Rev. sci. tech. Off. int. Epiz., 2006, **25** (3), 937-950

Risk assessment and surveillance for bovine spongiform encephalopathy

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Submitted for publication: 24 January 2006
Accepted for publication: 13 October 2006

Summary
The national risk of bovine spongiform encephalopathy (BSE) has not been assessed by many countries, and many countries are conducting little or no BSE surveillance. National measures implemented, including import restrictions, surveillance systems, and sanitary controls, should be based on actual BSE risk. Thus, as a first step, the national BSE status must be determined, particularly through assessment of the national risk. The World Organisation for Animal Health (OIE) provides recommendations for surveillance and risk assessment of BSE, which are considered the international standard by the World Trade Organization (WTO). This document describes the variables for determination of BSE status and gives guidance on specific options and practical considerations for meeting the BSE surveillance and risk assessment recommendations of the OIE.

Keywords
Bovine spongiform encephalopathy – Cattle – Risk assessment – Surveillance – Transmissible spongiform encephalopathy.

Introduction

The detection of bovine spongiform encephalopathy (BSE) in cattle in North America (1, 10, 29) has again highlighted the global nature of the disease and the ongoing need for all countries to proactively undertake risk assessments, to develop appropriate, cost-effective surveillance systems, and to institute preventive measures. Such approaches are justifiable, even before detection of a BSE case in a country, in order to achieve the goals of BSE control and reduction of the human exposure risk.

International recommendations are available to guide countries in assessing national BSE risk (40, 42, 43), establishing their national BSE status (40) and developing appropriate surveillance systems (44), as well as in managing trade-related risks associated with the presence of the BSE agent in cattle (40). The Agreement on the Application of Sanitary and Phytosanitary (SPS) Measures of the World Trade Organization (WTO) designates the World Organisation for Animal Health (OIE) as the standard-setting body for issues of animal health and zoonoses (45), therefore the OIE *Terrestrial Animal Health Code* (referred to here as the *Terrestrial Code*) is considered the international standard for these issues.

According to the *Terrestrial Code*, a scientifically based national assessment of domestic BSE risk is the required first step in determining the BSE risk status of the cattle population of a country and in subsequently applying measures for trade, as well as in developing an appropriate, efficient surveillance system (44). The WTO SPS agreement also directly includes a similar statement (45). However, the majority of countries worldwide have not conducted an assessment of their national BSE risk.

In order to guide countries in the process of assessing their BSE risk and developing and implementing a reasonable, cost-effective BSE surveillance system, this document presents and discusses the various options and

considerations. Measures for control and prevention of BSE are not discussed. In addition, aspects of risk communication are outside the scope of this document and are presented elsewhere (25).

Bovine spongiform encephalopathy status of countries

Since the emergence of BSE in the world, many countries have recognised the need to know their own BSE status as well as that of their trading partners. Classification is important so that countries can:

– implement appropriate measures domestically, including an appropriate level of surveillance, and

– judge the risk of trade, and adequately implement import conditions to prevent introduction of the BSE agent.

Many countries worldwide have claimed to be 'BSE-free' based entirely on the fact that no BSE cases have been reported. However, reporting of cases is affected by many national variables, including quality of veterinary services, veterinary diagnostic infrastructure, and national disease awareness, as well as political and economic influences. Therefore, presence or absence of reported cases alone cannot be considered as a sufficiently objective criterion for classification.

Consequently, the recommendations given in the *Terrestrial Code* for determining the BSE risk status of the cattle population of a country are not based on reported disease, but on the outcome of a national BSE risk assessment (41). In addition, other national factors such as disease awareness programmes, the system of notification and investigation of BSE cases, the implementation of a risk-based surveillance system, and available laboratory competence should be considered.

After evaluation of all these factors, countries, zones or compartments can be classified according to the BSE risk status of the cattle population. Prior to 2005, the OIE classified countries into five BSE categories: free, provisionally free, minimal risk, moderate risk, and high risk. The OIE resolved to publish a list of BSE-free and provisionally free countries and has published protocols for country classification based on this system. To date, only a few countries have submitted any data to the OIE and are listed by the OIE as being free or provisionally free from BSE (41). These countries will maintain their current status until May 2008, when they will be reassessed according to the *Terrestrial Code* standard valid at that time.

In 2005, the former five-category system was modified into the current system of three categories: negligible risk, controlled risk, and undetermined BSE risk (40). All future country applications will be assessed and designated as belonging to one of these three categories.

Risk assessment

General principles of risk assessment methodology are available from the OIE (43); they allow the outcome of the assessment to be useful for international trade as well as for decision-making at the country level. In general, risk assessments should be:

– science-based, in accordance with current knowledge about the disease;

– transparent, open, rational, and easily understood by decision-makers;

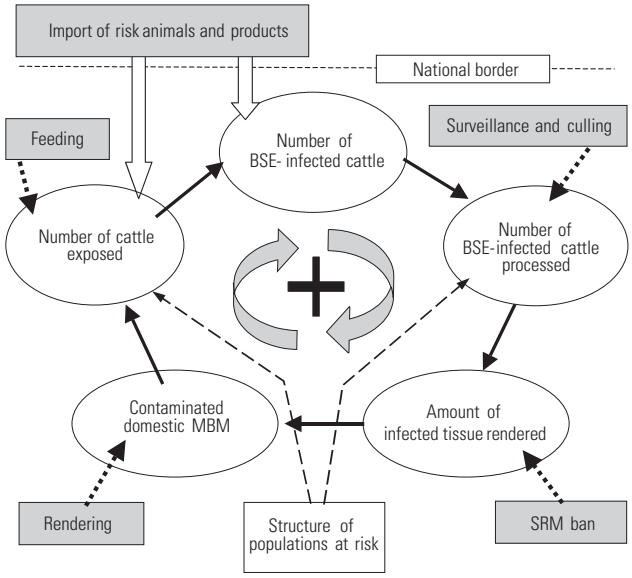
– objective and consistent, so that valid comparisons of risk can be made among countries;

– well-documented and supported by published literature, surveillance data, and expert opinion. Assumptions used in the risk assessment should be fully described and uncertainty in input data captured or described.

Additional specific technical details of performing risk analyses and assessments are widely available elsewhere (7, 27, 38).

The validity of a risk assessment is critically dependent on the availability, quality and quantity of input data. Data should be validated whenever possible. Data from national BSE surveillance systems should be included if available, although initially the risk assessment might have to be performed in the absence of these data. Consequently, national risk assessments should be updated iteratively not only as surveillance data becomes available but also as the risk in other countries is acknowledged.

An OIE-based national BSE risk assessment estimates only the risk of BSE being present in the cattle population of a country, and not the likelihood of exposure of humans. In order to clearly identify and assess BSE risks related to exposure of cattle, the concept of amplification of the BSE agent within the cattle population must be understood. Amplification can be described as a feedback loop in which by-product material from the slaughter of infected cattle is recycled back into the cattle population through feed containing infective agent, which results in exposure of additional cattle. In Figure 1, this loop is presented with the grey areas and dotted lines indicating points where control measures to reduce risk may be applied. The



MBM: meat-and-bone meal
SRM: specified risk materials

Fig. 1
Introduction and transmission of bovine spongiform encephalopathy (BSE) infectivity through the cattle system: the model used by the Scientific Steering Committee of the European Commission for the Geographic BSE-Risk Assessment
(Modified from 33)

structure of the populations at risk also influences the feedback loop, although it does not generally represent a point of control. To estimate the risk, the assessment should involve both a release assessment and an exposure assessment.

Bovine spongiform encephalopathy risk assessment: OIE guidelines

There is currently no standard BSE risk assessment protocol used consistently throughout the world, though specific factors to be considered in the risk assessment for BSE are given in the *Terrestrial Code*. They are mentioned generally in the chapter on BSE (40) and are presented in more detail as an Appendix with specific formal guidelines (42). To evaluate the risk, the OIE recommends that the following factors be considered.

Release assessment

Because the OIE guidelines assume that the BSE agent enters countries through the import of commodities contaminated with the BSE agent, the release assessment evaluates the likelihood that the BSE agent has been introduced via the importation of potentially infected live animals, meat-and-bone meal (MBM), greaves, feed potentially contaminated with MBM or greaves, and other potentially contaminated products of ruminant origin. It is assumed that countries importing these products from BSE-affected countries are more likely to experience BSE than those that do not.

For MBM and greaves or feed potentially contaminated with them (subsequently called MBM), the guidelines suggest that comprehensive data on origin, volume, composition (including initial processing data), and end-use of the imported materials should be considered. For live animals, import risk is related to the country of origin and the animals imported. Therefore, the guidelines suggest that comprehensive data on the date of import, country of origin, and volume of imports as well as the species, use, and fate of the imported animals should be considered.

In the OIE guidelines, the same general considerations apply to imports of products of animal origin, however, data should also be included on the species of origin of the imported product. It should be determined whether tissues known to contain the BSE agent are included, as well as the end-use and methods of disposal of waste associated with the products. Imported products of animal origin that, according to the *Terrestrial Code*, present negligible risk do not need to be included in the risk assessment.

Exposure assessment

The exposure assessment evaluates the likelihood of exposure of domestic cattle to the BSE agent, through consideration of domestic factors such as the probability of recycling and amplifying the agent. Specifically, the exposure assessment evaluates the ability of the domestic cattle production system to mitigate amplification of the BSE agent if it were to be released. If the system effectively eliminates or decreases any BSE infectivity release exposure will be limited. Otherwise, spread and amplification of the BSE agent within the country over time is more likely. Because it is assumed that BSE is transmitted to cattle primarily by the ingestion of MBM of ruminant origin, ultimately it must be determined whether ruminant-origin MBM is being or has been fed to cattle.

Because specified risk materials (SRM: those tissues/organs known to contain the highest BSE infectivity) and bovine fallen stock as well as slaughterhouse waste (animal by-products) may end up in the rendering system and thus be fed to cattle, the handling of animal by-products and the production of livestock feeds should also be considered. Specified risk materials are defined slightly differently

depending on the country, but generally include the skull, brain, spinal cord, vertebral column (including dorsal root ganglia), distal ileum, eyes, and tonsils from cattle of specific age categories.

The guidelines also assume that properly rendered material (at the standard treatment of 133ºC at 3 bars of pressure for 20 minutes) (36) can retain some transmissible spongiform encephalopathy (TSE) infectivity, and that there is a possibility of cross-contamination if MBM is used in any animal feeds. Therefore, comprehensive data on the ability to avoid or exclude the ultimate feeding of ruminant proteins to cattle, to largely inactivate BSE infectivity, and to remove/exclude bovine SRM from rendering should be considered. Data considered should include the fate of fallen stock and animal by-products, the definition and fate of SRM, the rendering system (including rendering parameters), general information on the production and composition of cattle feeds, particularly the use made of MBM, and methods used to control cross-contamination. The assessment should also consider the monitoring and enforcement of all of these factors.

In addition, the assessment should consider how the risk of exposure could be affected by the BSE surveillance system (e.g. active targeted vs. passive, regulations, scope, duration, and any data generated) and the presence of awareness programmes to improve compliance.

The Veterinary Services of countries are expected to perform these assessments and submit them to the OIE with all relevant supporting data. The assessments are then used as one aspect of determining the BSE status of the cattle population of a country, zone or compartment (40), as previously described.

Approach: qualitative versus quantitative assessments

Risk assessments can be qualitative (involving a subjective evaluation of the risks), quantitative (involving estimation of probabilities), or semi-quantitative (if elements of both approaches are used). The approach selected should depend on the scope of the question(s) being asked, the speed with which results are required in order to facilitate timely disease control decisions, the quality and quantity of input data, and other factors. Regardless of the approach, the objective should be to correctly assess the risk and obtain unbiased estimates of probabilities. The OIE does not make any recommendation as to whether BSE risk assessments should be qualitative or quantitative.

The mathematically sophisticated nature of quantitative assessments and the apparent simplicity of their numerical outputs can lend an air of accuracy and validity to the conclusions that might not be warranted (20). Therefore, results of quantitative predictions require careful and thoughtful interpretation. For BSE, the global problem of import data availability, quality, and validity must be considered by all countries in selecting their approach. This problem, combined with inconsistencies and uncertainties in export data from countries at risk (including from countries in Europe) affects the ability to make any quantitative assessment of BSE risk with valid outputs.

The OIE states that, for diseases where internationally agreed standards exist and risks are largely known, a qualitative assessment is sufficient (43). In addition, because qualitative assessments do not require advanced statistical modelling, they may be easier for many countries to perform. Considering these issues, as well as the problems with data availability and validity in BSE, it seems that qualitative approaches are probably more reasonable to apply.

Quantitative assessments

As of July 2006, only three countries have published quantitative assessments of their national BSE risk: Japan, Canada, and the United States of America (USA). These three assessment models have all been different.

In Japan, a mathematical model to assess the release risk for BSE was published after the first Japanese BSE cases were detected (35). The authors concluded that a certain risk existed. However, assessment of the exposure risk could not be completed due to missing information.

The assessment of Canada, conducted by the Canadian Food Inspection Agency (CFIA) was published in 2003 (26) and concluded that the likelihood of the introduction and establishment of BSE into Canada was negligible, just weeks prior to the reporting of a first case in that country in May 2003.

In 2001 the quantitative 'Harvard Risk Assessment' (6) for BSE was released, which concluded that BSE would be unlikely to become established in the USA. In a subsequent review of the assessment commissioned by the US Department of Agriculture, the Research Triangle Institute (30) reported weaknesses in the model, including that a '…lack of data to support assumptions… limits its predictive value.' In addition, the reviewers mentioned that the simulation type of model used is not adequately transparent for the structure of the model to be evaluated adequately, and they suggested that the quantitative model developed may have been too complex for the data available and the purposes intended.

Qualitative assessments

The European Commission (EC) adopted a qualitative approach for BSE risk assessment of countries based on OIE recommendations, called the Geographical BSE Risk Assessment (GBR). Currently, no other qualitative BSE risk assessment methodologies have been published. Because the GBR assessment has been the most widely applied BSE risk assessment, it is considered in detail in this document.

The EC's Scientific Steering Committee (SSC) began its work on the GBR in 1998. In July 2000, the methodology used and the first assessments of countries were published. The GBR is a standardised qualitative assessment and classification tool to allow comparison of country-level risk for BSE, i.e. the risk that one or more BSE-infected cattle are present in a country or a specified geographic region at the time of assessment. In countries already reporting BSE, the GBR gives an indication of the level of infection. The country to be assessed provides the relevant data, which are then validated and evaluated, initially by the SSC and currently by the European Food Safety Authority (EFSA) (18).

Using an objective set of criteria, the GBR then categorises countries into one of four levels of BSE risk according to the likelihood of the presence of one or more BSE-infected animals in the domestic cattle population:

– GBR I: highly unlikely

– GBR II: unlikely but not excluded

– GBR III: likely but not confirmed, or confirmed at a lower level (1 to 100 annual BSE cases per million adult cattle)

– GBR IV: confirmed at a higher level (greater than 100 annual BSE cases per million adult cattle).

The threshold of 100 cases per million cattle differentiating levels III and IV was set arbitrarily based on the OIE guidelines available at that time.

Because the GBR was developed based on the OIE guidelines for risk assessments (42), the OIE and GBR criteria are the same in principle. For example, the GBR also categorises variables as those relating to release assessment (called 'external challenge' in the GBR) and to exposure assessment (called 'stability' in the GBR).

The GBR considers the primary variable contributing to external challenge to be the import of live cattle and MBM from the United Kingdom (UK) and other BSE-infected countries (33). Initially, only exporting countries with reported BSE cases were considered, but since January 2002, all exports from GBR III countries have been included due to accumulating epidemiological evidence for a wider geographic distribution of the disease. Due to an overall lack of valid data, only live cattle and MBM imports are considered in the GBR assessment of external challenge. In the GBR, the external challenge is regarded as independent of the size and structure of the cattle system in the importing country.

When assessing the risk of recycling and amplification of the agent in the country, the factors considered in the GBR are very similar to the OIE guidelines for exposure assessment. However, the risk of cross-contamination is more strongly emphasised in the GBR assessment. The GBR assumes that as long as potentially BSE-contaminated MBM exists in the country and feeding of MBM to farmed animals is legally possible, cross-contamination of cattle feed with animal protein (therefore potentially BSE-contaminated ruminant protein) is difficult to exclude. Exclusion is even more difficult if only a ruminant-to-ruminant feed ban is implemented.

The GBR did not consider surveillance in the assessment until 2004, because national BSE surveillance systems were generally not effective enough to alter risk. Now, as in the OIE guidelines, surveillance data are being used as a variable in the GBR assessment, primarily as a tool for categorising a country after the initial assessment has been made. Once countries are effectively implementing a risk-based surveillance system (discussed below, i.e. they are relatively likely to find the disease if it is there), the resulting data may be used by the GBR to refine the assessment. For example, during the reassessment of Sweden and Norway in 2004, both countries were assessed to fall between GBR II and GBR III. Through evaluation of their surveillance systems and the data gathered, each country was finally designated as GBR II.

Whenever the required information is not complete, the GBR uses worst-case scenarios, which assume that country conditions allow the BSE agent to enter, be recycled, and/or be spread within the country.

The OIE recommendations cover countries, zones, or compartments, but available GBR assessments only address entire countries. If complete data sets were available for other defined geographical areas, the GBR would assess them in the same way.

In addition, the OIE guidelines suggest that the assessment be reviewed annually. The GBR should be theoretically reviewed when new countries at risk are detected. However, because the process is time consuming, updating and review have not been done regularly.

The most recent assessments (and reassessments) were published in June 2005 (Table I; 18), and included the categorisation of Canada, the USA, and Mexico as GBR III. Although only Canada and the USA have reported cases,

Table I
Categorisation of countries assessed by the Geographical BSE Risk Assessment (GBR) as of June 2006

GBR level	Countries
GBR I: highly unlikely	Argentina (I*), Australia (I), Iceland, New Caledonia, New Zealand (I), Panama (I), Paraguay (I), Singapore, Uruguay (I), Vanuatu
GBR II: unlikely but not excluded	Botswana (I), Brazil (I), Colombia, Costa Rica (II), El Salvador (I), India, Kenya, Mauritius, Namibia (I), Nicaragua (I), Nigeria, Norway (I), Pakistan, Sweden (II), Swaziland (I)
GBR III: likely but not confirmed or confirmed at a lower level	Albania, Andorra, Austria, Belarus, Belgium, Bulgaria, Chile (I), Croatia, Denmark, Canada (II), Cyprus, Czech Republic, Estonia, Finland, Former Yugoslav Republic of Macedonia, France, Germany, Greece, Hungary, Ireland, Israel, Italy, Latvia, Lithuania, Luxembourg, Malta, Mexico, Poland, the Netherlands, Romania, San Marino, Slovak Republic, Slovenia, South Africa, Spain, Switzerland, Turkey, United States of America (USA) (II)
GBR IV: confirmed at a higher level	United Kingdom, Portugal

Source: developed from the European Food Safety Authority Scientific Report on GBR Assessments (18)
* Countries reassessed as of 2004 have former GBR level in parentheses

the historically open system of trade in North America suggests that it is likely that BSE is present also in Mexico. Table I shows the classification of the 65 countries assessed by the GBR as of June 2006. The validity of the GBR assessment has been confirmed, as ten 'BSE-free' countries initially assessed as GBR III (i.e. likely but not confirmed) subsequently reported BSE cases (Table I).

Limitations of bovine spongiform encephalopathy risk assessments

Bovine spongiform encephalopathy (BSE) risk assessments rely heavily on the availability and validity of data, and all assessments must rely on the openness and transparency of the country being assessed. Many domestic and international sources of data are incomplete or unreliable, and therefore precise assessment is difficult. For example, import and export data may be inconsistent when the records of the trading partners are compared. Moreover, it might be possible that countries wishing to appear to have a low risk might provide incomplete or incorrect data. For these reasons, the GBR uses the worst-case scenario when data are incomplete or unreliable.

Similarly, the BSE status of trading partners, and therefore the risk of import, is often difficult to judge. Because many exporting countries have not been assessed, importing countries wishing to assess their national BSE risk have had to base their own exposure risk on incomplete data from the non-assessed countries exporting to them. For example, the assessment in an importing country will show a greater level of risk when a previously 'BSE-free' exporting country reports a first BSE case or conducts a risk assessment indicating that some risk is present. This situation will improve when all countries have conducted scientifically based national BSE risk assessments. National risk assessments should be updated iteratively; not only as initial or additional surveillance data become available, but also as the risk in other countries is acknowledged. Clearly, for rational trade decisions to be made based on BSE risk assessments, the risk of all countries worldwide must be evaluated.

Surveillance for bovine spongiform encephalopathy

According to the *Terrestrial Code* (44), surveillance systems for BSE can have one or more goals; depending on the risk category of a country, goals may include:

– to determine if BSE is present in the domestic cattle population

– to support a claimed BSE status or to (re)-gain a higher BSE status

– to monitor the level and progression of the disease (when present), which will aid in determining control measures and evaluating their effectiveness.

Effective and well-designed surveillance systems that meet OIE guidelines thus may potentially answer the following specific questions:

– Is BSE present in cattle and if yes what is its prevalence?

– If BSE has been present for several years, is the prevalence decreasing, unchanged or increasing? Changes must be interpreted in the context of implementation and enforcement of BSE control measures.

– How are BSE cases spatially distributed? Is there evidence of freedom in some regions of a country?

– Has the age distribution of BSE cases changed?

Considerations for planning a bovine spongiform encephalopathy surveillance system

For each country, the most important initial step in planning a BSE surveillance system is to clearly define a set of objectives. Because the BSE surveillance system implemented in a country should be based on the outcome of the national BSE risk assessment, the specific objectives, and consequently the scope and methodology, will vary considerably among different countries. In addition to the national risk, the overall infrastructure of the country must be considered when a national surveillance system is being designed. Some of the most important practical considerations, including possibilities for testing and data handling, are listed below.

General

– Is there adequate political will, including legislative support and the definition of a suspect animal, for the system to allow implementation and enforcement?

– Who will administer the programme?

– Is the veterinary infrastructure adequate to manage the surveillance system?

– Are all procedures adequately documented and are systems in place for auditing and control?

– What are the direct costs needed to run the system (including personnel considerations for sample collection, laboratory evaluation, data handling/analysis/evaluation, and public awareness campaigns), and are they properly allocated, and who will pay the costs?

Sample collection and shipment

– What are the specific procedures for sample collection?

– Who will collect samples for each category of animals to be tested? Are trained people available?

– How will the quality of the samples be assured?

– What are the specific procedures for sample packing (e.g. what type of containers are used for transport of samples) and shipping (e.g. refrigerated, overnight, courier, mail)?

– What can be done to ensure that samples reach a testing laboratory in the shortest time possible (ideally within 24 hours)?

– Will containers be labelled with an animal's identification or will the identification be included only on submitted paperwork?

Diagnostic testing

– Which test(s) will be used, in what order, how are the results confirmed and will the same testing scheme be used for all risk categories of cattle tested?

– Is there adequate laboratory capacity (space, equipment, trained personnel) in all regions of the country?

– Will there be a reference laboratory in the country for confirmation or will samples be shipped elsewhere, and if so, where, when and how?

– How will laboratories be accredited and validated (including confirmation of random negative samples using a reference test)?

Data, analysis and reporting

– What individual and herd-level data will be collected with each sample? Will there be a mechanism for validation of data?

– How and where will the data and test results be sent?

– How will the data be entered and what database will be used for storage? Who will be responsible and who will have access?

– What methods of analysis will be used and how frequently will analyses be done?

– What reports will be generated from the data, how often will they be done, and to whom will they be distributed?

Laboratory diagnostic testing

Laboratory tests are required in BSE surveillance systems because a diagnosis cannot be confirmed clinically (4). Usually, much of the routine screening using rapid tests for BSE can be performed in approved governmental and private diagnostic laboratories throughout a country. All testing must follow the recommended protocols in the OIE *Manual of Diagnostic Tests and Vaccines for Terrestrial Animals* (39). For confirmation of positive results from rapid screening tests, a reference laboratory should be available domestically or outside the country.

When certain rapid tests for BSE were evaluated using brain samples from clinically affected cattle, the tests showed a high sensitivity (11, 12, 17, 32). The diagnostic sensitivity of the tests might thus actually be lower within

the spectrum of field samples, which would be expected to include samples containing lower concentrations of BSE agent. The same evaluation studies also found that most of the available tests also have specificities > 99%. This is desirable given the low prevalence of BSE, because if test systems have specificities of < 99.9%, the predictive value of positive results will be only low to moderate. False BSE-positive results, especially if poorly communicated, could be economically disastrous to a country's local and export cattle markets.

The EC has conducted further evaluation trials and validated several rapid tests for post-mortem diagnosis of BSE (11, 12, 17, 19). These evaluations followed published recommendations for evaluation of diagnostic tests (21, 24), and thus the validated tests have met minimum performance standards of diagnostic sensitivity, diagnostic specificity, detection limits and reliability.

Other countries have independently validated and approved some of these tests. Final selection of the test(s) to be approved for use in a given country will depend on many factors including their cost, rapidity, ease of performance, possible laboratory throughput, and robustness when testing brain samples of varying quality (e.g. autolysed, contaminated with blood). Tests approved in specific countries are generally described on the website of the designated competent agricultural or veterinary authority in the country.

Types of surveillance systems for bovine spongiform encephalopathy: passive and active

Passive surveillance

Passive BSE surveillance depends entirely on the compulsory reporting of clinically suspect cattle by cattle owners, veterinarians, and others involved in handling animals and the follow-up of these animals by government Veterinary Services, including testing of brain samples for BSE. The term 'passive' refers to the reliance on notification to the appropriate authority by individuals in the field, thus the first requirement for a passive system is that BSE must be an officially 'notifiable' disease in the country. In addition to the general surveillance considerations given above, the following information must be determined and/or be considered in order for an effective passive system to be developed:

a) The knowledge level and disease awareness of cattle owners and veterinarians regarding BSE, including the ability to recognise clinical signs of BSE in cattle.

Underreporting often results from difficulties in identifying clinical BSE suspects, as the clinical signs are variable, often subtle, and not pathognomonic for BSE (4). It has been shown that cattle owners tend to be very aware of subtle changes in the health, production, and personalities of their animals, and are therefore the most able to detect the subtle early changes seen with BSE. Countries with a longer experience with BSE have better disease awareness, as is shown by the increased number of suspects reported (23).

b) The willingness of cattle owners and veterinarians to report suspected cases of BSE.

Mistrust as well as lack of knowledge about BSE and the correct procedures to be followed may result in underreporting (46). Motivation to report is lowest in countries that have not reported a first case. The extension of routine ante-mortem examinations at the slaughterhouse to include consideration of BSE can also improve identification and removal of clinical BSE cases before slaughter as well as improve compliance in reporting. If cattle owners are aware that the cattle will be carefully checked, they might be more wary of sending suspect animals to routine slaughter.

In addition, providing a clear description of compensation for suspected and/or confirmed cases and notification procedures, as well as assuring that consequences of reporting seem reasonable to cattle owners (e.g. herd culling, cohort culling) (22), can make the system more transparent, decrease mistrust, and ultimately lead to better compliance.

Optimisation of passive surveillance requires optimisation of all these considerations, especially the willingness to report.

Despite these constraints, most countries should be able to implement and enforce a passive system for BSE. When effectively implemented, passive surveillance allows the identification and removal of animals with clinical signs, and therefore animals with the highest infectivity, before they enter the food and feed chains.

The major advantage of a passive system is its low cost for each case detected. In Switzerland, approximately 40% of clinically suspect cases are later confirmed with BSE (9), and this percentage of positives is higher than for testing all other subpopulations of cattle.

The most important disadvantage is poor compliance and underreporting of potential cases. Also, low prevalence diseases that are not contagious and have incubation periods of many years, such as BSE, are difficult to capture in a passive reporting system (9). Moreover, because many factors affect the identification and reporting of clinical

suspects, the number of BSE cases identified using passive systems underestimates the true prevalence in the country. Therefore, comparison of passive BSE surveillance data among countries is inherently problematic (9).

Active surveillance

Many countries have opted to include active surveillance to complement the data from passive systems. The term 'active' refers to the systematic collection of data, and is essential for countries to obtain unbiased estimates of prevalence and to evaluate the effectiveness of national control strategies.

Different strategies for sampling in an active surveillance system include:

– risk-based sampling where the cattle population is categorised into high risk groups including fallen stock and emergency slaughter cattle (including non-ambulatory 'downer' cattle) and low risk groups (apparently healthy cattle at routine slaughter)

– population-based sampling without regard to risk grouping.

In a statistical context, when the prevalence (or risk) of BSE is low, a higher level of surveillance (e.g. a larger sample of the population) is required to detect it (31). Therefore, theoretically, a very large sample should be taken to detect cases in countries where the BSE risk assessment shows a very low level of risk. However, this would not be logical or practical for low-risk countries. The OIE recommendation that the BSE surveillance system implemented in a country should be commensurate with the outcome of the national BSE risk assessment (40) is generally taken to mean that in low-risk countries, a reasonable (low) level of surveillance can be implemented rather than a very high one. This concept is reflected in the *Terrestrial Code* chapter on BSE surveillance, adopted in May 2006 (44), which states that:

– when the risk assessment demonstrates non-negligible risk, the country should conduct surveillance which will allow the detection of BSE at a prevalence of at least one case per 100,000 in the adult cattle population

– when the risk assessment demonstrates negligible risk, the country should conduct surveillance which will allow the detection of BSE around a prevalence of at least one case per 50,000 in the adult cattle population.

In order to be able to compare surveillance systems among countries, the OIE guidelines assign a risk-based value for every tested sample based on the population and age of the animal sampled, i.e. the lowest value is given for routine slaughter cattle below two or above nine years of age; the highest value is given for clinical suspects between four and seven years of age. All the samples tested in a country are assigned points according to this guideline and then the points are added together to give a total. A given number of total points, based on the number of adult cattle in the country and the risk, must be reached within seven years.

This risk-based sampling protocol maximises the detection of BSE and decreases the cost of detection per BSE case, as more cases are likely to be detected for the same fixed testing cost. For BSE, the population with the highest number of positive results per number sampled is the population of clinical suspects. The second most appropriate population to target in order to detect BSE is the population of cattle which have died on farm or in transit, 'fallen stock', and stock sent for emergency slaughter (44), i.e. the population of cattle in the risk categories. Targeting this population is also economically more efficient than testing cattle at routine slaughter. This is shown in Table II, which compares the relative frequency of detection for BSE among clinical suspects, emergency slaughter cattle (as well as those identified with non-specific signs of disease on ante-mortem examination), cattle dead or killed on the farm, and cattle tested at routine slaughter. The table also shows the calculated costs of finding one positive in each population. In addition, targeting this population allows for a more sensitive evaluation of changes in prevalence. The number of risk animals is generally estimated to be approximately 2% of the total adult cattle population.

Within each of the aforementioned sampling options, it is possible to consider testing all or a subset of the population (5). However, sampling all animals in risk categories might exceed available resources, and the allocation of limited national resources to BSE testing in addition to testing for other important food-borne illnesses and production-

Table II
Frequencies and estimated costs in Euros (€) of detection of bovine spongiform encephalopathy (BSE) cases through testing of various populations of cattle in the European Union in 2004
(see text for definitions of cattle populations)

Cattle population	Number of tests	Number of BSE-positive animals	Frequency of positive animals	Cost per detected case (Euros) [a]
Clinical suspects	3,207	174	1/18	1,290
Emergency slaughter	329,332	208	1/1583	110,832
Dead or killed (on farm)	1,149,318	312	1/3684	257,859
Routine slaughter	9,551,469	166	1/57,539	4,000,000*

a) Assuming €70/sample tested)
*Approximately
Source: European Commission (16)

limiting diseases needs to be considered in all countries. In this case, the selection of animals for testing could be further refined. For example, in some countries dairy breeds might be sampled preferentially because in most production systems dairy cattle have a much higher probability of being exposed to feeds containing MBM than do beef cattle.

Although a few animals younger than 24 months have been identified with BSE, most positive cases have been older (13, 14, 15). Therefore, it is very unlikely that testing of cattle, especially routine slaughter cattle, younger than 24 months will identify positive cases. Most countries restrict active surveillance and testing of routine slaughter cattle to adult animals, i.e. those above 30 months, although some countries do test cattle > 24 months. Even without precise data on animal age, this age range can be easily estimated by examining the dentition, as the first set of permanent incisors erupts at approximately 20 months and the second set at approximately 30 months.

In addition, although BSE testing of cattle at routine slaughter is not an efficient way to identify cases, often it is done with the intent of minimising the diversion of BSE suspect animals to the slaughter plant. In some countries it might also have been used to generate large numbers of negative test results with the aim of boosting the justification for a more favourable BSE status. However, according to current OIE surveillance guidelines, only very low numbers of points can be achieved through testing of routine slaughter cattle (44).

As with a passive system, the following information (in addition to the general surveillance considerations given above) must be determined and/or considered in order for an effective active system to be developed:

a) number of adult cattle and herds, the annual number of cattle slaughtered or rendered by risk group and the geographic source of cattle exiting through each location

b) possible 'exit routes' for adult cattle and the number in each category

c) the number and location of slaughter plants and rendering plants selected for sample collection, the person responsible at each location, and the required training of sample collectors

d) disposal of fallen stock (e.g. proportion buried, rendered)

e) the location and detailed logistics of sampling (e.g. where on the slaughter line will sampling occur, the acquisition of sampling spoons and sample containers)

f) whether all high-risk animals and animals at routine slaughter will be tested, or if a random sample of these animals will be tested, and if it is the latter, the number of samples collected and the frequency of sampling

g) whether there is an effective system for individual animal identification that provides traceability from slaughter to the herd of origin, and a method of verification of identification.

Non-compliance is also a challenge in implementing active surveillance, especially in countries not having reported a first BSE case. Non-compliance is generally manifested as diversion of fallen stock to avoid identification and testing, e.g. by burying fallen stock on the farm.

Evaluation and updating of bovine spongiform encephalopathy surveillance systems

Surveillance systems require periodic evaluation to improve quality, cost-effectiveness, and determination of equivalence in the context of international trade. However, the adequacy and effectiveness of any surveillance system can only be evaluated if its goals are clearly defined. Evaluations should be objective, systematic and transparent and might involve the use of fault trees, scenario analysis and classification methods (34). In some cases, the goals of the surveillance system will have changed between evaluations; hence it is optimal to time the evaluations to coincide with iterations of the national BSE risk assessment so that the evaluation can be used to update the surveillance system appropriately.

In addition, the surveillance system should be described transparently and results made available to the international community using data that make evaluation possible. For example, reporting the total number of cattle tested at routine slaughter or fallen stock is not useful without a breakdown of number tested by age.

Examples of current national surveillance systems

Switzerland

In January 1999, Switzerland initiated an active, targeted surveillance scheme to enhance the detection of BSE cases in the adult cattle population (8). In addition to a passive system including the mandatory reporting and testing of all suspect clinical cases, all cattle in risk groups and that

have at least four permanent incisors (i.e. over 30 months) are tested. Additionally, approximately 3% of the total number of adult cattle sent to routine slaughter are randomly sampled and tested, to minimise diversion of suspected BSE cases to routine slaughter. The increase in BSE cases detected after implementation of targeted surveillance in Switzerland was the first indication of the importance of this methodology.

European Union

In January 2001, the EU introduced active screening of cattle for BSE, in which the entire risk population (i.e. all cattle that have died or been killed on farm or during transport, fallen stock, and cattle sent to emergency/sick slaughter) over 24 months of age are tested. Additionally, all cattle subject to routine slaughter over 30 months of age (in some countries also younger animals) are tested. Through this programme, the number of detected cases in the EU increased.

Japan

Systematic BSE testing was initiated in Japan after the first BSE case was detected in 2001. In addition to testing the risk population, until recently the Japanese system also included testing of all routine slaughter cattle of all ages. This testing was implemented as a consumer confidence measure, and was therefore not directly related to surveillance for the disease.

Canada and the United States of America

Before the first cases were identified, Canada and the USA initiated testing of a proportion of the national cattle populations. Canada tested primarily animals from the risk groups (1). In 2004, the USA initiated increased surveillance of the risk population for a 12 to 18 month period (3, 37).

New Zealand and Australia

The BSE surveillance systems in New Zealand (28) and Australia (2) are primarily passive with a small number of animals tested through active surveillance.

Conclusions and recommendations

Although undertaking a national risk assessment for BSE requires substantial political will and human resources, it is crucial not only for meeting requirements for international trade but also for understanding the domestic situation as regards BSE, animal health, and food safety. By expending resources on a comprehensive, valid risk assessment, countries with negligible risk can also justify implementing a lower level of surveillance.

In undertaking risk assessments, countries must acknowledge the national benefits of evaluating the domestic risk honestly and accurately, so that the data included are as valid and complete as possible and the results are useful for decision-makers. Quantitative assessments are not necessarily more useful than qualitative assessments, although they require substantially more effort. It is also important that risk assessments be reviewed externally.

Implementation and enforcement of any level of BSE surveillance requires substantial financial and human resources. There has been some criticism for spending resources on BSE surveillance that could be spent on zoonotic diseases with higher morbidity, and the level of surveillance required for countries assessed as having a negligible risk is discussable. However, for most countries, implementing targeted surveillance at a minimal level based on the national risk is important in terms of estimating the baseline prevalence, with the goal of minimising risks to animal and public health. Consideration of the lessons learned during the early years of the outbreak in Europe can allow other countries to develop and initiate more cost-effective surveillance for BSE initially, and implement only those specific aspects into national surveillance systems that are important as determined by the national risk assessment.

Appréciation du risque et surveillance de l'encéphalopathie spongiforme bovine

D. Heim, I. Gardner, E. Mumford & U. Kihm

Résumé
Le risque national d'encéphalopathie spongiforme bovine (ESB) n'a pas été évalué par nombre de pays, et nombreux sont ceux qui ne pratiquent qu'une surveillance sommaire de l'ESB, ou même qui s'en abstiennent totalement. Les mesures nationales mises en œuvre, notamment les restrictions à l'importation, les systèmes de surveillance et les contrôles sanitaires doivent reposer sur le risque réel d'ESB. Ainsi, la première étape consiste à déterminer le statut national au regard de l'ESB, en particulier grâce à une appréciation du risque national. L'Organisation mondiale de la santé animale (OIE) formule des recommandations pour la surveillance et l'appréciation du risque d'ESB, qui sont considérées comme les critères internationaux par l'Organisation mondiale du commerce (OMC). Le présent document décrit les variables utilisées pour la détermination du statut au regard de l'ESB et fournit une orientation sur les options spécifiques et les considérations d'ordre pratique permettant de se conformer aux recommandations relatives à la surveillance et à l'appréciation du risque d'ESB formulées par l'OIE.

Mots-clés
Appréciation du risque – Bovin – Encéphalopathie spongiforme bovine – Encéphalopathie spongiforme transmissible – Surveillance.

Determinación del riesgo y vigilancia de la encefalopatía espongiforme bovina

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Resumen
Hay muchos países que aún no han determinado el riesgo de encefalopatía espongiforme bovina (EEB) en su territorio y en los que la vigilancia de esa enfermedad es escasa, a veces inexistente. Las medidas que aplique cada país, entre ellas las restricciones a la importación, los sistemas de vigilancia y los controles sanitarios, deberían depender del riesgo real de EEB. Por ello el primer paso debe ser el de determinar la situación del país al respecto, concretamente a través de un proceso nacional de determinación del riesgo. La Organización Mundial de Sanidad Animal (OIE) formula recomendaciones en materia de vigilancia y determinación del riesgo de EEB, que la Organización Mundial del Comercio (OMC) considera preceptivas en el plano internacional. Los autores describen las variables que entran en juego al determinar la situación de un país con respecto a la EEB y ofrecen pautas sobre opciones concretas y consideraciones prácticas para cumplir las recomendaciones de la OIE en la materia.

Palabras clave
Bovino – Determinación del riesgo – Encefalopatía espongiforme bovina – Encefalopatía espongiforme transmisible – Vigilancia.

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