by influenza type A viruses, members of the family *Orthomyxoviridae*. Influenza viruses are classified on the basis of their hemagglutinin (H) and neuraminidase (N) subtypes. Currently 16 H subtypes and 9 N subtypes have been identified (Swayne and Suarez, 2000; OIE, 2004; Fouchier et al., 2005).

AIV has been reported from 12 orders and 88 species of free-living birds. Most isolates are reported from species in the orders Anseriformes and Charadriiformes. It is recognized that species in Anseriformes (ducks and geese) represent important reservoirs of AIV. Morbidity and mortality in wild birds is rare (Alexander, 2000; Stallknecht and Shane, 1988). Most of the evidence obtained from different AI occurrences in poultry in different geographic areas supports the view that primary introduction of AIV is from wild birds (Alexander, 2000). The H5N1 strain circulating in South East Asia

since late 2003 is the exception in that it affects wild birds clinically (OIE, 2006).

AIV are categorized according to their pathogenicity. According to the OIE Terrestrial Animal Health Code, notifiable avian influenza is defined as follows (OIE, 2005a):

- "Notifiable avian influenza (NAI) is defined as an infection of poultry caused by any influenza A virus of the H5 or H7 subtypes or by any AI virus with an intravenous pathogenicity index (IVPI) greater than 1.2 (or as an alternative at least 75% mortality) as described below. NAI viruses can be divided into highly pathogenic notifiable avian influenza (HPNAI) and low pathogenicity notifiable avian influenza (LPNAI).

- HPNAI viruses have an IVPI in 6-week-old chickens greater than 1.2 or, as an alternative, cause at least 75% mortality in 4-to 8-week-old chickens infected intravenously. H5 and H7 viruses which do not have an IVPI of greater than 1.2 or cause less than 75% mortality in an intravenous lethality test should be sequenced to determine whether multiple basic amino acids are present at the cleavage site of the hemagglutinin molecule (HA0); if the amino acid motif is similar to that observed for other HPNAI isolates, the isolate being tested should be considered as HPNAI.

- LPNAI are all influenza A viruses of H5 and H7 subtype that are not HPNAI viruses."

To date all HPAIV have been of the H5 or H7 subtype. However, only a small number of H5 or H7 subtype viruses have been highly pathogenic (Swayne and Suarez, 2000).

HPAIV can be transmitted by (OIE, 2002):

- Direct contact with secretions from infected birds, especially feces
- Contaminated feed, water, equipment and clothing
- Clinically normal waterfowl and sea birds introducing the virus into flocks, and
- Broken contaminated eggs infecting chicks in the incubator

AIV are inactivated by heat at 56°C/3 hours or 60°C/30 min, pH 2 or lower, oxidizing agents such as sodium dodecyl sulfate, lipid solvents, and ß-propiolactone, and disinfectants such as formalin and iodine compounds. However AIV remain viable for long periods in tissues, feces and water (OIE, 2002). AIV are stable at a pH range of 5-12 (Lu et al., 2003).

The virulence of H5 and H7 AIV is controlled by the cleavability of the H molecule, HA0. HPAIV have multiple basic amino acids at the cleavage site of the H, this characteristic allows cellular proteases present in all tissues to cleave the H resulting in systemic infections affecting several organs, brain and skin. LPAIV in contrast, do not have multiple basic amino acids at the H cleavage site and are cleaved only by extracellular proteases present in the respiratory or gastrointestinal tracts. This results in localized infections (Rott, 1992; Vey et al. 1992; Senne et al., 1996; Pasick et al., 2005). LPAIV-

infected birds may show mild clinical signs, but often are totally asymptomatic (Mo et al., 1997; Alexander, 2000; Swayne and Suarez, 2000; Ito et al., 2001).

Release assessment

This step of the process describes the biological pathways leading to the presence ("release") of the agent of concern in the animal or product to be exported. The probability of LPAIV being present in exported chicken meat depends on the flock prevalence of LPAIV and the likelihood of the bird being viremic at slaughter (Pharo, 2002).

Description of model parameters

A – Probability of a flock being infected by an H5 or H7 LPAIV

The risk assessment calculations are based on the probability of exporting at least one infectious bird carcass from an LPAIV-infected flock (H5 or H7). To calculate the probability of a flock being infected, the number of flocks infected prior to detection is required. On this basis, the risk period is the time elapsed between infection and detection and the number of affected flocks during that period. The concept of the risk period assumes that once infection is detected exports will be stopped.

Usually, very few commercial flocks are involved in LPAIV outbreaks. For example, surveillance for AIV in the US has been able to detect LPAIV infections at an early stage. In 2004, there were only two commercial broiler flocks affected by LPAIV. Even in extreme years, such as 2002, in which 201 premises were infected in Virginia, retrospective investigation showed that at

the time of detection there were only 6 farms infected (4 turkey breeders and 2 turkey grow-out farms) (CEAH, 2002).

During the LPAIV outbreak in Virginia in 2002, the index farm, was detected based on clinical signs (Akey, 2002). Samples taken that day were negative in the agar gel immunodiffusion (AGID) test but positive for virus isolation. Repeat blood samples taken 4 days later were AGID positive. Based on this combination of evidence, the onset of infection is likely to have been only 2-4 days prior to detection (B. Akey*, personal communication). Other occurrences of AI may take more time to be detected, particularly if clinical signs are not evident. Three scenarios were modeled with different time periods prior to detection (Table 6.2).

The yearly number of broiler flocks in the US is estimated at 223,496 flocks (CEAH, 2004). There are five production cycles in a year; therefore at any given time there are approximately 44,700 flocks on the ground. The estimate of the prevalence of LPAIV-infected flocks prior to detection was modeled as a beta distribution: Beta (s+1, n-s+1), where "s" is the number of affected flocks prior to detection and "n" is the number of flocks at a given point in time.

Table 6.2 – Estimated number of infected farms prior to detection

Time to detection	Number of infected farms		
	Minimum	Most likely	Maximum
1 week	1	2	6
2 weeks	2	4	12
3 weeks	3	6	18

* Bruce L. Akey. Chief, Office of Laboratory Services. Virginia Dept. Agriculture and Consumer Services (2002).

B - Proportion of birds infected within a flock

AIV tend to spread rapidly in affected flocks. Perhaps surprisingly, virulent viruses have shown much poorer transmission from infected to susceptible chickens and turkeys than viruses of low pathogenicity (Alexander et al. 2000). Empirical evidence from the Virginia outbreak suggests that LPAIV can infect a large proportion of birds, up to 80%, in a few days (B. Akey, personal communication). A triangular distribution with a minimum value of 0.2, a most likely value of 0.5, and a maximum value of 0.8 was used to model the within-flock prevalence.

C - Infected flock is not detected during routine surveillance or ante- or post-mortem inspection

LPAIV may be asymptomatic or occasionally produce mild clinical signs (Mo et al. 1997; Alexander et al., 2000; Swayne and Suarez, 2000). The first broiler flock in the outbreak in Virginia was detected by testing at slaughter of poultry without clinical signs (B. Akey, personal communication).

In the United States avian influenza monitoring and surveillance is conducted by various sectors of the Government (State and Federal) and private industry (CEAH,2002; CEAH, 2004). Federally accredited veterinarians and State laboratory systems are required to report any suspect case to the State and Federal authorities. A thorough investigation is conducted after suspect cases are found. This investigation involves collaboration with the National Veterinary Services Laboratories (NVSL) (an OIE Avian Influenza reference laboratory), State and Federal veterinarians, and other animal health officials, as appropriate.

National Poultry Improvement Plan (NPIP)

NPIP monitors the health status of commercial flocks through monitoring of genetic stock and multiplier flocks. NPIP is implemented by state authorities in cooperation with the USDA and the poultry industry. NPIP establishes the regulatory standards for sample collection, diagnostic tests performed, and the laboratory protocols for conducting tests.

For parent flocks and multiplier flocks that are included in NPIP in each state, NPIP coordinates ongoing sample collection and testing. This ensures that flocks meet the certification standards for freedom from disease. NPIP requires sampling of 30 birds every 90 days for primary breeder flocks and 30 birds every 180 days for parent flocks.

Testing in the states

State laboratories perform AI testing on any case presenting respiratory or neurologic signs and also randomly on poultry submissions. Any positive finding in a State laboratory triggers reporting of the case, a determination of the circumstances, and the sending of follow-up samples to the NVSL for confirmation and further identification.

In addition to government programs, industry performs constant monitoring, usually using slaughter blood in serologic testing. Many high-technology commercial farms continually analyze flocks serologically to monitor the general flock health status. Any positive sample discovered during this testing is reported to the State government for further investigation.

Although clinical signs may not be observable in live birds, during post-mortem inspection a proportion of birds will show lesions, such as air saculitis, that are suggestive of LPAIV infection. A flock will be condemned if such signs are found. It is unlikely that routine post-mortem inspections would not find these signs in one or more birds

Given the multiple surveillance activities and sources of diagnostic test results, it is not possible to estimate accurately the probability of detection of an infected flock. Most experts consider the system to be effective. In general, surveillance for AI in the US is very effective and most outbreaks are detected at a very early stage with very few premises involved. It is possible, however, that some infected flocks might be missed due to the lack of clinical signs. To allow for this possibility, failure of detection was modeled with a triangular distribution with parameters (0.2, 0.3, 0.6) which represents a conservative subjective estimate. These values can be adapted to reflect the lack of sensitivity of passive surveillance systems in each country.

D - Virus is present and survives in the carcass.

LPAIV does not produce a systemic infection and invades almost exclusively the respiratory and gastrointestinal tracts (Mo et al., 1997; Alexander, 2000; Swayne and Suarez, 2000). Thus, the risk of importing LPAIV in meat products has been considered negligible (Swayne and Suarez, 2000). However, until recently, there was very little information on the occurrence, onset, and length of viremia in LPAIV infections (Alexander et al., 2000). One of the few studies in the literature on transmission of AIV through meat was

conducted in 1931 using a strain of HPAIV (Purchase, 1931). More recently, a study using intratracheal inoculation of different HPAIV and medium pathogenicity AIV (MPAIV)[4], failed to detect viral antigen by immunohistochemistry in skeletal muscle of birds inoculated with MPAIV, whereas viral antigen was detected in muscle with all HPAIV strains in the study (Mo et al., 1997). However, these results are inconclusive as immunohistochemistry is not as sensitive as virus isolation (D. Swayne*, personal communication).

Recently, a study was conducted to determine the presence or absence of LPAIV in muscle of intranasally infected birds and to determine if transmission was possible by feeding meat to susceptible birds (Swayne and Beck, 2005). The study found no virus in thigh or breast muscle of LPAIV-inoculated birds and failed to transmit LPAIV by feeding meat from intranasally-inoculated chickens to susceptible chickens. In contrast, the same study found virus in thigh and breast muscles from birds inoculated with a HPAIV strain. This study is the most conclusive evidence to date on the absence of LPAIV in muscle tissue.

The release assessment results are extremely sensitive to this parameter. It is not scientifically possible to demonstrate the absence of virus in meat in absolute terms. However, all available scientific evidence substantiates the absence of LPAIV in muscle. From a molecular perspective, the HA0 molecule of LPAIV can only be cleaved by proteolytic enzymes, such as

[4] The current terminology used to describe AIV has abandoned the term medium pathogenicity and considers only LPAIV and HPAIV following the criteria laid down in the OIE Terrestrial Animal Health Code (OIE 2005a).

* David E. Swayne. Laboratory Director, USDA/ARS/Southeast Poultry Research Laboratory.

trypsin, restricting the range of tissues where virus can replicate to the digestive and respiratory systems. In addition, experimental evidence using a natural route of infection confirms the molecular basis for virulence (Swayne and Beck, 2005).

Developing a quantitative estimate for this parameter presents difficulties. Given the limited number of birds used in the study, a conventional Bayesian approach using an uniform prior distribution yields unreasonably high values which do not take account of the molecular basis for virulence, empiric observations, and expert opinion.

Therefore, to model this parameter quantitatively, two approaches can be used. The first is to use zero as a single point estimate for the probability of LPAIV in meat, which yields a final probability of zero, this represents the current state of knowledge on the presence of LPAIV in poultry meat. The second approach is to truncate the possible distribution of values for the presence of virus in muscle at an arbitrary maximum value. The results presented are based on the second approach, which represents a worst-case scenario.

E – Number of flocks exported

World poultry exports amount to nearly 8.3 million metric tons (MT) a year (GTA, 2005). Exports by the European Union, Brazil, and the United States constitute 95% of this volume. For the purpose of this assessment, the median volume imported by the top twenty poultry importing countries from United States was used. This volume (46,000 MT) was converted into the

number of birds and number of flocks, assuming that exports consisted of broiler carcasses exclusively. If the volume of exports is composed of chicken pieces, it can be converted back to the number of birds contributing to it using the weight ranges in table 6.3.

Table 6.3 – Weight range for different poultry products (USDA, 2003).

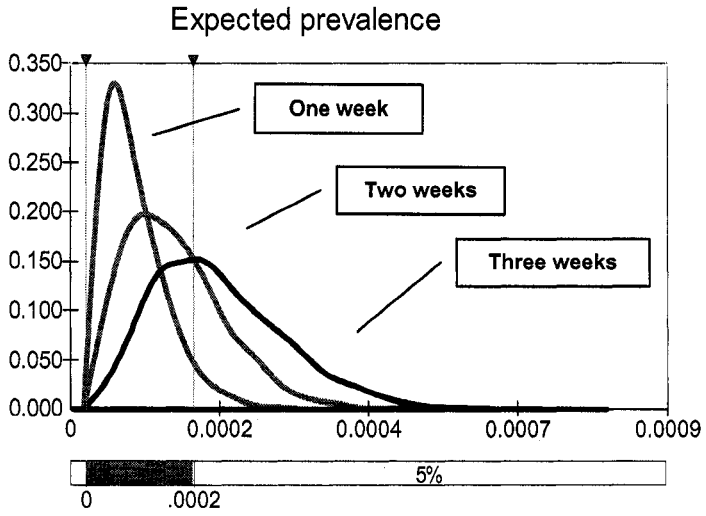
Commodity	Weight range
Small broiler chicken (without neck and giblets)	1.13-1.70 Kg
Large broiler chicken (without neck and giblets)	> 1.70 Kg
Leg quarters	240-680 g
Chicken legs	142-496 g
Thighs	71-298 g
Drumsticks	71-198 g

Release assessment results

As mentioned above, the results represent only the release assessment step of the risk assessment process. It is worth remembering that the release assessment results are based on the hypothetical presence of LPAIV in meat. Available scientific evidence suggests that LPAIV is not present in poultry meat and cannot be transmitted by feeding meat to susceptible chickens (Swayne and Beck, 2005). The pathways for exposure need to consider the volume of poultry meat that would be discarded uncooked and fed in turn to poultry. The exposure assessment would likely lead to a greatly reduced probability.

Flock prevalence during the risk period

Figure 6.1 shows the values and distribution of the expected prevalence of LPAIV under three different times before detection.



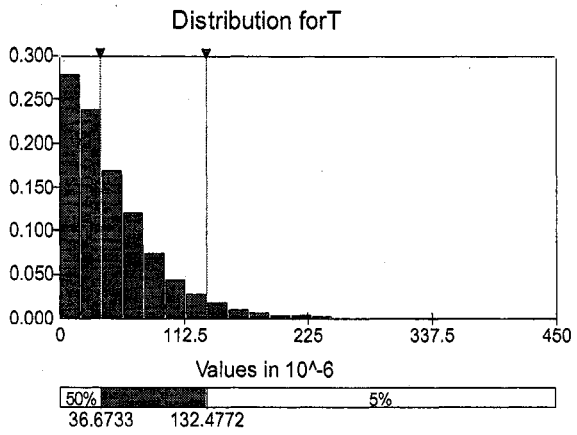
	Time to detection		
Distribution descriptors	**One week**	**Two weeks**	**Three weeks**
5%	2.44E-05	5.29E-05	8.50E-05
mode	6.52E-05	0.0001	0.0001
median	8.05E-05	1.45E-04	2.10E-04
95%	1.84E-04	2.99E-04	4.07E-04

Figure 6.1 – Probability density functions of flock prevalence 1-3 weeks prior to detection
A probability density function (PDF) represents the distribution of possible outcomes and their relative frequency (probability density) for defined ranges of values (Vose 2000, Miller et al. 1983).

Yearly probability of introduction of LPAIV in meat (T)

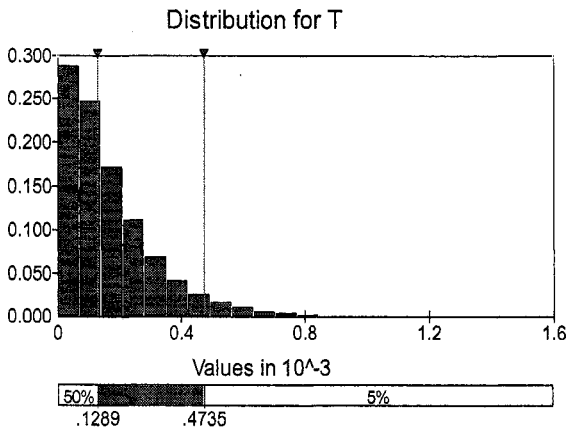
The probability of exporting at least one infected bird with LPAIV in muscle varies depending on the length of time prior to detection. The results can be expressed as the probability value, or alternatively as at least one infected bird with LPAIV in meat exported in a given number of years of trade at the current level, or equivalently, at least one infected bird with LPAIV in meat in a given number of metric tons exported. Figures 6.2-6.4 show the results for the three different times to detection. The median values range from 3.6 $x10^{-5}$

^{5} for a time lag of one week to detection to 2.8 x 10^{-4} for a three week lag to detection.



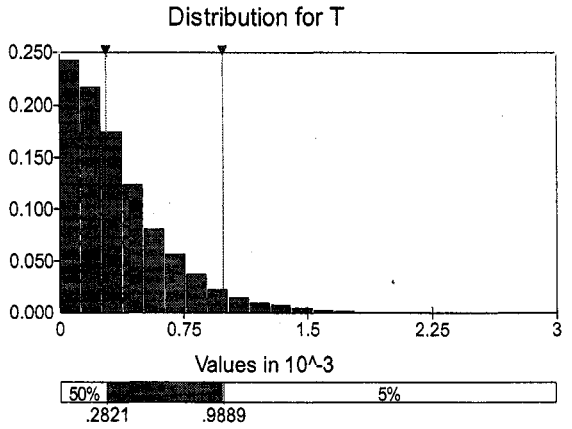
Distribution descriptors	T	At least 1 infected carcass in "x" years	At least 1 infected carcass in "x" exported Tons
5%	3.46469E-06	288,626	13,276,782,902
mode	1.27216E-07	7,860,625	361,588,748,819
median	3.66733E-05	27,268	1,254,319,131
95%	0.000132477	7,548	347,229,647

Figure 6.2 - Probability of exporting at least one infected carcass with LPAIV in muscle tissue per year assuming one week to detection.



Distribution descriptors	T	At least 1 infected carcass in "x" years	At least 1 infected carcass in "x" exported Tons
5%	1.18E-05	84,795	3.9E+09
mode	4.65E-07	2,152,612	9.9E+10
median	0.000129	7,760	3.57E+08
95%	0.000474	2,112	97,146,653

Figure 6.3 - Probability of exporting at least one infected carcass with LPAIV in muscle tissue per year assuming <u>two weeks</u> to detection.



Distribution descriptors	T	At least 1 infected carcass in "x" years	At least 1 infected carcass in "x" exported Tons
5%	2.66E-05	37,646	1,731,707,594
mode	1.19E-06	840,784	38,676,050,628
median	0.000282	3,545	163,054,951.6
95%	0.000989	1,011	46,517,308.89

Figure 6.4 - Probability of exporting at least one infected carcass with LPAIV in muscle tissue per year assuming <u>three weeks</u> to detection.

Measuring the effect of additional flock surveillance on the estimation of risk

The OIE guidelines for surveillance for AI call for increased surveillance in domestic poultry to ensure the early detection of infection. Three different surveillance scenarios were modeled based on three different samples sizes per exported flock (Table 6.4).

Table 6.4 – Sample sizes per flock under three different proposed surveillance scenarios

Scenario	Confidence level	Design prevalence	Sample size per flock*
A	95%	25%	11
B	95%	10%	29
C	95%	5%	59

*Sample sizes calculated based on Martin et al., 1987.

In the United States, the (NPIP) recently has proposed to expand its surveillance activities, currently directed only at breeder birds, to include meat-type chickens and layers. The effect of surveillance as a mitigation measure to reduce the yearly probability of introduction of LPAIV in meat was quantified based on each scenario and one, two, or three weeks delay in detection of infection.

Calculations to reflect the effect of surveillance are based on the same model structure used to calculate the non-mitigated probability. The only difference is that the flock prevalence estimate is replaced by the probability of a test-negative flock being infected.

Probability of a test-negative flock being infected

The probability of a flock being infected given that it is test negative, denoted as p (F inf| T-), is calculated:

p (F inf| T-) = 1 – NPVflock

Where:

NPVflock is the negative predictive value at the flock level. The negative predictive value at the flock level (NPV) is calculated as:

NPVflock = q Fsp / (q Fsp + Fp (1-Fse))

where:

Fsp = flock specificity

Fse = flock sensitivity

Fp = flock prevalence

q = 1-Fp

Flock level sensitivity and specificity

The sensitivity and specificity of the testing approach at the flock level need to be determined to assess the probability of a test negative flock being infected. Flock sensitivity is defined as the probability of a truly infected flock being classified as infected by the test. Flock specificity is the probability of a truly non-infected flock being classified as non-infected by the test (Noordhuizen et al., 1997).

Flock specificity (Fsp) is calculated as:

$Fsp = Sp^n$

where Sp is the specificity of the test and n the number of tests per flock.

If the critical number of positive results to classify a flock as positive is set to one (i.e. a flock is considered infected if a single positive test result is found), flock sensitivity is calculated as:

$Fse = 1 - (1-AP)^n$

Where AP is the apparent prevalence, calculated as $AP = Se\ p + ((1-p)(1-Sp))$ where:

Se = test sensitivity

Sp = test specificity

p = within-flock prevalence

Sensitivity and specificity of the AGID test

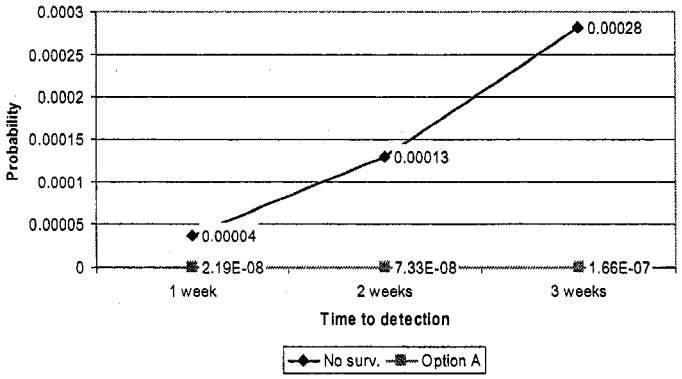
The literature on the sensitivity and specificity of the AGID test is scarce. One of the few studies attempting to validate diagnostic tests for AI compared the AGID test and a competitive ELISA test against the hemagglutination inhibition (HI) and neuraminidase inhibition (NI) tests. The AGID had a relative sensitivity to HI of 96.2% and a relative specificity of 99.5% (Schafer et al., 1998). The AGID test is very sensitive to detect AIV antibodies when used at the flock level (D. Senne* personal communication).

Effect of additional surveillance on the yearly probability of introduction of LPAIV in meat

The effect of surveillance at the flock level on the probability of importing meat from at least one infected bird was measured and contrasted against

* Dennis Senne. National Veterinary Services Laboratories (NVSL). USDA-APHIS-VS

the non-mitigated estimate. Results show a significant decrease in the probability when the proposed surveillance approach is applied (Figure 6.5).



Time to detection	Surveillance option			
	No surveillance	A	B	C
1 week	3.67E-05	2.19E-08	0	0
2 weeks	0.000129	7.33E-08	2.46E-14	0
3 weeks	0.000282	1.66E-07	4.26E-14	0

Figure 6.5 - Probability of introducing at least one infected carcass (median values). (Surveillance options B and C are not graphed, given the scale of the graph they would appear on the x axis.)

Conclusions

The results of this study are only a part of the risk assessment. They represent the release assessment step of the risk assessment process, i.e., the probability of exporting at least one infected chicken with LPAIV in muscle tissue during the risk period prior to detection of the first LPAIV-infected flock.

In the model, the large number of birds per flock characteristic of chicken flocks in the US, the high level of infectiousness of LPAIV in poultry flocks, and the use of a non-zero probability for the presence of LPAIV in meat imply

that if a flock is infected, the probability of at least one bird having virus in muscle is relatively high. However, the small flock prevalence during the risk period makes this event unlikely.

Additional surveillance would reduce the probability estimate in the release assessment significantly. The current OIE Code chapter emphasizes the importance of surveillance as the most important tool for early detection.

All available scientific evidence, both from a molecular perspective, as well as from an experimental perspective, shows that LPAIV is not present in poultry muscle or bones. The assumptions made in this assessment represent a pessimistic worst-case scenario and most likely lead to an overestimation of the true probability of introduction. Clearly, the presence of LPAIV in muscle tissue is critical to the results of the assessment.

A complete risk assessment would need to include the exposure and consequence assessments. Given the different systems of production and potential exposure pathways in different countries, this was not feasible. However, chicken products are imported for human consumption; consequently, only a small proportion of meat would be discarded uncooked and potentially fed to poultry. In addition, experimental data have shown that susceptible birds fed meat from LPAIV-infected birds failed to seroconvert and were not infected (Swayne and Beck, 2005). The combined probability of release and exposure is likely to be insignificant.

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Appendix 1 – Derivation of the probabilistic approach

The following parameters were used:

x – Infected poultry carcass with LPAIV in muscle

A – Flock prevalence

B – Within-flock prevalence

C – Probability of not detecting an infected flock through passive surveillance

D – Probability of LPAIV presence in muscle

n – Number of birds per flock

E – Number of flocks exported prior to detection

The probabilistic approach was derived as follows:

- Probability of a bird being infected and having LPAIV in muscle BD
- Probability of NO birds in a flock are infected and have LPAIV in muscle $(1-BD)^n$
- Probability of at least one infected bird with LPAIV in muscle in a flock $1-(1-BD)^n$
- Probability of a flock being infected, undetected and with at least one infected bird with LPAIV in muscle $A\times C\times(1-(1-BD)^n$
- Probability of NO exported flocks infected, undetected and with at least one infected bird with LPAIV in muscle $1-(A\times C\times(1-(1-BD)^n)^E$
- Probability of **<u>at least one</u>** exported flock infected, undetected and with at least one infected bird with LPAIV in muscle $P(x\geq 1)=1-[1-(A\times C\times(1-(1-BD)^n))^E]$

Appendix 2 - Mathematical model

	A	B	C	D	E	F
1						
2						
3		**Metric tons exported**	**Average carcass weight (Kg)**	**Birds**	**Flocks/Year**	
4						
5	Median top 20 recipients US exports	46,000	1.4	32,508,834	1,026	
6	Average flock size (n)	31,690				
7	Broiler flocks in the US/year	223,496		(CEAH 2004)		
8						
9						
10	**Risk period**					
11	Time to detection (weeks)	3				
12	Number of flocks exported (E)	59		(E5/52)*B11		
13						
14	Number of broiler flocks infected prior to detection	9		RiskTriang(3,6,18)		
15	Number of risk periods in a year	1		RiskPoisson(1.22)		
16						
17						
18	**Probability calculations**					
19	**A** - Flock prevalence	0.000223708		RiskBeta(B14+1,(B7/5)-B14+1)		
20	**B** - Within flock prevalence	0.50		RiskTriang(0.2,0.5,0.8)		
21	**C** - Failure to detect an infected flock (routine surveilance and ante- and post-mortem inspections)	0.4		RiskTriang(0.2,0.3,0.6)		
22	**D** - Virus present in meat	5.00E-06		RiskBeta(0+1,50-0+1,RiskTruncate(0,0.00001))		
23	**E** - Flocks exported during the risk period	59		B12		
24	**Q**	2.50E-06		B*D		
25	**R**	7.62E-02		1-(1-Q)^n		
26	**S**	6.25E-06		A*C*R		
27	**T**	**3.70E-04**		1-(1-S)^E		
28						
29						
30						

	A	B	C	D	E	F
32	**Effect of surveillance on U**					
33						
34	**Flock Se and Sp calculations**					
35	Se	0.962				
36	Sp	0.995				
37	Expected w/flock prev.	0.50		RiskTriang(0.2,0.5,0.8)		
38	Number tested per flock	11		NPIP		
39	Aparent prev.	0.4835		(B34*B36)+((1-B36)*(1-B35))		
40	Flock Se	0.999302132		1-(1-B39)^B38		
41	Flock Sp	0.94635458		B35^B37		
42	Prob. of true neg. flock	0.946142873		(1-B19)*B40		
43	Prob. of false neg. flock	1.56119E-07		B19*(1-B39)		
44	Pred. Value neg.	0.999999835		B41/(B41+B42)		
45						
46	**Probability calculations**					
47	**A** - P(flock inf | T-)	1.65005E-07		1-B43		
48	**B** - Within flock prevalence	0.5		RiskTriang(0.2,0.5,0.8)		
49	**C** - Failure to detect flock clinical surveillance	0.4		RiskTriang(0.2,0.3,0.6)		
50	**D** - Virus present in meat	5.00E-06		RiskBeta(0+1,50-0+1,RiskTruncate(0,0.00001)		
51	**E** - Flocks exported during the risk period	59		B23		
52	**Q**	2.50E-06		B*D		
53	**R**	0.0762		1-(1-Q)^n		
54	**S**	4.61E-09		A*R		
55	**T**	**2.73E-07**		1-(1-S)^E		

Note: The number of birds tested per flock and the number of flocks exported during the risk period varies depending on the time lag to detection and the surveillance option (A, B or C).

Chapter 7

Analytical approaches for risk assessment for animal health programs: Methodological issues and solutions

Introduction

Quantitative risk assessment frequently involves the use of stochastic processes to simulate a desired outcome of interest. The advantage of using stochastic processes is that they allow incorporating uncertainty and variability in the final outcome (Vose, 2000). In animal health, the most common building blocks to develop stochastic models are the distributions used in the binomial, hypergeometric and Poisson processes. The application and use of these distributions and their parameters have been discussed elsewhere (Vose, 2000; Murray, 2002). Several studies, in particular animal health trade risk assessments, have successfully used this type of approach (MAF, 1999; Ahl et al., 1993; McDiarmid, 1993; Vose, 1997; Zepeda, 2007) that has become the conventional internationally applied methodology (OIE, 2004).

Occasionally, insufficient data may lead to unreasonable or questionable outcomes in relation to the current scientific understanding on the subject at hand. When modeling parameters for which limited data are available, the 'conventional' approach yields very widespread distributions reflecting a high level of uncertainty. The effect of such parameters in stochastic probabilistic models can be very significant, leading to potentially erroneous conclusions. In face of this type of situation, the analyst needs to be able to recognize the limitations of the approach and explore alternative solutions.

An example of this situation surfaced when attempting to model the presence of low pathogenic avian influenza virus (LPAIV) in poultry meat (Chapter 6). The objective of this chapter is to explore alternative approaches under a specific modeling situation in which the conventional approach is limited. The advantages and disadvantages of these alternative approaches are discussed.

Limitations of conventional modeling approaches

The outcome of the risk assessment presented in Chapter 6 is the product of two previous quantitative risk assessments performed by the author to support international trade negotiations on poultry meat exports from the United States (unpublished results). A stochastic model was initially constructed to calculate the probability of at least one exported poultry carcass with LPAIV. At the time of the development of the first model, the current scientific knowledge indicated that LPAIV is not present in poultry meat. This is based on the molecular characteristics of the cleavage site of the hemagglutinin (HA) (Rott, 1992; Vey et al., 1992) and expert opinion

indicating that LPAIV infections are restricted to the respiratory and digestive tracts of infected birds. However, until recently, there was very little information on the occurrence, onset, and length of viremia in LPAIV infections; no formal experiments demonstrating the absence of LPAIV in poultry meat had been conducted or had used methods that were not considered to have enough sensitivity (Mo et al., 1997). For the stated reasons, the probability of LPAIV being present in poultry meat was initially modeled with a uniform distribution (0,1). One of the outcomes of a risk assessment is to identify gaps in scientific knowledge. As a result of the initial risk assessment, Swayne and Beck (2005) conducted an experimental study to determine if LPAIV could be present in poultry meat. The study showed that, with LPAIV infections, there is no viremia and virus cannot be found in muscle tissue.

One of the limitations of experimental studies that require the use of biosecure laboratory (biosafety level 3 (BSL3)) facilities is that cost and space constraints usually force researchers to use a limited number of animals. Although Swayne and Beck's study provided extremely useful information, the study used only 50 birds.

One way to model the presence of LPAIV in poultry meat using the data from that study is to use a beta distribution with the format Beta (s+1, n-s+1) where 's' is the number of successes and 'n' the number of trials, in this case zero successes in fifty trials. Figure 7.1 and Table 7.1 show the results of 1000 iterations using a spreadsheet (Excel, Microsoft Corp.) and simulation software (@Risk, Palisade Corp.).

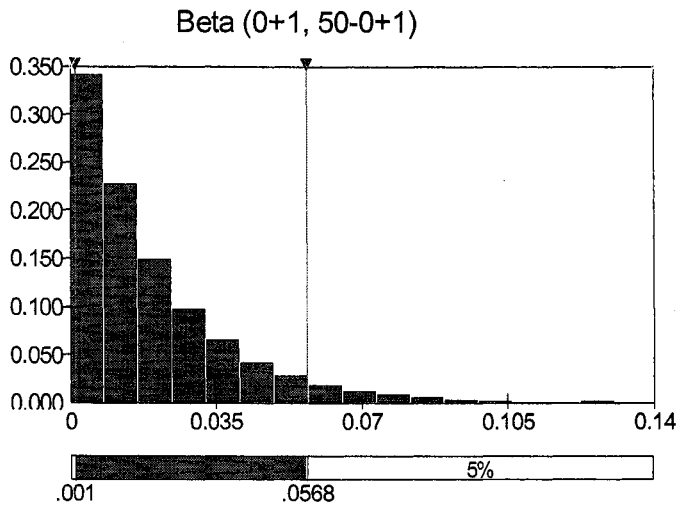

Figure 7.1 – Probability of LPAIV presence in poultry meat using a Beta (0+1, 50-0+1) format.

Table 7.1 – Distribution descriptors of a Beta (0+1, 50-0+1) distribution

Distribution descriptors	Probability
5%	9.9 E-04
50%	1.35 E-02
mean	1.92 E-02
95%	5.68 E-02

Although Swayne and Beck's study found no evidence of LPAIV in muscle, the median probability for the presence of LPAIV in poultry meat using this approach is approximately 1.3%, which is excessively high and does not reflect the prevailing scientific opinion. When this distribution is used in the larger context of the model used in Chapter 6, the overall probability of at least one exported carcass with LPAIV is unreasonably high and might lead decision makers to overly conservative decisions that could be considered to be trade restrictive and not scientifically based.

For the purpose of this chapter three different approaches are explored:

a) Increasing the number of animals used in the study

b) Truncating the original Beta distribution

c) Incorporating expert knowledge as a prior distribution

Effect of increasing the number of animals used in the study

The median value obtained with the Beta (s+1, n-s+1) distribution in Figure 7.1 is a function of the number of animals used in the study. To analyze the effect of increasing the number of animals four different scenarios were compared, all assume that no positive results are found, i.e. s = 0.

Table 7.2 and Figure 7.2 show the effect of increasing the sample size on the probability of LPAIV presence in muscle tissue. It is evident that a larger number of experimental animals will result in a lower probability. It is difficult to define a minimum threshold for the number of experimental animals. However, in order to obtain a median value similar to the effect of truncating the distribution (Figure 7.3) between 135,000-140,000 experimental animals would be needed. Clearly, cost and laboratory space limitations preclude the use of large sample sizes in this type of experimental studies.

Table 7.2 – Effect of sample size on the probability of LPAIV presence in muscle

	Number of experimental animals			
Distribution descriptors	**50**	**500**	**1000**	**5000**
5%	9.89E-04	1.01E-04	5.04E-05	1.02E-05
50%	1.35E-02	1.38E-03	6.91E-04	1.38E-04
Mean	1.92E-02	1.99E-03	9.99E-04	2.00E-04
95%	5.67E-02	5.94E-03	2.97E-03	5.97E-04

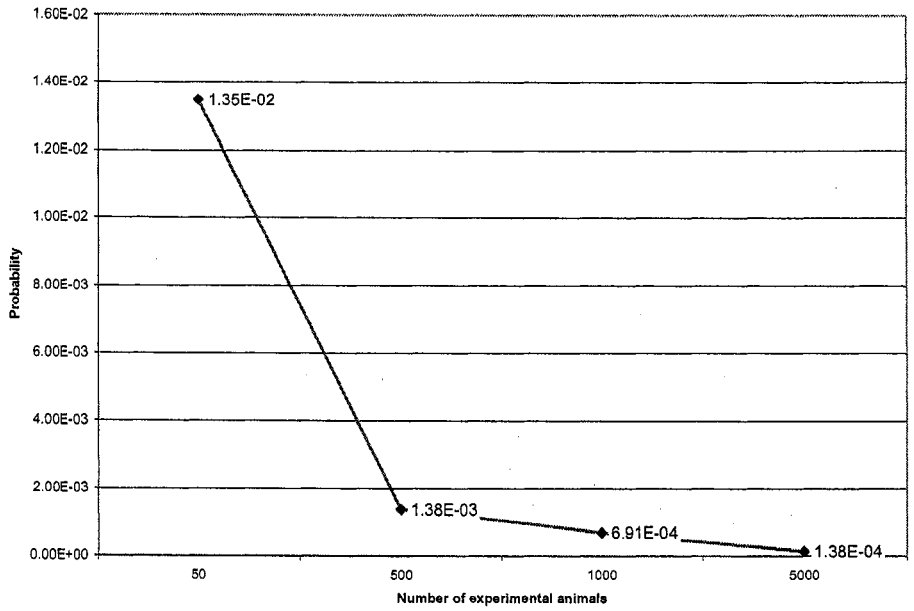

Figure 7.2 – Median probability values for a Beta (s+1, n-s+1), assuming zero successes and four different scenarios n = 50, 500, 1000 and 5000 experimental animals.

Truncation of the original Beta distribution

On occasion, access to suitable experts may be difficult, and the analyst is unable to create a distribution reflecting their knowledge and may only be able to elicit a plausible maximum value from a single expert. This approach involves using experimental data and setting an upper limit to the distribution, ideally derived from expert opinion. Although this approach generates results that might be closer to the scientific consensus (Figure 7.3), it only represents a point estimate from a single expert. However, it may be useful when expert opinion is limited and only a best guess on the upper limit of the probability is available.

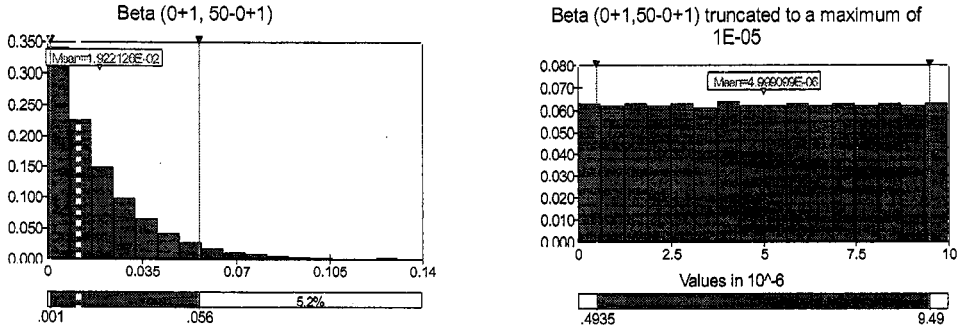

Figure 7.3 – Effect of truncation on a Beta (0+1, 50-0+1) distribution at a defined maximum value.

Incorporation of expert knowledge as a prior distribution

A third alternative is to elicit expert opinion creating a distribution that can be used as a prior distribution. In a Bayesian context, a Beta distribution (s+1, n-s+1), is a posterior distribution that assumes a Beta (1,1) prior distribution, which is equivalent to a Uniform (0,1) distribution (Figure 7.4) (Vose, 2000; Murray, 2002).

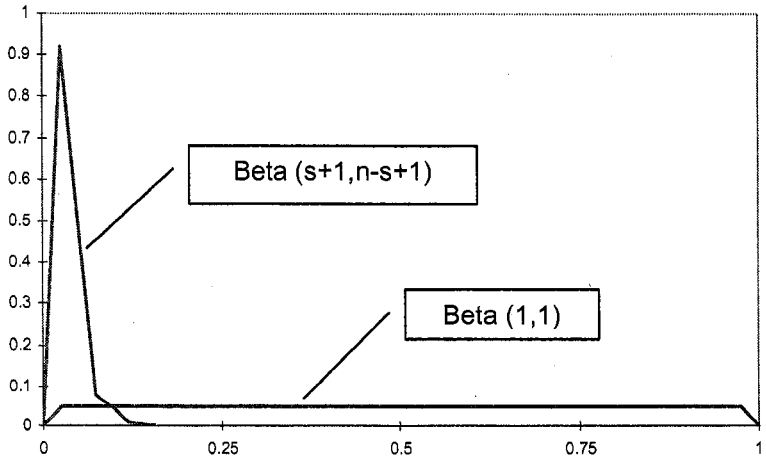

Figure 7.4 – A Beta (1,1) prior distribution and the resulting Beta posterior distribution incorporating experimental data from Swayne and Beck (2005).

Expert opinion can be expressed in the form of a Pert distribution with a minimum, a most likely and a maximum value. A Pert distribution is a form of the Beta distribution (equations 1 to 4) (Vose, 2000).

$$Pert(a,b,c) = Beta(\alpha_1,\alpha_2)\times(c-a)+a \qquad \text{Eq. 1}$$

Where: a = minimum, b= most likely, c= maximum and

$$\alpha_1 = \frac{(\mu-a)\times(2b-a-c)}{(b-\mu)\times(c-a)} \qquad \text{Eq. 2}$$

$$\alpha_2 = \frac{\alpha_1\times(c-\mu)}{(\mu-a)} \qquad \text{Eq. 3}$$

$$mean(\mu) = \frac{a+4b+c}{6} \qquad \text{Eq. 4}$$

In general terms a Beta distribution (s+1, n-s+1), can be rewritten as Beta ($s+\alpha_1$, $n-s+\alpha_2$), where α1 and α2 are the parameters of the prior Beta distribution (Murray, 2002). Thus, a posterior Beta distribution using a Pert distribution as a prior, can be written as:

$$Beta_{post} = Beta(s+\alpha_1, n-s+\alpha_2)\times(c-a)+a \qquad \text{Eq. 5}$$

Assuming that a panel of experts was convened and that they collectively agreed that a suitable distribution for the presence of LPAIV in muscle would be Pert (0, 1e-07, 1e-06), a posterior Beta distribution could be obtained taking into consideration experimental evidence. Figure 7.5 and Table 7.3 show the results of a simulation with 1000 iterations.

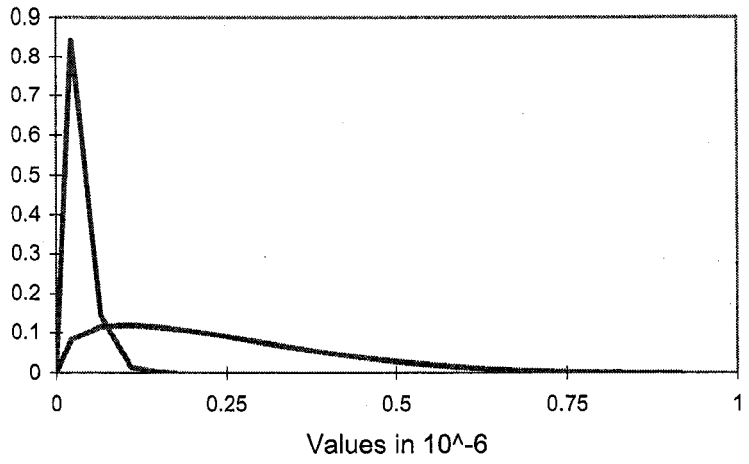

Figure 7.5 – Effect of combining experimental results from Swayne and Beck (2005) and expert opinion in a Bayesian context

Table 7.3 – Main distribution descriptors of a Beta (0+1, 50-0+1), a Pert (0, 1e-07, 1e-06) and a posterior Beta distribution combining both distributions

Distribution descriptors	Posterior w/uninformed prior	Informed prior (Pert)	Posterior w/informed prior
5%	1.00E-03	3.00E-08	2.65E-09
Mean	1.92E-02	2.33E-07	2.49E-08
50%	1.35E-02	2.03E-07	1.96E-08
95%	5.70E-02	5.42E-07	6.58E-08

Eliciting expert opinion should not be taken lightly; several issues can arise that may lead to inaccurate estimates. Some of these issues are presented by Vose (2000) and include the ability of the experts to recall past events (availability), the ability to see the overall picture and avoid focusing excessively on the details of the problem; and being influenced by unrepresentative data (representativeness), as well as adjustment and anchoring which might lead to overconfidence and too narrow estimates.

Murray (2002) and Van der Fels-Klerx (2002) describe a process to conduct a workshop of experts to elicit their knowledge and derive the appropriate distributions to include in a stochastic model.

Effect of the four modeling approaches on the results of the full model used in Chapter 6

In order to evaluate the effect of each alternative approach on the results of the model used in Chapter 6 to assess the probability of at least one infected poultry carcass with LPAIV in muscle, four simulations with 10,000 iterations each were run. The results are presented in figures 7.6 and 7.7. The median value obtained by using only the experimental data is around 4%, which contradicts what avian influenza experts think about the presence of LPAIV in meat. It is worth recalling that the experiments conducted by Swayne and Beck (2005) failed to detect a viremia in LPAIV infected birds, could not isolate LPAIV in different muscle groups and could not transmit the infection by feeding ground meat from LPAIV infected birds, while birds infected with a highly pathogenic avian influenza virus (HPAIV) developed a viremia, virus was recovered from muscle, and birds fed ground meat from infected birds became infected. Increasing the number of experimental animals to a thousand birds has almost no effect in reducing the probability. The two approaches that combine experimental data and expert opinion significantly reduce the probability of exporting at least one carcass with LPAIV. While the 'expert opinion' used in the latter two approaches was not elicited using formal methods, the values used are not unreasonable.

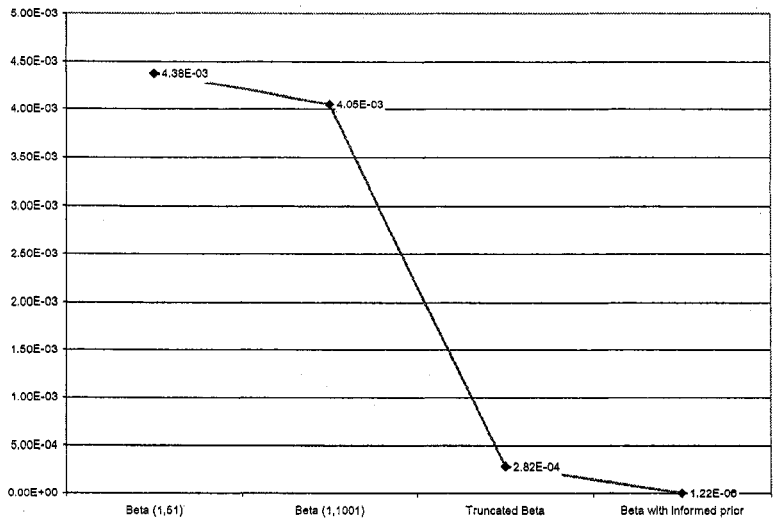

Figure 7.6 – Median values of four simulations of the LPAIV model with the four modeling approaches

Distribution descriptors	Beta (1,51)	Beta (1,1001)	Truncated Beta	Beta with informed prior
5%	1.63E-03	1.26E-03	2.69E-05	1.34E-07
50%	4.38E-03	4.05E-03	2.82E-04	1.22E-06
Mean	4.90E-03	4.60E-03	3.63E-04	1.93E-06
95%	9.99E-03	9.79E-03	9.80E-04	6.09E-06

Table 7.4 – Main distribution descriptors of four simulations of the LPAIV model with the four modeling approaches

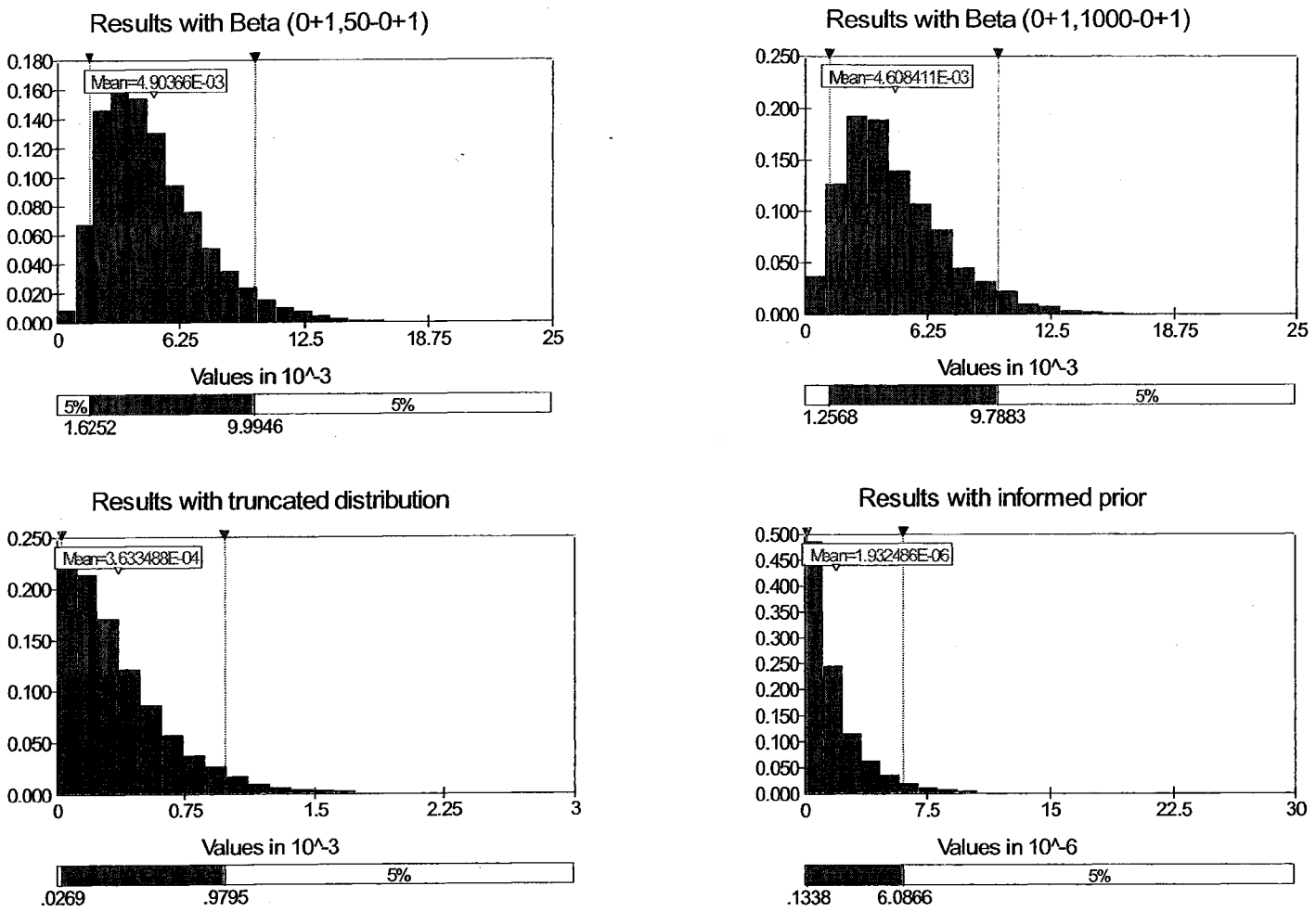

Figure 7.7 – Probability of at least one infected poultry carcass with LPAIV in muscle using four different modeling approaches

Discussion

While it would seem that an increase in the number of experimental animals would lead to a significant reduction in the probability of the presence of LPAIV in meat (Figure 7.2 and Table 7.2), the results presented in Figure 7.6, 7.7 and Table 7.4 demonstrate that there is no significant advantage in obtaining additional experimental data with more observations. Additionally, as mentioned above, the cost and logistic constraints of this approach frequently force researchers to limit the number of experimental animals used.

The last two approaches, i.e. truncating the distribution at a defined maximum value and using an informed prior distribution, come closer to reflecting the current scientific opinion that LPAIV is not present in muscle. Eliciting expert opinion to generate an informed prior distribution should be the preferred approach. Although the cost of deriving expert opinion (e.g. travel, and workshop expenses) and availability of suitable experts may make this approach difficult to implement, it is a more efficient and practical approach compared to conducting large scale experimental studies requiring BSL3 laboratory conditions.

Stochastic simulation models are a useful tool in animal health risk assessment. On occasion, insufficient data may lead to the use of subjective estimates based on expert opinion. A risk assessment report must explicitly state the variables of the model for which subjective estimates were used and the assumptions made. Sensitivity analysis will help determine how sensitive

the model is to variations in these variables and will provide an indication if further efforts should be made to refine the estimates used.

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Chapter 8

Compartmentalization in aquaculture production systems[5]

Introduction

Zoning and compartmentalization are disease management strategies that pursue the same objective; both aim at establishing animal populations with a distinct health status based on effective separation of these populations and application of biosecurity measures to prevent the reintroduction of the infection. Zoning relies more heavily on geographic factors, such as natural or man-made barriers, while compartmentalization focuses more on management and biosecurity within establishments comprising the compartment to ensure the maintenance of the health status (OIE, 2007a). The key difference between both concepts is that, in zoning, the application of control measures is under the direct responsibility of the competent authority, while, in compartmentalization, biosecurity measures are the responsibility of the management of the compartment. Therefore, to achieve international recognition of compartments, it is essential that the competent

[5] Zepeda C., Jones B. and Zagmutt F. (accepted for publication, 2008) Compartmentalisation in aquaculture production systems. OIE Scientific and Technical Review 27 (1).

authority establishes an audit and certification process in close coordination with the management of the compartment.

Although the term "compartmentalization" is relatively new for the purpose of international trade, many disease control programs have applied it historically. Traditional control programs for diseases, such as bovine tuberculosis and brucellosis, have relied on certifying disease-free herds (CFR, 2006a, b) as the building blocks leading towards eradication.
The concept of a disease-free herd is the basis for compartmentalization. The current interpretation of a compartment extends to all the epidemiologically linked units of a production system (Scott et al., 2006). In vertically integrated industries, such as the poultry, swine and some aquaculture industries, compartmentalization allows the recognition of all the production units, including the slaughterhouses or packing plants, as having a uniform animal health status, ensuring the uninterrupted flow of animals, vehicles and goods between the different units within the compartment.

Aquaculture production systems pose a particular challenge for the application of compartmentalization. The high potential for contact with pathogens through water means that the effective separation between compartments, essential to maintain the integrity of the system, can only be guaranteed under specific production conditions.

The Australian AQUAVETPLAN categorizes aquaculture production systems into four groups (DAFF, 2004):

- Open systems - Systems where there is no control of either host movement or water flow (e.g. wild caught fisheries)
- Semi-open systems - Systems where there is control of host movement but no control of water flow (e.g. net pen culture, sea cages, mollusk rack culture)
- Semi-closed systems - Systems where there is control of host movement and some control of water flow (e.g. land based farm with tanks, ponds or raceways)
- Closed systems - Systems where there is good control of both host movement and water flow (e.g. aquaria, recirculating farms in a building on land).

Compartmentalization is ideally suited for closed and semi-closed systems. Some industries, such as salmon farming, may have a combination of systems ranging from closed systems to semi-open systems. In this case, a mixed approach of zoning and compartmentalization may be appropriate.

Implementation of compartmentalization

A compartment free of a specified disease is expected to thoroughly document all the procedures supporting its disease status claim. Scott et al. (2006) identified seven factors for a successful implementation of compartmentalization:

- Definition of the compartment
- Epidemiologic separation of the compartment from potential sources of infection
- Documentation of factors critical to the definition of compartment

- Supervision and control of the compartment
- Surveillance for the agent or disease
- Diagnostic capabilities
- Emergency response, control, and notification capability

The specific details pertaining to each factor will not be repeated here, but their application will be demonstrated below, using a shellfish or shrimp hatchery as an example. It is important to stress that, as in zoning, the burden of proof lies with the disease-free compartment. It is the responsibility of the compartment to implement all the appropriate measures that guarantee the integrity of its status.

Certification and Biosecurity

A compartment must identify all the potential pathways for the introduction of infection. The critical points for the most significant pathways must be addressed in a comprehensive biosecurity program and documented in a biosecurity plan. For international trade purposes, the recognition of compartments necessarily involves a process of official certification by the appropriate governmental authority i.e. the competent authority according to the OIE Code (OIE, 2007a).

This certification requirement implies that the biosecurity program and all the measures applied within the compartment must be auditable and transparent. Biosecurity measures must be subjected to a control and verification process based on hazard analysis and critical control points (HACCP) including the following (FDA, 2001):

- Conduct a hazard analysis

- Determine critical control points
- Establish critical limits
- Establish monitoring procedures
- Establish corrective actions
- Establish verification procedures
- Establish record-keeping and documentation procedures

The evaluation of biosecurity measures using the HACCP methodology is shown below, using a salmon farm as an example.

Surveillance

Continuous surveillance within and outside the compartment will be the ultimate proof that the biosecurity measures aimed at preventing the introduction of infection are effective. Internal surveillance must be maintained and directed not only to the pathogen for which the compartment has been defined but also towards other pathogens of importance, in particular OIE listed diseases.

The finding of another disease agent that shares one or more pathways of introduction may indicate a breach in the biosecurity that needs to be corrected immediately. For example, the detection of a boring sponge in the shells of trochus spat (*Trochus niloticus*) at a high-health recirculating marine hatchery facility was of concern even though the sponge, of itself, was not causing mortalities; however, its presence indicated a breach of biosecurity which might allow entry of more lethal pathogens (J. B. Jones, unpublished data). External surveillance will indicate whether significant changes in the level of exposure have occurred and might trigger a review of the biosecurity

measures applied; for example, a change in the prevalence of a disease outside the compartment may require a review of the sample strategy for surveillance for the disease within the compartment.

Uses of compartmentalization

Compartments can be defined under two scenarios:

- as a disease management tool in an endemic but stable situation
- as a disease management tool in the event of an outbreak

In countries or zones with endemic disease, compartmentalization offers the possibility to direct resources more efficiently. Disease-free compartments can be defined and trade in situations where disease eradication at the country or zone level is not deemed feasible in the short term or in situations where infected wildlife or vectors are involved. In most situations, compartmentalization will entail a significant investment and eradication of the infection should be the most cost-effective approach.

In the event of an outbreak, compartmentalization can be used as a tool to limit the economic impact of the disease by allowing trade from disease free compartments. Ideally, a country should define its compartmentalization strategy as a precautionary measure before an outbreak as a way to expedite the resumption of trade. If compartments are defined and bilaterally agreed upon in 'peace time', in the event of an outbreak, disease-free compartments could resume to trade once the situation has been demonstrated to be stable both in terms of incidence and geographic distribution. However, if the compartmentalization strategy is established once the disease has been

introduced, the time required to define the compartments, conduct a thorough pathways analysis to identify potential routes of entry, set up biosecurity measures, and establish certification procedures, will be significant and the benefits of applying such a strategy may be lost.

Occasionally, a mixed approach combining zoning and compartmentalization may be suitable. For example, the European Union under Council Directive 91/67/EEC and subsequent decisions, recognizes disease free zones for two fish diseases (infectious haematopoietic necrosis [IHN] and viral haemorrhagic septicaemia) and two shellfish diseases (*Bonamia ostreae* and *Marteilia refringens*) (OIE, 2007b). The zones are based on geographical characteristics, but one of the features of this program is that there are also individual farms with this recognition.

Compartmentalization applied to "high health" shellfish or shrimp hatcheries

A "closed system", such as a finfish farm using recirculated water or a shellfish or shrimp hatchery of high health status, is the easiest form of compartment in which to apply management practices to achieve biosecurity. This is because all of the animals forming the subpopulation within the compartment are identifiable and it is possible to establish a clear epidemiological separation from other aquatic animals and other potential pathways for disease introduction. All of the perimeter inputs (water, air, personnel, feed, vehicles and stock) are under the control of an operator and are capable of being independently monitored and audited. The activities within the compartment can all be routinely monitored and tested such that

deviations from normal can be identified and investigated. The example below is taken from a shellfish hatchery but could be easily adapted to fit any building-based aquaculture ventures (such as fish farms operating with recirculated water).

Definition of the compartment

The subpopulation of animals within the compartment must be clearly defined, including identification of, and traceability of the aquatic animals. This step should be carried out in consultation with the competent authority and might, for example, involve a single hatchery or a group of hatcheries owned by a company, or a group of hatcheries belonging to an industry association. All of the aquatic animals within the compartment and those leaving the compartment will be identifiable by a method which enables trace-back to the hatchery of origin and the batch production date. Where a compartment is comprised of a number of establishments, these will share many common elements of the biosecurity plans which together will form the criteria for the definition of the compartment.

Epidemiologic separation of the compartment from potential sources of infection

Animals in the compartment need to be recognizable through a clear epidemiological separation from other aquatic animals and all things presenting a disease risk. Therefore, potential sources of infection and the risk of spread of infection into the compartment must be assessed. Methods for performing a disease risk assessment are well documented, for example (Arthur et al., 2004; OIE, 2004; Jones, 2006). In addition, HACCP analysis,

with which business managers are often more familiar, can be invaluable for identifying processes, hazards, and critical control points (NRM, 2007). An example of a HACCP generic process flow diagram for a typical shellfish or shrimp hatchery is shown in Figure 1.

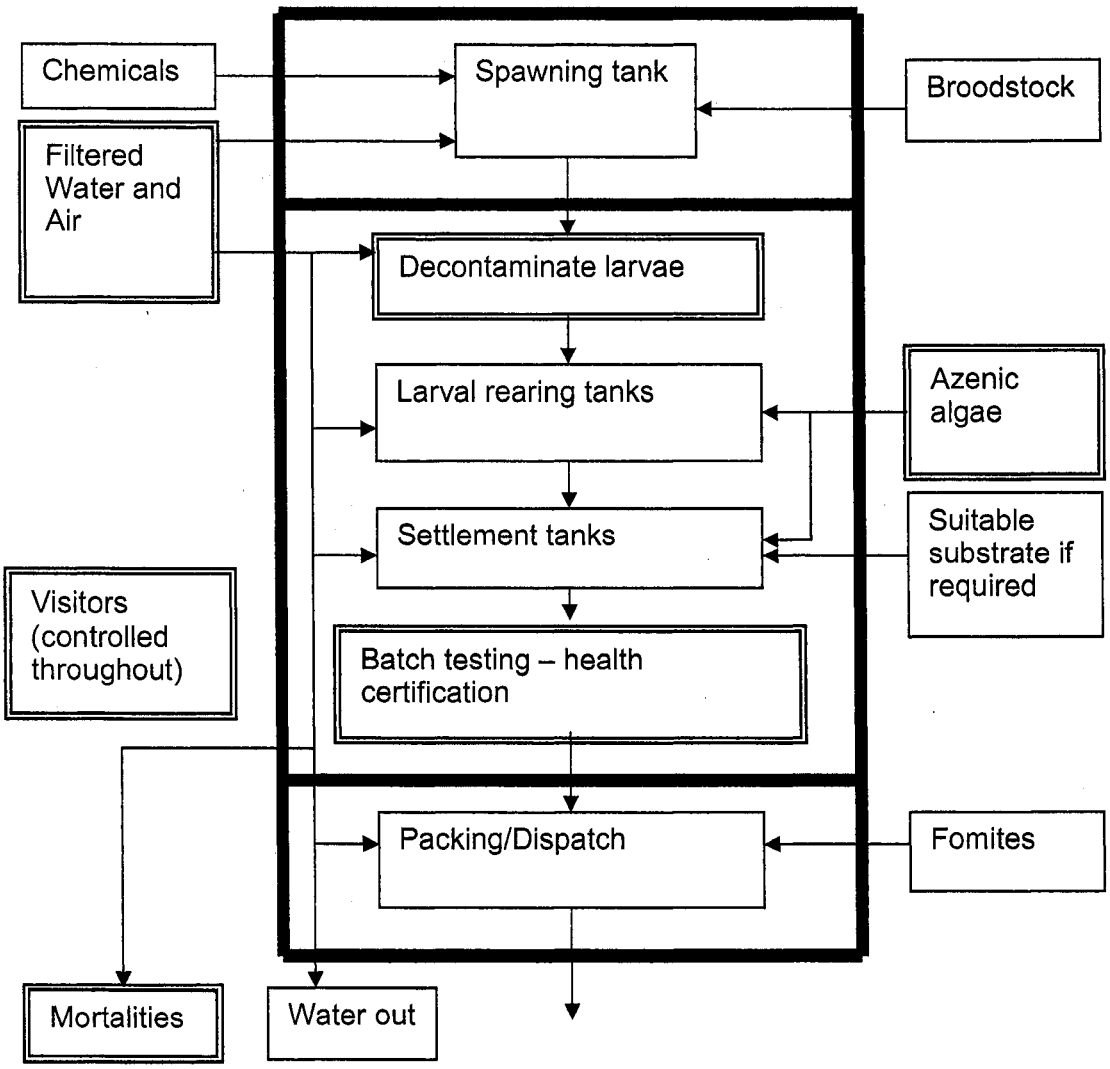

Figure 1. HACCP style generic flow diagram: shellfish or shrimp hatchery. The compartment is shown within heavy lines, the three sections have separate biosecurity. The boxes with double outline are Critical Control Points in the process.

Documentation of factors critical to the definition of compartment

For land-based hatcheries, the most common source of infection is through the incoming water supply, particularly if aquatic animals in that water supply may carry the diseases of concern. A secure water source (such as a well) is the preferred option, but for most hatcheries incoming sea water must be filtered to remove bacteria and other potential pathogens (Arndt and Wagner, 2003, Ford et al., 2001). Filtration can be accompanied by protein fractionation and sterilization (typically UV) where viruses are of concern.

The fish pathogen, *Amyloodinium ocellatum,* is the only aquatic pathogen that has been associated with airborne dispersal (Roberts-Thompson et al., 2006), but the air can bring dust (for example, dust rich in iron promotes growth of *Vibrio* bacteria), birds (McAllister and Owens, 1992; Vanpatten et al., 2004), insects, and aerosols which may include toxic chemicals from nearby industrial or agricultural sites (Pathiratne and George, 1998). Toxic compounds negatively affect the immune-status of the stock. If an assessment of the risk requires it, air supply into a building or parts of a building can be controlled.

Feed is a common source of pathogens. The risk of pathogen introduction can be controlled by using processed foods, such as pellets, crumbed feeds or algal pastes. Live, freshly dead, or frozen feeds are more problematic. For shellfish this is usually overcome by using azenic algal culture, keeping bacterial counts to below $2x10^6$ cfu/ml (Lewis et al., 1986). In shrimp hatcheries, care must be taken to ensure that feed does not become infected with shrimp pathogens, such as white spot syndrome virus (Vijayan et al.,

2005). The use of fresh or frozen crustacean tissues to condition broodstock should be avoided.

Other supplies coming onto the site can be a potential source of infection. These include fomites, such as transport crates, settlement slats and netting; and other at risk items such as non-food grade plastics that may lead to toxic insults (Jones, 2006), especially in mollusk hatcheries that result in immune suppression and consequent infection by pathogenic organisms.

Water leaving the compartment should also be treated to prevent the escape of individuals and/or pathogens to the environment. Such a breach may affect the status of other compartments and the environment.

Contingency plans should be in place to ensure continuity of power supply, particularly to pump, heat or aerate water. Utility staff might travel from one establishment to another, representing a potential biosecurity hazard that should be assessed.

A full set of daily records should be kept of all production figures, sources of supplies and feed (Juarez et al., 1996). Daily records for each tank should be kept of water quality parameters, stock movements, feeding schedules, morbidity and mortality records and medications. Maintenance and cleaning schedules for all tanks, pipe work and associated infrastructure should be recorded when due and when completed. If the hatchery has a "dry out" or fallowing period in the production cycle, then that must be documented together with other maintenance and cleaning that may be undertaken.

A compartment must have a biosecurity plan, addressing all of the above potential pathways for the introduction of pathogens into the facility, together with the assessment of the risk and management measures required for each risk, the production and stock records, feed sources, surveillance results, visitor logbook, morbidity and mortality history, medications, vaccinations, documentation of training, and any other criteria necessary for risk mitigation.

Supervision and control of the compartment

Staff and visitors entering and leaving the site(s) are a biosecurity risk. Personnel should not visit "at risk" sites prior to arrival for work and should, where practicable, not enter and leave multiple times during the day - especially where a compartment is surrounded by high risk factors. Visitors, particularly if they have visited other establishments, may also pose a biosecurity risk. Mud and other biological contaminants on vehicles and vessels entering and leaving the site are also a biosecurity risk which needs to be evaluated and managed. It is important to keep a visitor book, to record all visits and visitors to the site to enable a swift and effective trace-forward and trace-back in case of disease.

The management of broodstock is a major problem and a major source of contamination in shellfish and shrimp hatcheries. Broodstock, particularly shellfish and mollusk broodstock, may have an unknown disease history (Brock and Bullis, 2001). Since many aquatic pathogens may be refractory to non-sacrificial tests and yield false-negative results, broodstock, their feces and water and any fomites associated with their arrival should be treated as a

potential source of infection. The holding and conditioning facilities for broodstock should be physically separated from the larval rearing areas, all equipment should be segregated and kept in the broodstock area, the water supply should be separate and staff should not move freely from broodstock to larval areas without application of risk mitigation procedures.

Within the farm or hatchery, it is a good practice to subdivide the space into areas based on activity and risk, for example larval grow-out areas should be separate from broodstock areas, feed preparation from administration, and workflow should, where practical, go from clean activities to dirty areas and then staff should exit from the facility. Many establishments separate work areas through the use of internal partitions and require the use of foot baths and hand washing facilities between work areas.

Egg production and fertilization should be carried out in a way that ensures that fertilized eggs are washed and do not carry adhering pathogens into the larval area (Brock and Bullis, 2001). Egg batches should be kept separate where possible and be tested for pathogens of concern as soon as practical. Many aquatic pathogens can persist in aquatic populations at prevalences far below those assumed by standard sampling methods. For this reason, routine testing of stock may not detect disease. In such cases, if broodstock are destroyed after spawning, they should be tested for vertically transmitted diseases of concern, and if positive, the offspring should be assumed to be infected, even if testing using standard sample sizes provides negative results.

Equipment in the facility should undergo regular maintenance and testing to ensure that it is operating within acceptable parameters. For example, refrigerator or heating unit motors may appear to be working but may not be operating at the specified temperature.

A compartment must be auditable. The biosecurity plan should define the relationship between the relevant enterprise/industry and the competent authority and their respective responsibilities including the processes for oversight and independent audit of the operation of the compartment by (or on behalf of) the competent authority

Surveillance for the agent or disease

A testing regime is an essential part of the concept of a compartment. Testing should be planned, regularly carried out and encompass both disease surveillance and hygiene issues (for example, shellfish hatcheries routinely monitor bacterial loads in pipelines, which should be below 10^4 bacteria/ml for larval survival (Lewis et al., 1986), and changes to normal bacterial plate-counts can give an early indicator of filter failure). Surveillance for pathogens of concern should occur regularly on larvae in the facility, in accordance with a sampling plan approved by the competent authority.

Finally, whether required by the competent authority or not, all larvae leaving the facility should be tested for pathogens of concern by an independent laboratory. This is as much about ensuring the reputation of the

establishment as it is about the quality of the larvae, and can avoid expensive disputes should mortalities subsequently occur.

Diagnostic capabilities

Most hatcheries will routinely monitor larvae for condition and growth, and also for bacterial loading in tanks, pipes and on surfaces. Commercial test kits for common pathogens are being increasingly used. However, it is essential for compartments, in consultation with the competent authority, to have ready access to a well equipped diagnostic laboratory and to appropriate veterinary assistance. This will speed the implementation of control measures, should a health problem be present.

Emergency response, control, and notification capability

In addition, the biosecurity plan should have a section on what to do if a disease emergency occurs in the vicinity of the establishment, in the broodstock area, or in the larval area. This should be detailed, and include , responsibilities of staff, isolation of affected areas, sample collection for diagnostic purposes, phone numbers to call for notification to the competent authority and for diagnostic assistance (including after-hours contact details) and with action sheets to tick as tasks are completed. The biosecurity plan should be an officially approved document with relevant sections laminated and readily available to staff in wet areas, and with copies available to relevant personnel off-site.

The biosecurity plan should include a section on disaster recovery (for example; from where stocks of veterinary drugs are available, where

emergency generators be leased and where tons of dead fish can be disposed of).

An example of the evaluation of biosecurity measures on salmon farms using the HACCP methodology

The cornerstone of compartmentalization is the establishment of an auditable biosecurity plan. The following example illustrates the steps required to apply a HACCP approach to biosecurity.

Salmon farming can be divided in two general phases: the fresh water and the saltwater stages. The fresh water stage comprises all the production steps from spawning, to fry production, to the production of smolts that are ready to be transferred to the ocean. The saltwater stage starts with the introduction of smolts in sea pens and finishes at harvest. In some operations, the broodstock (i.e. adult fish that will be spawned) are kept in a separate saltwater facility, but for the purposes of this example the broodstock is extracted directly from the saltwater farm.
Within these two broad stages, there are several intermediate steps intended to reproduce the natural life cycle of salmonids. Often the transition between intermediate steps involves moving the fish to and from different physical units, increasing the risk of spread of infectious diseases among separate production units.

Briefly, the production cycle starts when the broodstock is selected from saltwater farm(s) and transported to freshwater ponds in the hatchery. The

adult fish are spawned and the eggs are manually fertilized and transferred to incubation units. The hatched alevins remain in the incubators until their yolk sacs are consumed. As alevins become fry, they are transferred to (bigger) fry tanks usually located in the same facility, and after they reach a certain size, they are transported to open pens in large freshwater bodies such as lakes.

Salmon that are physiologically ready to migrate to saltwater are called smolts. They are moved as a cohort to floating pens usually located in protected bays or estuaries. After the fish reach a certain average weight (2.5-4.5 kg, depending on the species), they are transported in well boats to processing plants where they are slaughtered and processed for human consumption.

Most of the long distance transportation of fish between production units is done in water tanks on specially designed hauling trucks, or in well boats, whereas the transfer within a production facility can be made using nets, containers or by diverting water flow. Fish in different production stages are commonly graded and split in different tanks/cages based on size to obtain a more homogeneous populations.

Depending on the country, region, and company/producer, the farming cycle may present many variations. For example, some countries allow for smolts to be grown in lakes, whereas in other areas smolts are grown only in ponds in-land; some operations will keep a separate broodstock, whereas others will gather the broodstock from the sea pens; fry can be grown in ponds in the

hatchery or moved to fry facilities elsewhere. Also, depending on local regulations, slaughter can occur on the sea site[6] or in the processing plant.

One important characteristic of the salmon farming industry is that companies are often vertically integrated. In other words, a single company manages the entire production cycle, from spawning to harvest. However, smaller companies may use external resources for some of the stages that require expensive inputs or technology. For instance, smaller operations may skip the freshwater cycle by buying smolts, or also outsource the harvest and processing of the food-size fish.

The aforementioned characteristics make disease management in farmed salmon complex, since populations are moved, mixed (i.e. grading and split), and fish in some stages are kept in open cages, facilitating the contact with wild fish populations, and the spread of diseases through water.

Compartments

Several stages of salmon farming occur in open systems (i.e. smolts in freshwater pens, and adults in saltwater cages), making the definition of a compartment particularly challenging. The hatchery stage may be defined as a compartment for one or more diseases if correct biosecurity measures are in place. For example, some modern facilities integrate the entire freshwater cycle - from spawning to smolts - in a single site, with tight biosecurity measures and constant surveillance for diseases of importance, including

[6] Carcasses are placed in iced bins and transported to the processing plant. Most regulatory agencies require that when sea site harvest occurs, blood and/or any fish parts are not released into the ocean.

filtration and disinfection of incoming water supply, restricted access to personnel and vehicles, and routine sampling for economically important diseases like infectious pancreatic necrosis (IPN), vibriosis and bacterial kidney disease (BKD), among others. Even in highly controlled systems, the broodstock can be an important source of infection so testing and culling of broodstock for relevant diseases like IPN and BKD is common practice (Gudmundsdottir, 2000; Pascho et al., 1991). Since most testing methods do not return immediate results, egg batches are separated and only groups from siblings with undetectable or very low levels of the agent are kept for hatching.

Most agents causing OIE listed salmon diseases such as infectious salmon anaemia and IHN can be present in both the freshwater and saltwater stages of the fish. Hence, although a compartment can be established for a hatchery, the open cage stages where broodstock are held must also be assessed and included in the compartment.

Depending on the disease, the open stages in lakes and oceans could also be defined as compartments, if the disease is not known to be present in wildlife populations and if proper biosecurity measures, and surveillance of both wild and farmed populations are in place. The following section will exemplify the evaluation of biosecurity measures in the different production stages of a typical salmon farm, using the HACCP framework.

Biosecurity assessment

Zagmutt (2001) used the HACCP framework to assess risk factors for the introduction and spread of IPN virus (IPNV) in salmon farms in Chile. Parts of this study are used to exemplify the use of the HACCP methodology to evaluate biosecurity measures.

The definition of the units of study and the evaluation of all the potential pathways for introduction and spread of diseases are two basic components to assess the on-farm biosecurity measures. Clearly defined pathways will greatly facilitate the identification and ranking of critical control points for disease introduction and spread, hence special care should be placed on this stage. Field visits are very helpful to identify pathways since the assessor can capture practices that may not be described in the company's management guidelines, or may be omitted by the experts consulted. For the following example, several field visits were performed on each production stage, and the pathways were reviewed and revised with experts.

- Units of study: the different units to be studied will depend on the specific management of the industry or particular company to be assessed, and the epidemiology and ecology of the disease of interest. For this example, the salmon farming cycle was divided in four stages based on current management and production units visited (weight ranges below for Atlantic salmon [*Salmo salar*] cycle):

    a. Hatchery: freshwater facility housing individuals from spawning to fry up to approximately 0.5 g
    b. Fry: in-land facility housing fry from 0.5 g to roughly 20 g.

c. Smolts: open-cage facilities housing fry from 20 g to smolts of approximately 100 g
d. Saltwater: open-cage facilities housing fish from smolt to harvest size (4.2-4.5 kg)

- Flow diagrams

Diagrams showing the pathways for potential introduction and spread of pathogens to and from the different stages provide a good way to conceptualize different risk sources. For simplicity, only pathways for the hatchery and saltwater stages are shown in Figures 2 and 3, respectively.

In Figure 2, "Eggs from outside supplier" come from outside sources, enter the facility, and then are placed in "Eggs with eye" tanks. Dead fry/eggs (mortality) from each population unit exit the facility as "carcasses". Some farm management is specific to certain populations of fish (i.e. disinfection of eggs) whereas other routine management like cleaning is applied to all populations in the farm (not shown in the figure).

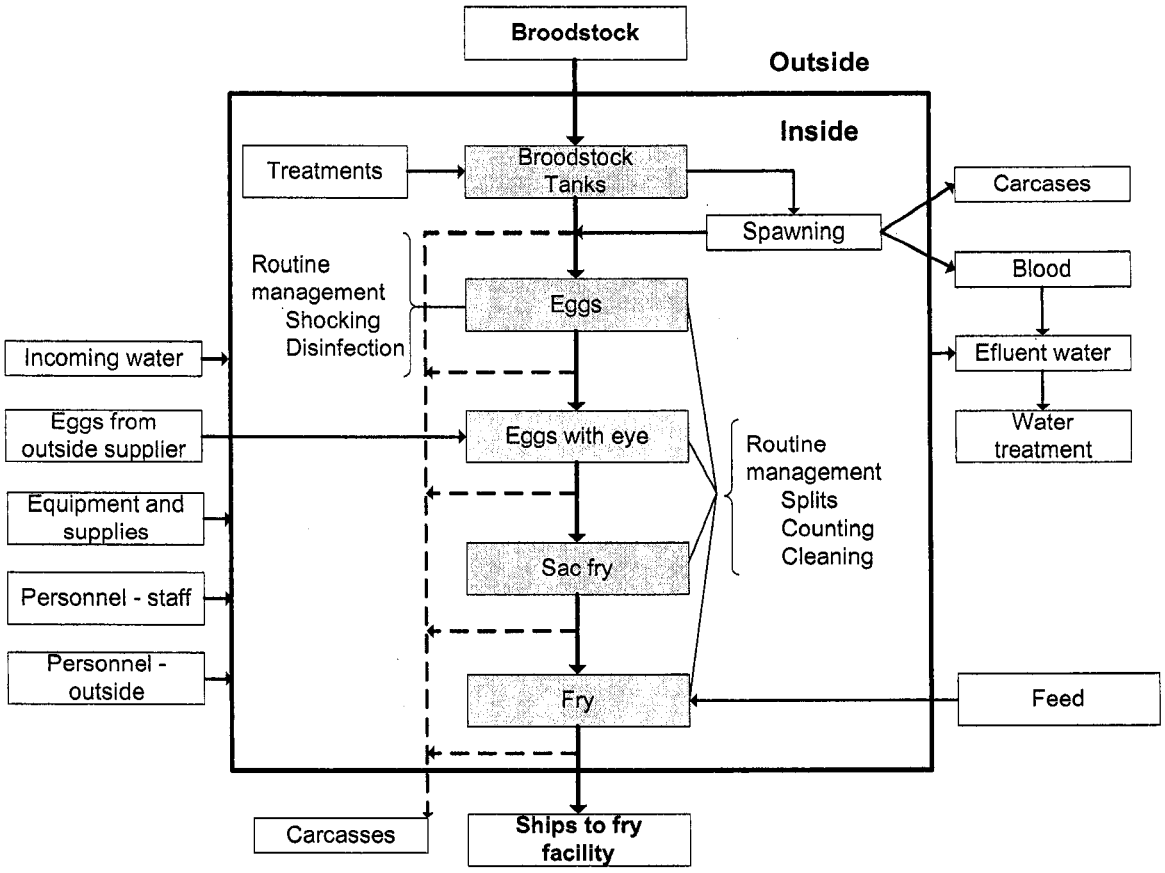

Figure 2: Pathways for potential introduction and spread of pathogens in the hatchery. The larger frame represents the farm. The population units are represented in grey boxes. Solid arrows indicate source and end of the event of interest, and discontinuous arrows indicate mortality removed from the system.

In Figure 3, the farming unit is not an enclosed facility, but instead is a group of floating pens situated in the ocean. Hence, the system is naturally permeable since it shares the same environment and water with other aquatic species like wild fish and sea birds that may carry disease-causing pathogens (Cusack, 1995; Menezes, 1992; NRM, 2007; Olivier and MacKinnon, 1998; Shaw and Opitz, 1996).

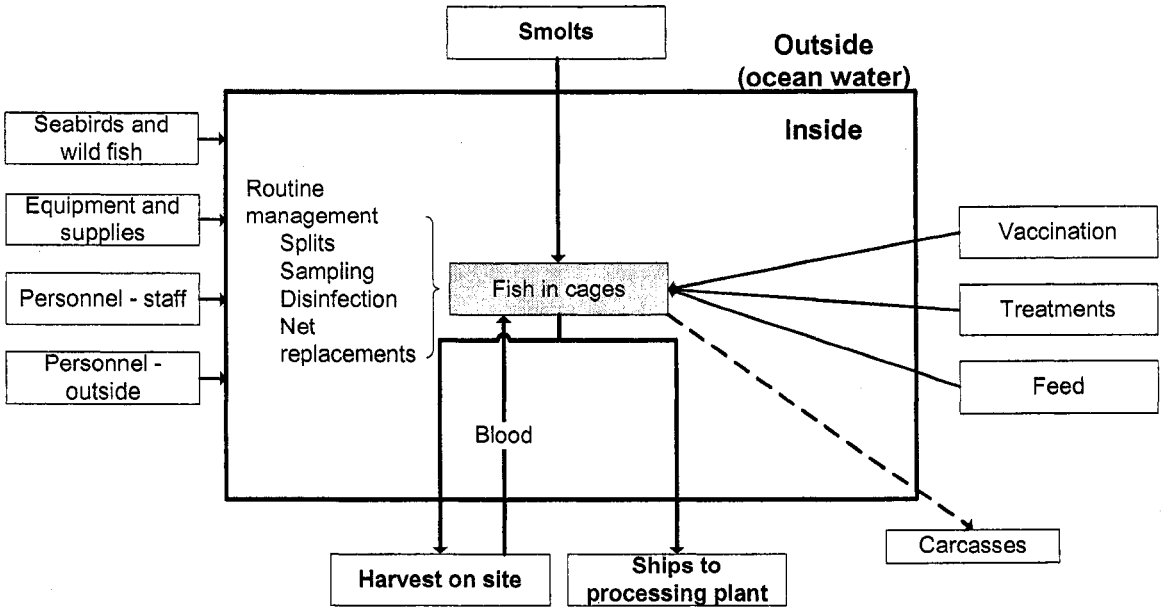

Figure 3: Pathways for potential introduction and spread of pathogens in the saltwater farm. The larger frame represents the sea site. The population units are represented in grey boxes. Solid arrows indicate source and end of event of interest, and discontinuous arrows indicate mortality removed from the system.

For compartmentalization purposes, special attention must be placed on events entering and exiting the farm or sea site, since those are potential risk factors for the introduction and spread of disease agents among farms. Also, the events with arrows inside the farm are potential risks for the spread of disease within the facility.

- Hazard analysis and critical control points

After performing field visits, expert consultation and reviewing the flowcharts, general critical control points for the introduction and spread of pathogens can be identified.

For the IPNV example, the general critical control points for viral introduction can be classified as Outside Genetic Material, Personnel, Water, and

Equipment and Supplies. Similarly, factors that may increase the risk of spread of the agent can be grouped as Routine Management, Personnel, Water, and Carcass Disposal.

Clearly, there are several options to asses in each risk group. For example, Outside Genetic Material can be imported or produced in the country, and genetic material can also come from the same company, or from another company.

Likewise, there may be different levels of risk depending on the water source and treatment. If a hatchery is supplied with UV-disinfected well water, the risk for introduction of infectious diseases will likely be smaller when compared to a hatchery with water supply from a river with native species that can harbour pathogens such as IPNV.

Given the wide variety of options and levels of risk, it is often impractical to measure the quantitative impact each risk has on the overall biosecurity of the farm. If risks can not be quantified, it may be possible to rank them or at least group them in broad categories like high, medium and low.

One popular option to rank risk factors is by eliciting expert opinion. For example, Horst et al. (1996) used experts to elicit different risk factors for the spread of contagious animal diseases, using Conjoint analysis. The methodology is based on the principle that a product or event can be evaluated as a composition or attributes (Fishbein, 1963). Hence, instead of asking the expert directly for a specific risk factor, the question presented is a

combination of factors and the expert is asked to rank the entire combination. This avoids the potential bias and extreme answers that can happen when a single option is presented (Green and Srinivasan, 1978).

In this example, a similar methodology was used to assess the relative importance of different risk factors and to evaluate the effectiveness of different biosecurity measures.

Table 1 shows the five risk factors the experts found most important for the introduction of disease into production facilities. Table 2 shows the five most important pre-emptive measures, as ranked by the experts.

Table 1. Ranked risk factors (first five) for the introduction of IPNV, based on expert opinion

Order	Risk
1	Culture in waters with high prevalence of IPN
2	Equipment and supplies from other centers, no disinfection
3	Personnel entering facilities without proper clothing
4	Personnel entering facilities with proper clothing, not obeying biosecurity measures
5	Imported eggs and/or smolts

Table 2. Ranked pre-emptive measure (first five) against the introduction of IPNV, based on expert opinion

Order	Pre-emptive measure
1	No access to visits or outside personnel
2	Properly disinfected equipment and supplies
3	New equipment and supplies
4	Domestically produced eggs and/or smolts
5	Personnel entering facilities with proper clothing, following biosecurity measures

The results from the expert elicitation can help identify critical control points where biosecurity should be focused, and which pre-emptive measures may adequately avoid the introduction of diseases into, and spread within, a compartment. Nonetheless, the identification of critical control points should not rely solely on expert advice, but should also be based on the available scientific evidence and, where possible, be underpinned with sound risk analysis methodologies.

Discussion

Increases in the variety and scale of global trade together with international travel movements have increased the difficulties faced by competent authorities in maintaining country and zone freedom status. Thus, the concept of on-farm biosecurity is becoming more acceptable to the agriculture and aquaculture sectors as there is growing awareness that on-farm biosecurity measures can provide another layer of assurance, complementing measures associated with country freedom and zone freedom and providing business security should country or zone measures be breached. It is also true that, in contrast to achieving country or zonal freedom, which depends on control measures imposed by regulatory agencies and is subject to availability of public funding, compartmentalization relies on establishing partnerships between the competent authority and the individuals managing the compartments.

With more aquaculture companies and individual farmers recognizing the benefits of seeking free compartment status, and with the costs and difficulties of proving country and zone freedom rising, it is likely that the

recognition of compartments will become the dominant form of disease freedom certification for international trade.

The successful establishment of a compartment will be very dependent on the characteristics of the production system. The concept naturally applies to closed systems like the oyster culture or salmon hatcheries described in this article, whereas it can be more challenging to implement in open systems like salmon farming in sea pens.

Several reasons may make the implementation of a compartment in open systems difficult. For example, some agents causing OIE-listed salmon diseases are present in both freshwater and saltwater stages of fish. Hence, a compartment for those diseases should not only include the hatchery but also the open cage stage. Open systems often share the same environment and water with other aquatic species like wild fish and sea birds that may carry disease-causing pathogens (Cusack, 1995; McVicar, 1998; Menezes, 1992; Olivier and MacKinnon, 1998; Shaw and Opitz, 1996), adding complexity to the establishment of the compartment. Nonetheless, if the disease is not present in wildlife populations and proper biosecurity measures and surveillance of both wild and farmed populations are in place, open stages in lakes and oceans could also be defined as compartments free of a particular disease.

Compartmentalization allows continuation of trade while providing the necessary assurances to avoid the spread of pathogens. Some argue that compartmentalization will be detrimental to competent authorities and

surveillance systems, the main criticism being that the majority of the resources will be directed towards highly integrated companies with export markets, while smaller operations and family production systems would be of secondary importance. Additionally, critics of the concept claim that compartmentalization will weaken the role of the competent authority by transferring too much authority and self certification responsibilities to the management of the compartment. Compartmentalization should be viewed as a tool to allow trade while a country reaches disease freedom. Under certain circumstances where disease eradication is not deemed possible, such as when there is a wildlife reservoir or the infection is transmitted by vectors, compartmentalization may be the only alternative. It is important to stress that the recognition of compartments by the competent authority of an importing country requires the direct involvement of the competent authority of the exporting country through providing certification of the health status of the compartments and certifying the particular commodity to be exported. Additionally, surveillance within and outside the compartment is mandatory to confirm disease freedom within the compartment and to understand the epidemiologic situation surrounding the compartment and thus, enable the adoption of appropriate safeguards to prevent the introduction of the infection.

Biosecurity is one of the critical components of compartmentalization. Although data are available to estimate the risk of spread of some diseases from the movement of processed fish (LaPatra et al., 2001), more studies are needed to integrate such data into biosecurity assessments, particularly when establishing compartments in endemic areas.

The feasibility of application of compartmentalization is largely dependent of the system of production and the epidemiology of the disease(s) for which the compartment is being defined. Therefore, the concept may not be universally applicable across all systems and diseases.

Compartmentalization provides an opportunity to develop and maintain strong operational relationships between the management of the compartments and the competent authorities. International trade is largely based on trust. However, trust cannot be achieved without transparency in the certification procedures used to document the health status of the compartment.

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Chapter 9

Discussion

The objective of this dissertation was to highlight the areas of interaction between epidemiology and the development of veterinary public policy at the national and international level.

Highlights of findings

The World Trade Organization's (WTO) Agreement on the Application of Sanitary and Phytosanitary Measures (SPS Agreement) has increased the demands placed on official veterinary services worldwide. The focus of Chapters 2-4 was on the challenges that international agreements place on veterinary services, the development of international standards and the use of risk analysis internationally. Although significant progress has been achieved over the past decade in the utilization of epidemiology in shaping veterinary public policy, there are areas where further efforts are still needed. This provides veterinary epidemiologists with new challenges and opportunities for the future.

The implementation of the SPS Agreement has highlighted the weaknesses and strengths of veterinary services and has led animal health officials to re-engineer the means for veterinary services to operate and embrace new alternatives for disease management and the delivery of animal health systems.

To date, many countries are still facing problems in implementing the SPS agreement. To address this problem, the WTO in conjunction with the World Bank, the World Animal Health Organization (OIE), the World Health Organization (WHO), and the Food and Agriculture Organization (FAO) launched the Standards and Trade Development Facility (STDF) as a financing and coordinating mechanism for SPS-related technical assistance and capacity building projects. The STDF medium term strategy, which will run from 2007 to 2011, places greater emphasis on acting as a mechanism for coordination in the provision of sanitary and phytosanitary technical cooperation (WTO, 2007). The STDF will fund projects and also serve as a link between the international donor community and recipient countries.

In support of the above initiative, and recognizing the difficulties in compliance that many countries still face, the United States Department of Agriculture's (USDA) Animal and Plant Health Inspection Service (APHIS) International Services (IS) recently launched the International Regulatory Capacity Building (ITRCB) program to coordinate the provision of scientific, technical and regulatory training provided by APHIS internationally (Hoffman, 2007). Similarly, USDA's Foreign Agricultural Service (FAS) under its Developmental Resources Division has established an initiative to promote

agricultural health and food safety seeking to enhance international trade and promote the development and improvement of food-safety systems in cooperating countries (FAS, 2007).

There is a need to develop mechanisms by which trained epidemiologists can provide their input in the development of regulations and policy. The OIE has taken steps in this direction and established the ad hoc group on epidemiology that has met regularly since 2003 and has contributed to the development of several chapters and guidelines included in the OIE Code. At the national level, many countries have established links with academia to seek the expertise required. The USDA-APHIS-VS Centers for Epidemiology and Animal Health (CEAH), in their capacity as an OIE collaborating center, have provided training in basic epidemiology for official veterinarians internationally. To date, over 400 participants from around the world have received this type of training. However, even though short courses provide basic tools and contribute to the development of awareness about the use of epidemiology in disease control programs, there is still a need to increase the number of epidemiologists trained at the post-graduate level. To date, several institutions around the world offer training in epidemiology at the Master of Science level or above. Official veterinarians in many developing countries face two important problems in order to obtain a degree in epidemiology: finding a funding source and the lack of guarantees to keep their position when they return. An alternative to solve the second problem is to conduct on-the-job training using a system of modules in which students perform course work for a period of one to two weeks and go back to their positions with homework and projects to develop. The Organismo Internacional

Regional de Sanidad Agropecuaria in Central America has conducted a post-graduate course on SPS measures for officials working in the animal and plant health areas in their respective countries (WTO, 2004).

The survey of OIE member countries in relation to the use of risk analysis showed that training in this topic is still needed. There are few available options in the field of animal health where such training can be obtained, in particular for the application of quantitative methods. The survey indicated that there is a continuing expectation that the OIE through its collaborating centers should help countries acquire this expertise. Once again, CEAH, as well as other institutions in Europe and elsewhere, have been active in providing such training internationally.

Chapters 5 and 6 focus on the use of risk assessment methods to assess the probability of transmission of pathogenic agents through the movement of live animals and products. Several approaches to calculate the probability of moving infected and undetected animals were developed. One of the main constraints to applying these approaches is the difficulty in obtaining good estimates of the sensitivity and specificity of diagnostic tests. In particular, it is difficult to obtain precise sensitivity estimates as the laboratory conditions required to conduct this type of studies limit the number of experimental animals used. This leads to wide confidence intervals associated with these estimates. Additional efforts are required to generate valid sensitivity and specificity estimates for OIE prescribed tests. The OIE through its Biological Standards Commission should endeavor to achieve this goal.

In addition, for certain selected diseases, the study reviewed the OIE recommendations for the importation of live animals. The approaches developed cover all potential situations contemplated in the OIE Code. Chapter 5 provides constructive criticism to some OIE standards, particularly in the cases where the OIE Code recommends applying the same test twice during a specified quarantine period. The expected correlation of test results limits the usefulness of this approach; a greater gain in sensitivity would be accomplished by using biologically independent tests. Some OIE Code recommendations already consider this; however, for some diseases, this is not the case. This issue has been brought to the attention of the OIE ad hoc group on epidemiology and hopefully will lead to revision of these recommendations.

Chapter 6 demonstrates the use of quantitative risk assessment using low pathogenicity avian influenza virus (LPAIV) in poultry meat as an example. Despite the fact that the OIE Code (OIE, 2007) does not recommend applying any restrictions for trade of poultry meat from LPAIV affected countries, many importing countries use LPAIV as a barrier to trade in poultry meat.

The absence of LPAIV in poultry meat cannot be demonstrated in absolute terms. The results of experimental studies with negative findings do not necessarily mean that the event of interest cannot occur. The scientific method cannot prove a negative. In the context of risk analysis, this situation poses particular problems as conventional approaches yield estimates that do not agree with expert opinion. Chapter 7 addresses some of these issues

and explores approaches to derive estimates that include expert opinion and experimental findings under a Bayesian framework.

Finally, Chapter 8 explores the application of compartmentalization to aquaculture production systems. Compartmentalization is a new concept to manage diseases for the purpose of international trade. It is hoped that the process outlined in Chapter 8 along with the guidelines for the application of compartmentalization in the Terrestrial Code will serve as the basis for equivalent guidelines in the Aquatic Code of the OIE.

Final comments

Epidemiology constitutes the core for the development of scientifically based veterinary public policy. It must be recognized, however, that the decision-making process is also influenced by economic and political considerations that cannot be ignored. Since the inception of the SPS agreement, significant progress has been seen in the way that many countries adopt animal health decisions. Nonetheless, several countries still operate under a policy of near zero or zero risk, which of course is unattainable.

It is worth recalling that the objective of the SPS agreement is to avoid the use of sanitary measures as unjustified barriers to trade. Many trade agreements have strived to eliminate or reduce quotas and tariffs for agricultural products. In practice, this has meant that SPS measures are the only legally valid way to restrict trade. Many producer groups, seeking an

economic advantage, exert considerable pressure on official veterinary services to use artificial sanitary arguments to limit or prohibit trade.

Countries have the sovereign right to develop policies to protect their producer groups and consumers. Veterinary public policy is both a science and an art (Schnurrenberger et al. 1987). It is the responsibility of veterinarians in public service to contribute to these policies by providing the scientific input in a useful and timely way. Decision-makers should find the optimal balance between science and politics. However, their credibility hinges on the application of transparent scientific principles.

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