CAPACITY BUILDING FOR SURVEILLANCE
AND PREVENTION OF BSE AND OTHER ZOONOTIC DISEASES

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course manual

# MANAGEMENT OF TRANSMISSIBLE SPONGIFORM ENCEPHALOPATHIES IN MEAT PRODUCTION

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AND PREVENTION OF BSE AND OTHER ZOONOTIC DISEASES

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# MANAGEMENT OF TRANSMISSIBLE SPONGIFORM ENCEPHALOPATHIES IN MEAT PRODUCTION

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# FOREWORD

To support countries with economies in transition and developing countries in the control and prevention of bovine spongiform encephalopathy (BSE), the project *Capacity Building for Surveillance and Prevention of BSE and Other Zoonotic Diseases*, is the result of collaboration between the Food and Agriculture Organization of the United Nations (FAO), Safe Food Solutions Inc. (SAFOSO, Switzerland) and national veterinary offices in partner countries, and funded by the Government of Switzerland.

The aim of the project is to build capacity, establish preventive measures and analyse risks for BSE. Partner countries are thus enabled to decrease their BSE risk to an acceptable level or demonstrate that their BSE risk is negligible, and thereby facilitate regional and international trade under the Agreement on the Application of Sanitary and Phytosanitary Measures (SPS Agreement) of the World Trade Organization (WTO). A brief project summary is included as an appendix to this course manual.

Activities of the project:

- The specific needs of partner countries are assessed.
- Four comprehensive courses to "train the trainers" are provided to selected participants to improve understanding of the epidemiology of and relevant risk factors for BSE and transmissible spongiform encephalopathy (TSE) and to develop specific knowledge and skills for implementing appropriate controls.
- In a third step, in-country courses are held by trained national personnel in the local language and are supported by an expert trainer.

FAO has the mandate to raise levels of nutrition and standards of living, to improve agricultural productivity and the livelihoods of rural populations. Surveillance and control of diseases of veterinary public health importance are contributions to this objective. SAFOSO, a private consulting firm based in Switzerland, is providing the technical expertise for this project.

This manual is a supplement to the training course *Management of transmissible spongiform encephalopathies in meat production*, which is given within the framework of the project. This practical course is targeted at governmental and industry personnel who will contribute to the development and implementation of the national BSE surveillance and control programme, and to the BSE risk assessment for the partner countries.

The information included in the manual is not intended to be complete or to stand on its own. For further reading, specific references are included at the end of the chapters. General background material and Web links, and a glossary of terms and frequently used acronyms, are included as appendices.

The preparation of this manual was a collaborative effort of the trainers of the *Management of transmissible spongiform encephalopathies in meat production* course offered in Switzerland and the project staff. The content of the manual reflects the expertise and experience of these individuals. FAO and SAFOSO are grateful to the professionals preparing the manual and to the Government of Switzerland for funding this public–private partnership project in support of safer animal production and trade..

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# COURSE OBJECTIVES

Upon completion of the lectures and exercises of the course on *Management of transmissible spongiform encephalopathies in meat production*, of the project *Capacity Building for Surveillance and Prevention of BSE and Other Zoonotic Diseases,* the participants should:

- understand basic principles of management in meat production, brain sampling and pathogen control for animal diseases in general and BSE and TSEs in particular;
- be able to apply the acquired knowledge practically in their daily job activities
- be able to transfer this knowledge effectively to others

Specifically, these principles include:

- basic information on BSE and TSEs, including transmission, pathogenesis, risk factors and epidemiology;
- international and national regulations in meat production, including guidelines for the use of animal by-products;
- knowledge of critical factors for BSE and TSE control at each step in the production chain, including at the farm, slaughterhouse and processing plant levels
- quality control and SRM control measures at each production step;
- meat inspection, assessment of meat production plants and HACCP principles, including oversight in implementation of BSE control measures;
- categorization of animal by-products and the risks of animal by-products in animal feed;
- collecting samples for BSE testing of slaughtered animals, including the appropriate technical skills.

# INTRODUCTION TO TRANSMISSIBLE SPONGIFORM ENCEPHALOPATHIES

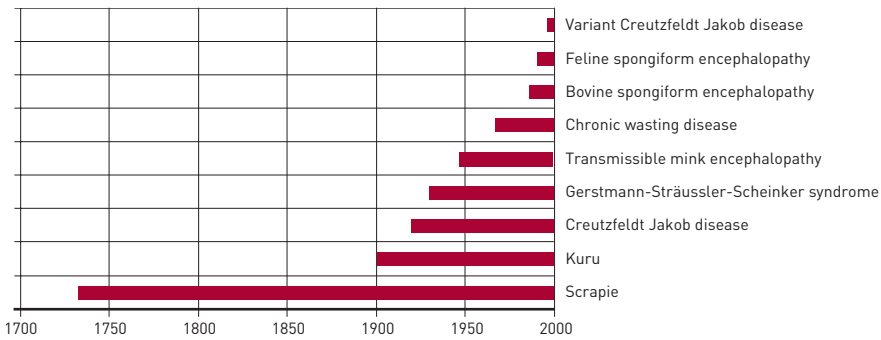
## 1. TRANSMISSIBLE SPONGIFORM ENCEPHALOPATHIES

Transmissible spongiform encephalopathies (TSE) are a class of neurodegenerative diseases of humans and animals characterized by spongiform degeneration of the brain and the associated neurological signs. TSEs are slowly developing and uniformly fatal.

Diseases include kuru, Gerstmann-Sträussler-Scheinker syndrome and Creutzfeldt-Jakob disease (all in humans), scrapie (in sheep and goats), feline spongiform encephalopathy (FSE; in cats), bovine spongiform encephalopathy (BSE; in cattle), chronic wasting disease (CWD; in cervids) and transmissible mink encephalopathy (TME; in mink). Most of these TSEs had already been reported before the first detection of BSE (Figure 1) (Lasmezas, 2003).

FIGURE 1

**Year in which the various TSEs were first reported**




The TSE with the longest history is scrapie, which was recognized as a disease of sheep in Great Britain and other countries of western Europe more than 250 years ago (Detwiler and Baylis, 2003). Scrapie has been reported in most sheep-raising countries throughout the world with few notable exceptions (e.g. Australia, New Zealand).

Transmissible mink encephalopathy (TME) was first described in 1947. It is a rare disease of farmed mink and has been recorded in countries including the United States of America (USA), Canada, Finland, Germany and the Russian Federation. Contaminated feed is suspected to be the main source of TME infection.

Chronic wasting disease (CWD) in captive and free-roaming North American deer and elk was first described in the 1960s. Initially, cases were only reported in captive deer and elk in Colorado (USA), but CWD in captive and/or free roaming deer, elk and moose has now been reported in several other states in the USA and in areas of Canada. The origin of CWD is still unknown.

Scrapie, kuru, Creutzfeldt-Jakob disease, Gerstmann-Sträussler-Scheinker syndrome, TME, and CWD are believed to be distinct from BSE. However, strain typing has indicated that some other TSEs are caused by the same strain of the TSE agent that causes BSE in cattle. Only four years after the initial BSE cases had been diagnosed in cattle in the United Kingdom of Great Britain and Nothern Ireland (UK), BSE in domestic cats (feline spongiform encephalopathy / [FSE]) was first reported. Almost all of the approximately 100 FSE cases diagnosed worldwide occurred in the UK. The most widely accepted hypothesis is that the affected domestic cats were exposed to BSE infectivity through contaminated commercial cat feed or fresh slaughter offal that contained brain or spinal cord from bovine BSE cases. Several large cats kept in zoos were also diagnosed with FSE. These included cheetahs, lions, ocelots, pumas and tigers. All of the large cats that were diagnosed with FSE outside the UK originated from UK zoos. It is suspected that these large cats acquired the infection by being fed carcasses of BSE-infected cattle.

Not long after BSE was diagnosed in cattle, sporadic cases of BSE in exotic ruminants (kudus, elands, Arabian oryx, ankole cows, nyala, gemsbock and bison) were diagnosed in British zoos. One zebu in a Swiss zoo was also BSE positive. In the majority of these cases, exposure to animal feed produced with animal protein (and therefore potentially containing BSE infectivity) was either documented or could not be excluded.

Moreover, there has long been concern that sheep and goats could have been exposed to BSE, because it has been experimentally demonstrated that BSE can be orally transmitted to small ruminants (Schreuder and Somerville, 2003). In 2005, the first case of BSE in a goat was confirmed in France (Eloit *et al.*, 2005), though there have been no confirmed BSE cases in sheep to date. It is difficult to distinguish between scrapie and BSE in sheep, as differentiation is currently not possible by clinical or pathological means.

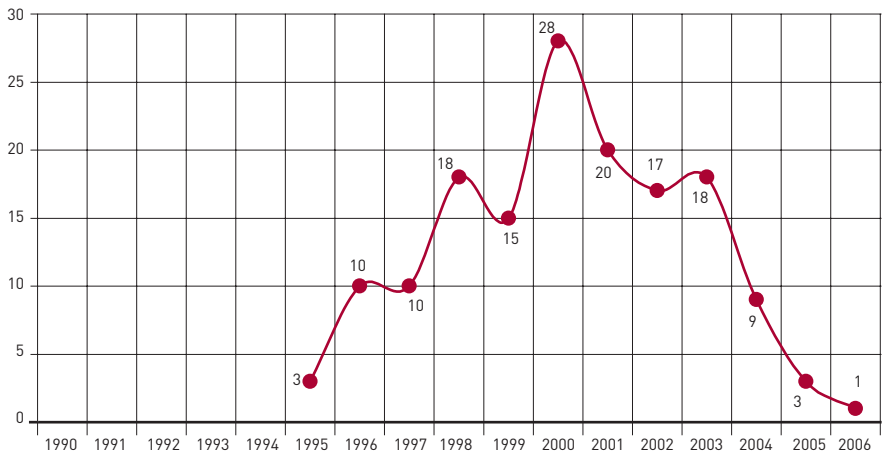
Several TSEs have been reported to occur in humans, including two forms of Creutzfeldt-Jakob disease (sporadic CJD and variant CJD [vCJD]), Kuru, Gerstmann-Sträussler-Scheinker syndrome, as well as fatal familial insomnia. Of these, only vCJD has been associated with BSE. Sporadic CJD was first identified in 1920 as an encephalopathy occurring almost exclusively in elderly patients worldwide. The incidence of sporadic CJD is approximately 0.3–1.3 cases per million individuals per year, and is similar in most countries. The duration of the disease is approximately six months. Approximately 80-89% of CJD cases are believed to be sporadic, 10% are familial (a result of a heritable mutation in the PrP gene), and the remainder are believed to be iatrogenic.

Variant CJD was first reported in March 1996 in the UK (Will *et al.*, 1996). In contrast to sporadic CJD, patients are young (average age 29 years) and the duration of the disease is longer (average 22 months). Epidemiologically, little is known about vCJD. In some cases the disease was seen in geographical clusters, and there are indications that special consumption patterns may have played a role. Genetic factors may also play a role in infection, as patients with clinical disease have been homozygous for methionine at codon 129 of the prion protein gene. In Europe, this genotype accounts for approximately 30% of the population.

The expected course of the vCJD epidemic is difficult to predict, since important variables such as human exposure rate, the infectious dose, the incubation period and human susceptibility are largely unknown. The predictions initially ranged from a few hundred to a few million expected cases. However, the lower predictions are more probable based on the current incidence of vCJD cases (Figure 2).

FIGURE 2

**Number of vCJD cases in the UK over time**




*Source:* Department of Health, UK (2006)

The link between BSE and vCJD is commonly accepted. Initially, the temporospatial association of the outbreaks suggested a causal relationship. Experimentally, inoculation of the BSE agent into the brains of monkeys produces florid plaques histologically identical to those found in the brains of vCJD patients. In addition, the agents associated with BSE and vCJD are similar, both by glycotyping (evaluating the glycosylation pattern) and by strain typing, whereas the prions associated with other TSEs (such as sporadic CJD, scrapie and CWD) are different.

## 2. BOVINE SPONGIFORM ENCEPHALOPATHY

### 2.1. Origin and spread

BSE was first diagnosed in cattle in the UK in 1986 (Wells *et al.*, 1987). Extensive epidemiological studies have traced the cause of BSE to animal feed containing inadequately treated ruminant meat and bone meal (MBM) (Wilesmith *et al.*, 1988). Although elements of the scenario are still disputed (e.g. origin of the agent; Wilesmith *et al.*, 1991; Prince *et al.*, 2003; SSC, 2001a), it appears likely that changes in UK rendering processes around 1980 allowed the etiological agent to survive rendering, contaminate the MBM and infect cattle. Some of these infected cattle would have been slaughtered at an older age, and therefore would have been approaching the end of the BSE incubation period. Potentially, they had no clinical signs or the signs were subtle and went unrecognized, though the cattle would have harboured infectivity levels similar to those seen in clinical BSE cases. The waste by-products from these carcasses would then have been recycled through the rendering plants, increasing the circulating level of the pathogen (which by now would have become well adapted to cattle) in the MBM, thus causing the BSE epidemic.

In 1989 the first cases outside the UK, in the Falkland Islands and Oman, were identified in live cattle that had been imported from the UK. In 1989 Ireland reported the first non-imported ("native" or "indigenous") case outside the UK, and in 1990 Switzerland reported the first indigenous case on the European continent. Indigenous cases were

then reported in many countries throughout Europe. In 2001, Japan reported the first indigenous case outside Europe, and this case has been followed by indigenous cases in Israel and North America.[1]

## 2.2. Epidemiology

Cattle testing positive for BSE have ranged from 20 months to 19 years of age, although most of the cases are between four and six years of age. A breed or genetic predisposition has not been found. Most cases of BSE have come from dairy herds, likely due to differences in feeding systems when compared to beef cattle. Additionally, beef cattle are typically younger at the time of slaughter. Because the average incubation period is four to seven years, infected beef cattle will generally not live long enough to develop clinical signs.

There is no experimental or epidemiological evidence for direct horizontal transmission of BSE, and there is still controversy regarding the potential for vertical transmission. No infectivity has thus far been found in milk (TAFS, 2007; SSC, 2001b), ova, semen or embryos from infected cattle (SSC 2002a, 2001c; Wrathall, 1997; Wrathall *et al.*, 2002). Some offspring of BSE cases in the UK were also infected, and a cohort study of UK cattle concluded that vertical transmission could not be excluded. However, the role of variation in genetic susceptibility or other mechanisms in this conclusion is unclear, and no offspring of BSE cases have been reported with BSE outside the UK. If some amount of maternal transmission does occur, it is clearly not enough to maintain the epidemic, even within the UK.

## 2.3. Pathogenesis

In the early 1990s, infectivity studies of BSE in cattle were ongoing. At that time, experimental inoculation of tissues from BSE-infected cattle into mice had only identified infectivity in brain tissue. Therefore, definition of specified risk materials (SRM; those tissues most likely to be infective) was based on scrapie infectivity studies. Scrapie replicates primarily in the lymphoreticular system, and scrapie infectivity has been found in numerous lymph nodes, tonsils, spleen, lymphoid tissue associated with the intestinal tract and placenta. During the later preclinical phase, infectivity is found in the central nervous system (CNS). In addition, scrapie infectivity has been detected in the pituitary and adrenal glands, bone marrow, pancreas, thymus, liver and peripheral nerves (SSC, 2002b).

The first results of BSE pathogenesis studies, in which calves were intracerebrally inoculated with tissue from BSE field cases and from cattle experimentally infected by the oral route, became available in the mid-1990s (Wells *et al.*, 1996; 1998). In cattle experimentally infected by the oral route, BSE infectivity has been found in the distal ileum at specific intervals during the incubation period, starting six months after exposure (Wells *et al.*, 1994). Furthermore, CNS, dorsal root ganglia and trigeminal ganglia were found to be infective shortly before the onset of clinical signs. Recently, low levels of infectivity early in the incubation period have been detected in the palatine tonsil. In one study, sternal bone marrow collected during the clinical phase of disease was infective; however, this result has not been reproduced (therefore it may possibly have been due to cross contamination) (Wells *et al.*, 1999; Wells, 2003).

[1] Current through January 2007.

## 2.4. TSE agents

Although some controversy still exists regarding the nature of the BSE agent, most researchers agree that a resistant prion protein is the cause of the disease. Research has shown the agent to be highly resistant to processes that destroy other categories of infectious agents, such as bacteria and viruses, and no nucleic acid has been identified.

In eukaryotic species, most cells contain a normal prion protein, termed $PrP^{C}$ (superscript "C" for "cellular"). This protein is normally degradable by proteases. TSEs are thought to be caused by an abnormal, infectious form of $PrP^{C}$, in which the steric conformation has been modified and which is highly resistant to proteinase degradation. This infectious form is most commonly termed $PrP^{Sc}$ (initially for "scrapie"), but may also be referred to as $PrP^{BSE}$ or $PrP^{Res}$ (for the portion that is "resistant" to a specific proteinase, proteinase K). Because prion protein is very closely related to the normal cellular $PrP^{C}$ protein, it does not induce the production of antibodies in infected animals.

The role of $PrP^{C}$ in normal animals is still under discussion. Genetically modified mice lacking the gene for $PrP^{C}$ (and expressing no $PrP^{C}$) can be experimentally produced, but these mice have no obvious physiological changes that can be attributed to lacking the protein. They cannot, however, be infected experimentally with TSE agents.

# 3. MEASURES FOR CONTROL AND PREVENTION

## 3.1. Aims of measures

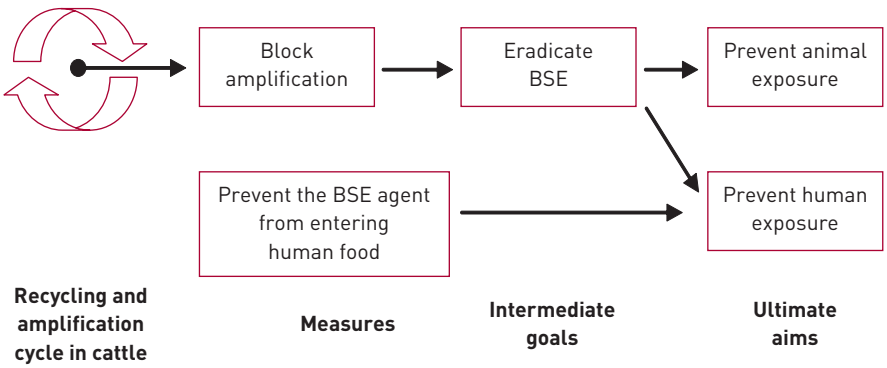
The ultimate aims of BSE control and prevention programmes are to reduce exposure risk both to cattle and to humans (Figure 3). Two levels of measures must therefore be considered:

- those that block the cycle of amplification in the feed chain;
- those that prevent infective material from entering human food.

Owing to the prolonged incubation period, it may be more than five years between effective enforcement of measures and a detectable decrease in the number of BSE cases, i.e. before the effect of the measures is seen. This interval may be even longer if the measures are not enforced effectively, as is usually the case for some time after implementation.

FIGURE 3

**Reducing BSE exposure risk to both cattle and humans**



Risk management for BSE is not globally harmonized. In Europe, the member states of the European Union (EU) have common rules for the implementation of measures, and other countries in Europe and countries wanting to join the EU are adapting their measures accordingly. However, the implementation of these measures still varies considerably from one country to another.

## 3.2. Measures to protect animal health

### Feed bans

Recognition of MBM as a source of infection led to bans on feeding MBM to ruminants in order to break the cycle of cattle re-infection (DEFRA, 2004a; EC, 2004; Heim and Kihm, 1999). Implementation of a "feed ban" may mean different things in different countries. Feeds containing MBM of ruminant or mammalian origin might be banned, or the ban might include all animal proteins (i.e. mammalian MBM, fishmeal and poultry meal). The ban might prohibit feeding of the materials to ruminants or to all livestock species, or might entirely prohibit use of the material.

In some countries, a feed ban of ruminant MBM to ruminants was implemented as the first step. The ban was then often extended to mammalian MBM due to the difficulty in distinguishing between heat-treated MBM of ruminant origin and MBM of other mammalian origin. This extended ban was generally easier to control and enforce.

Even when no MBM is voluntarily included in cattle feed, there is still a risk of recycling the agent through cross contamination and cross feeding. Experience has shown that small amounts of MBM in feed are sufficient to infect cattle. These traces may result from cross contamination of MBM-free cattle feed with pig or poultry feed containing MBM, e.g. from feed mills that produce both types of feed in the same production lines, from transport by the same vehicles or from inappropriate feeding practices on farms. Apparently, using flushing batches as a safeguard against such cross contamination in feed mills is not sufficient. The traces of MBM in cattle feed that have been detected in European countries are most often below 0.1%, which seems to be enough to infect cattle. Therefore, as long as feeding of MBM to other farmed animals is allowed, cross contamination of cattle feed with MBM is very difficult to eliminate. Dedicated production lines and transport channels and control of the use and possession of MBM at farm level are required to control cross contamination fully. In most European countries, a ban on feeding MBM to all farm animals has now been implemented.

More detailed information on measures for livestock feeds can be found in the *Capacity Building for Surveillance and Prevention of BSE and Other Zoonotic Diseases* project course manual entitled *Management of transmissible spongiform encephalopathies in livestock feeds and feeding* (FAO, 2007a).

### Rendering parameters

Rendering of animal by-products (e.g. bovine tissues discarded at the slaughterhouse) and fallen stock into MBM, which is then fed to ruminants, can recycle the agent and allow amplification. When rendering processes are properly applied, the level of infectivity is reduced. It has been determined that batch (rather then continuous) rendering at 133 ºC and 3 bars of pressure for 20 minutes effectively reduces infectivity (providing that the particle size is less than 50 mm) although it does not completely inactivate the agent (Taylor *et al.*, 1994; Taylor and Woodgate, 1997, 2003; OIE, 2005a). Therefore, using these parameters does not guarantee absolute freedom from infectivity in the

MBM, especially when material with high levels of BSE infectivity enters the rendering process.

More detailed information on measures for rendering can be found in the *Capacity Building for Surveillance and Prevention of BSE and Other Zoonotic Diseases* project course manual entitled *Management of transmissible spongiform encephalopathies in livestock feeds and feeding* (FAO, 2007a).

### Specified risk materials

Specified risk materials (SRM) are tissues that have been shown (or are assumed) to contain BSE infectivity in infected animals, and that should be removed from the food and feed chains (TAFS, 2004a). If these materials are removed at slaughter and then incinerated, the risk of recycling the pathogen is markedly reduced. In addition, in order to remove infectivity further from the feed chain, carcasses from high-risk cattle (e.g. fallen stock) should also be treated as SRM. Countries define SRM differently, and definitions sometimes change as new information becomes available, however most definitions include the brain and spinal cord of cattle over 30 months (Table 1).

## 3.3. Measures to prevent human exposure

The above measures to protect animal health indirectly protect human health by controlling the amplification of the BSE agent. The most important direct measures for preventing human exposure to the BSE agent in foods are described in the following pages.

**TABLE 1. A summary of designated SRM in Europe (as of October 2005)**

| Species and tissue | European Union | UK and Portugal | Switzerland |
|---|---|---|---|
| | | *Age* | |
| **CATTLE** | | | |
| Skull (including brain and eyes) | >12 months | - | >6 months |
| Entire head (excluding tongue) | - | > 6 months | >30 months |
| Tonsils | All ages | All ages | All ages |
| Spinal cord | >12 months | >6 months | >6 months |
| Vertebral column *(including dorsal root ganglia but NOT vertebrae of tail or transverse processes of lumbar and thoracic vertebrae)* | >24 months | >30 months | >30 months *(includes tail)* |
| Intestines and mesentery | All ages | All ages | >6 months |
| Spleen | - | >6 months | - |
| Thymus | - | >6 months | - |
| **SHEEP AND GOATS** | | | |
| Skull (including brain and eyes) | >12 month | >12 months | >12 months |
| Spinal cord | >12 months | >12 months | >12 months |
| Tonsils | >12 months | >12 months | All ages |
| Ileum | All ages | All ages | All ages |
| Spleen | All ages | All ages | All ages |

### Ban of SRM and mechanically recovered meat for food

Excluding SRM and mechanically recovered meat (MRM) from the human food chain effectively minimizes the risk of human exposure and is the most important measure taken to protect consumers (TAFS, 2004a). MRM is a paste derived from compressed carcass components from which all non-consumable tissues have been removed. These carcass components include bones as well as the vertebral column with the spinal cord and dorsal root ganglia often attached. The MRM is then used in cooked meat products, such as sausages and meat pies, and, if ruminant material is included, is regarded as a major BSE risk factor.

### BSE detection at slaughter

Measures for minimizing risks for human health require the identification and elimination of clinically affected animals before slaughter, which can only be achieved through an adequate surveillance programme including an ante mortem inspection specific for BSE. Because the SRM from clinically affected animals is known to contain infectivity, removal and destruction of these animals **prior** to entering the slaughterhouse have two clearly positive effects:

- The risk of infective material entering the food and feed chains is reduced.
- There is less contamination of the slaughterhouse, and less potential for cross contamination of normal carcasses.

In addition, most countries in Europe have been conducting laboratory testing of all slaughter cattle over 30 months of age (or even younger) for BSE since 2001 (TAFS, 2004b).

The **benefits** of testing ordinary slaughter cattle are:

- It identifies the very few positive animals that may not yet be showing clinical signs.
- It decreases the risk of contaminated material entering the food chain in those countries where other measures (e.g. ante mortem inspection, SRM removal) may not be effectively implemented.
- It could increase consumer confidence in beef and beef products.
- It may allow import bans to be lifted (although some imports bans may be in violation of WTO rules).

The **drawbacks** are:

- It is extremely expensive.
- It may give a false sense of security to consumers.
- It may diminish the incentive to implement and enforce effectively other, more effective measures (such as ante mortem inspection).
- It could lead to increased contamination within slaughterhouses due to processing of a greater number of positive carcasses if other measures are not implemented.

All currently available methods for diagnosing BSE rely on the detection of accumulated $PrP^{Sc}$ in the brain of infected animals. Therefore, cattle must have already been slaughtered before confirmation of disease status can be made, potentially increasing the risk of contamination of carcasses with an infectious agent. To prevent this, identification and removal of clinically affected animals by the farmer or veterinarian during an ante mortem inspection are optimal control steps.

### Measures to avoid cross contamination of meat with SRM

It has been shown that the use of certain types of captive bolt guns to stun cattle prior to slaughter causes brain tissue to enter the blood stream that could be disseminated throughout the carcass (including muscle). Therefore, pneumatic bolt stunning and pithing are now forbidden by many countries in Europe and elsewhere. Hygienic measures taken in the slaughterhouse to reduce potential contamination of meat with SRM are also important.

More detailed information on SRM removal and other meat production issues can be found in subsequent chapters in this course manual.

## 3.4. On-farm measures

Classical control measures for infectious diseases (biosecurity, quarantine, vaccination) do not generally apply to BSE. Given all available evidence, the BSE agent is not transmitted horizontally between cattle but only through feed, primarily ingestion of contaminated MBM during calfhood. When a BSE case is detected, it has been shown that other cattle within that herd are unlikely to test positive for BSE, despite the likelihood that many calves of similar age to the case all consumed the same contaminated feed.

However, some on-farm strategies, primarily those that focus on feed as a source of infection, and some culling programmes do contribute to the control and eradication of BSE. Culling strategies vary among countries, and often change over time. Some different culling strategies that have been applied include (SSC, 2000; 2002c):

- the index case only
- all cattle on the farm where the index case was diagnosed
- all cattle on the farm where the index case was born and raised
- all cattle on the index case farm and on the farm where the index case was born and raised
- all susceptible animals on the index case farm (including sheep, goats and cats)

} Herd culling

- "feed-cohort" (cattle that could have been exposed to the same feed as the index case)
- "birth-cohort" (all cattle born one year before or one year after the index case and raised on the same farm)

} Cohort culling

While herd culling may be a politically expedient means of increasing consumer confidence and facilitating exports, it is unlikely to be an efficient risk management measure (Heim and Murray, 2004). There are significant problems in implementing such a strategy. Farmers see it as a radical approach because it results in a considerable waste of uninfected animals. Although there may be sufficient compensation for culled animals, farmers may not believe it is reasonable to cull apparently healthy, productive animals. In addition they are likely to lose valuable genetic lines and/or their "life's work". For these reasons, farmers may be less willing to notify suspect cases if culling of their entire herd could result.

Evidence from a number of countries indicates that, in those herds where more than one case of BSE has been detected, the additional case(s) were born within one year of the index case. As a result, culling a birth cohort is a more rational risk management strategy as it focuses on those animals within a herd that have the greatest chance of

having BSE. Even so, depending on the initial level of exposure and the original size of the cohort, it is likely that relatively few additional cases of BSE will be detected in the birth cohort of a herd index case. Cohort culling is, however, likely to be much more acceptable to farmers when compared with herd culling.

### 3.5. Import control

The best means of preventing the introduction of BSE is to control the import of certain BSE risk products from countries with BSE or countries that are at risk of having BSE. Most countries do not ban imports of potentially infective materials until the exporting country has reported their first BSE case. This is usually too late, however, because the risk already existed before the first case was detected. Materials that should be considered risky for import (unless appropriate safety conditions are met) include any mammalian derived meals (including MBM and other protein meals), feed containing MBM, live cattle and offal. Import of beef and beef products for human consumption, including processed beef products, whole cattle carcasses and bone-in beef, should also be controlled, especially for the exclusion of SRM. Deboned beef meat is generally considered as non-risky for import.

### 3.6. Enforcement

Although implementation of each measure decreases the overall risk of exposure, combining measures decreases the risk more profoundly (Heim and Kihm, 2003). For example, feed bans implemented in conjunction with an SRM ban for feed have a stronger impact. Also, measures must be effectively implemented and enforced. Simply issuing a regulation or ordinance without providing the necessary infrastructure and controls will not achieve the desired goals. Education of all people involved is required at all levels and in all sectors in order to improve understanding and capacity, and thus improve compliance.

## 4. CLINICAL SIGNS

In contrast to many BSE cases pictured in the media, most cattle with BSE have subtle signs of disease. Signs are progressive, variable in type and severity, and may include depression, abnormal behaviour, weight loss, sensitivity to stimuli (light, sound, touch) and gait or movement abnormalities. Other signs that have been noted in some BSE cases include reduced milk yield, bradycardia and reduced ruminal contractions (Braun *et al.*, 1997).

Differential diagnoses for BSE include bacterial and viral encephalitides (e.g. borna disease, listeriosis, sporadic bovine encephalitis, rabies), brain edema, tumors, cerebrocortical-necrosis (CCN), cerebellar atrophy, metabolic diseases and intoxications, as well as other causes of weight loss and neurological abnormalities.

Because none of the clinical signs are specific (pathognomonic) for the disease, a definitive clinical diagnosis cannot be made. With experience, however, farmers and veterinarians can become efficient at early identification of BSE suspects. These suspicions should always be confirmed through laboratory testing.

# 5. DIAGNOSIS OF BSE

## 5.1. Biosafety

Microorganisms are classified by the World Health Organization (WHO) according to their pathogenicity for humans and animals. According to this classification, precautions must be taken when handling these agents primarily to protect the people handling them, and also to protect the general human population and livestock from accidental exposure. Depending on the classification of the microorganism, precautions must also be taken to protect laboratory workers and the community from possible exposure and infection. Thus, WHO has defined four biosafety level (BL) categories for laboratories. These categories correlate somewhat with the WHO risk group categories, but also reflect what is being done with the microorganism in the laboratory.

The most internationally well accepted guideline on the classification system for and the handling of microorganisms is the WHO Laboratory biosafety manual (WHO, 2003). This manual defines the risk groups, the requirements for risk assessments, and the requirements for each of the laboratory BLS.

In 2000, the EU published a directive based on the WHO guidelines, which defines a new risk group for BSE and related animal TSEs based on BSE agent characteristics (e.g. limited risk for laboratory personnel and the community, inability to exclude aerosol transmission). This new risk group is called 3**, which means risk group 3 with some alleviations. Scrapie, on the other hand, is still classified as risk group 2.

According to the Swiss Expert Committee for Biosafety, different biosafety levels are required when handling BSE materials, depending on the type of material (Swiss Expert Committee for Biosafety, 2006). For example, histology and Immunohistochemistry (IHC) on formic acid-inactivated BSE material can be performed in a BL 1 laboratory, and routine BSE diagnostics can be performed in a BL 2 laboratory with some additional measures. A reference laboratory for TSE must be BL 3, but some modifications are allowed. Attention should be paid to the fact that BSE laboratory requirements often differ among countries.

## 5.2. Sample collection

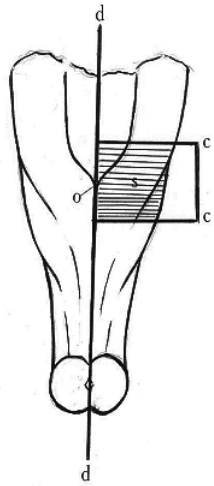
Because both the highest concentration of $PrP^{Sc}$ and the most prominent related lesions tend to be located in the area of the obex region of the brainstem (Figure 4), sampling this region optimizes sensitivity, regardless of the diagnostic test method used. If this region is not sampled correctly, false negative results may be obtained. This requires that individuals collecting samples are familiar with the anatomy of this region.

All animals clinically suspected of having BSE should be examined post mortem. Optimally, several representative areas of the brain of clinical suspects are examined; therefore, the whole head of the animal should be removed and sent to the laboratory. This also allows tests to be performed for other differential diagnoses. At the laboratory, the brain is removed as soon as possible for further testing and one half is fixed in formalin (for histopathology and IHC). The remaining half of the brain is first sampled for rapid tests and then frozen at -20 °C or -80 °C.

In cases of emergency slaughter, fallen stock or routine screening, only the caudal brainstem (medulla oblongata) is generally removed for testing, without opening the skull. The caudal end of the brainstem should be visible through the foramen magnum after separation of the head, and a specially designed spoon can be used to remove the brainstem (including the obex region) through the foramen. The brainstem is then split

FIGURE 4

**Tissue selected for testing for BSE (histopathology and rapid tests), (s), includes the obex region (o)**




longitudinally, and one half fixed in formalin for histopathology and IHC while the other half is reserved and sampled for rapid tests. The fresh tissue remaining after sampling for rapid tests is then frozen at -20 °C or -80 °C.

For neuropathology and IHC, tissue is fixed in formalin, inactivated with formic acid, and then embedded in paraffin. The embedded brain samples are sectioned and placed on glass slides. For neuropathologic examination, sections are then stained with standard haematoxylin and eosin (H & E) stain.

## 5.3. Neuropathology and immunohistochemistry

Visualization of typical neuropathologic changes requires that the tissue structure be intact. Therefore it may not be possible to evaluate even slightly autolytic samples (e.g. samples from fallen stock or cadavers, samples improperly fixed for transport). Freezing of samples also destroys the tissue structure.

After characterization of the histopathologic features present in a sample, BSE must be differentiated from other neural diseases showing similar lesions. The term "spongiform" is purely descriptive and is sometimes used interchangeably with other terms, such as *vacuolation, spongiosis, spongy degeneration* or *microcavitation*. Vacuolation of the neuropil can be seen in many different diseases and even in a normal brain, so possible causes of spongiform changes must be differentiated (e.g. normal vacuolation vs pathological vacuolation vs vacuolation from post mortem artifacts). "Encephalopathy" refers to the fact that the disease is primarily degenerative and, apart from gliosis, does not show any inflammatory changes.

After neuropathologic examination, IHC can be used to identify $PrP^{Sc}$ directly in the sample by labelling it with specific antibodies. In some cases, IHC may allow a definitive diagnosis of BSE to be made when questionable or even no neuropathologic changes are seen.

However, because the normal PrP protein ($PrP^{C}$) present in the brain cells has the same amino acid sequence as $PrP^{Sc}$, antibodies normally used in IHC detect both $PrP^{Sc}$ and $PrP^{C}$. Therefore, in order to be able to determine if there is any $PrP^{Sc}$ present, the

two proteins must first be differentiated. Proteinase K is an enzyme that causes total proteolysis of normal $PrP^{C}$, although $PrP^{Sc}$ is resistant to proteolysis by proteinase K to a large extent. Only small parts at the beginning and at the end of $PrP^{Sc}$ are digested and the remaining part, generally referred to as the core fragment or $PrP^{Res}$, is still detected by the antibodies. Therefore, proteinase K is used in IHC to digest totally the $PrP^{C}$ present in the sample, ensuring that any PrP detected will be $PrP^{Sc}$. Without this step, samples could yield a false positive result owing to the detection of normal $PrP^{C}$. Similarly, incomplete digestion could lead to false positive results.

For most antibodies used in testing, the respective epitope on PrP is not accessible in the native PrP conformation. Therefore, an additional step to demask the appropriate epitope on $PrP^{res}$ is required. Demasking can be accomplished by denaturation of the protein or by using non-specific proteases.

## 5.4. Rapid BSE tests

Tests are available to analyse BSE suspect materials rapidly (OIE, 2005b). Which rapid tests are licensed and approved in various countries throughout the world is variable and lists are constantly being updated (EFSA, 2006).

All currently licensed BSE rapid tests have several things in common. First, they use material from the brainstem, i.e. they are post mortem tests. Second, current rapid tests are based on the same principles of homogenization, proteinase K digestion (with the exception of the IDEXX HerdChek BSE Antigen EIA) and detection. Although the principles of these steps are similar among tests, there are significant differences in the execution. The materials and procedures are specific to each test system and test performance is validated under these specific conditions, thus protocols cannot be modified or interchanged among tests.

Initially, the sample of central nervous system (CNS) material must be homogenized with a specific buffer containing stabilizers and detergents. After homogenization, proteinase K is used to digest the $PrP^{C}$ (with the exception of the IDEXX HerdChek BSE Antigen EIA) and the epitope is demasked. Then, the proteinase K resistant fragment of $PrP^{Sc}$, if present, is detected with specific monoclonal or polyclonal antibodies using western blot or enzyme-linked immunosorbent assay (ELISA) technology.

Although there are differences between the tests, the overall performance (sensitivity and specificity) is comparable. Great differences can be found in the handling and the versatility of the tests for high and low throughput laboratory set-ups.

## 5.5. New developments

Work is constantly being done on the development of new rapid tests. New tests may be based on the refinement of an established procedure or on the replacement of procedures by completely new concepts.

All new tests are still based on post mortem sampling as they use brain material from the obex region. Of course, the ability to diagnose BSE ante mortem would be a huge advantage, and much research is being done in this field. Reports on possible ante mortem tests are published regularly. However, none of these tests has so far passed the validation process, and an imminent breakthrough in ante mortem testing is not foreseen.

Diagnosis of TSEs is covered in depth in the *Capacity Building for Surveillance and Prevention of BSE and Other Zoonotic Diseases* project course manual *Diagnostic techniques for transmissible spongiform encephalopathies* (FAO, 2007c).

# 6. SURVEILLANCE SYSTEMS

## 6.1. Objectives of surveillance

The two major objectives for BSE surveillance are to determine whether BSE is present in the country and, if present, to monitor the extent and evolution of the outbreak over time. In this way, the effectiveness of control measures in place can be monitored and evaluated. However, the reported number of BSE cases in a country can only be evaluated within the context of the quality of the national surveillance system and the measures taken. BSE risk can still exist in a country, even if no cases are found with surveillance. Surveillance aims to supplement the more comprehensive data that is provided by a risk assessment (Heim and Mumford, 2005).

General guidelines for disease surveillance and specific guidelines for an appropriate level of BSE surveillance for the different categories of national risk are provided in the OIE *Terrestrial Animal Health Code* (OIE, 2005 c,d). These recommendations are considered by WTO (WTO, 1994) and the international community as the international standards.

## 6.2. Passive surveillance

In most countries, BSE is listed as a notifiable disease, which is a basic requirement for a functioning passive (as well as active) surveillance system. However, some countries have no national passive surveillance system for BSE, or only a weak system.

Until 1999, BSE surveillance in all countries was limited to the notification of clinically suspected cases by farmers and veterinarians (and others involved in handling animals) to the veterinary authorities (passive surveillance). It was assumed that this would allow early detection of an outbreak (Heim and Wilesmith, 2000). However, because passive surveillance relies solely on the reporting of clinical suspects and is dependent on many factors, including perceived consequences on the farm and diagnostic competence, it is not necessarily consistent or reliable. Thus, although passive surveillance is a crucial component of any BSE surveillance system, it has become increasingly obvious that passive surveillance alone is not sufficient to establish the real BSE status of a country.

For a passive system to function effectively, several factors must be in place:

**Veterinary structure:** The disease must be notifiable.

**Case definition:** A legal definition of BSE must exist and must be broad enough to include most positive cases.

**Disease awareness:** The appropriate individuals (farmers, veterinarians) must be able to recognize clinical signs of the disease.

**Willingness to report:** There must be minimal negative consequences to the identification of a positive case at the farm level and measures must be considered "reasonable".

**Compensation scheme:** The costs of culled animals must be reasonably compensated.

**Diagnostic capacity:** There must be adequate laboratory competence.

Because these factors vary greatly, both among countries and within countries over time, the results of passive BSE surveillance systems are subjective and evaluation and comparison of reported numbers of BSE cases must be made carefully.

## 6.3. Active surveillance

To optimize identification of positive animals and improve the surveillance data, those populations of cattle that are at increased risk of having BSE should be actively targeted within a national surveillance system. With the introduction of targeted surveillance of cattle risk populations in 2001, a large number of countries in Europe and also the first countries outside Europe detected their first BSE cases.

Cattle with signs of disease non-specific to BSE and cattle that died or were killed for unknown reasons may be defined in different countries as sick slaughter, emergency slaughter, fallen stock or downer cows. The probability of detecting BSE-infected cattle is higher in these populations, as it may have been BSE that led to the debilitation, death, cull or slaughter of these animals. Many of these cattle may have exhibited some of the clinical signs compatible with BSE, which were not recognized. The experience of many countries in the last years has shown that, after clinical suspects, this is the second most appropriate population to target in order to detect BSE. Targeted surveillance aims to sample cattle in these risk groups selectively, and testing of these risk populations is now mandatory in most countries with BSE surveillance systems in place.

| | | | |
|---|---|---|---|
| Healthy cattle | => | Routine slaughter | |
| Cattle with non-specific signs (e.g. weight loss, loss of production) and Cattle that died for unknown reasons (on the farm, during transport) | => | Sick/emergency slaughter, fallen stock, downer cows | } Risk groups |
| Cattle with specific signs of BSE (or suspicion of BSE) | => | BSE suspects | |

The age of the population tested is also important, as the epidemiological data show that cattle younger than 30 months rarely test positive for BSE. Therefore, targeted surveillance aims to sample cattle over 30 months of age selectively in the risk populations, which may be identified on the farm, during transport or at the slaughterhouse.

However, despite the fact that correctly implemented sampling of risk populations would hypothetically be sufficient to assess BSE in a country, testing a subsample of healthy slaughtered cattle should be considered. This is needed to minimize diversion of questionable carcasses to slaughter, i.e. to improve compliance. If farmers are aware that random sampling is occurring, and when the probability of being tested is large enough, they are less likely to send suspect animals directly to slaughter.

The specific surveillance approaches vary among the different countries. The EU and Switzerland are testing the entire risk population over 24 and 30 months of age, respectively. In the EU, additionally, all cattle subject to normal slaughter over 30 months of age are currently tested, whereas in Switzerland a random sample of approximately 5% is tested. Countries outside Europe have implemented a variety of different testing systems. From the experiences gained in Europe, it is clear that it is most efficient to assure the effective implementation of passive and targeted surveillance in risk populations rather than to focus on testing the entire normal slaughter population.

Surveillance for TSEs is covered in depth in the *Capacity Building for Surveillance and Prevention of BSE and Other Zoonotic Diseases* project course manual entitled *Epide-*

*miology, surveillance, and risk assessment for transmissible spongiform encephalopathies* (FAO, 2007c).

## 7. RISK ASSESSMENT

### 7.1. BSE status and international standards

For a long time, BSE was considered a problem exclusively of the UK. Even after the detection of BSE cases in several countries outside the UK, the risk of having BSE was categorically denied by many other countries. Only after the introduction of active surveillance did several "BSE-free" countries detect BSE.

Before 2005, the OIE described five BSE categories for countries, but in May 2005 a new BSE chapter was adopted (OIE, 2005e) reducing the number of BSE status categories to the following three:

- Country, zone or compartment with a negligible BSE risk
- Country, zone or compartment with a controlled BSE risk
- Country, zone or compartment with an undetermined BSE risk

According to the OIE, a primary determinant for establishing BSE risk status of a country, zone or compartment is the outcome of a science-based national risk assessment. This assessment may be qualitative or quantitative, and should be based on the principles given in the Code Chapters 1.3.1 and 1.3.2 on Risk Analysis and the Appendix 3.8.5 on Risk Analysis for BSE (OIE, 2005f,g,h). The OIE Code Chapter on BSE (OIE, 2005e) lists the following potential factors for BSE occurrence and their historic perspective that must be considered in such an assessment:

*Release assessment*[1]

- the TSE situation in the country;
- production and import of meat and bone meal (MBM) or greaves;
- imported live animals, animal feed and feed ingredients;
- imported products of ruminant origin for human consumption and for in *vivo* use in cattle.

In addition, surveillance for TSEs and other epidemiological investigations (especially surveillance for BSE conducted on the cattle population) should be taken into account.

*Exposure assessment:*

- recycling and amplification of the BSE agent;
- the use of ruminant carcasses (including from fallen stock), by-products and slaughterhouse waste, the parameters of the rendering processes and the methods of animal feed manufacture;
- the feeding bans and controls of cross contamination and their implementation;
- the level of surveillance for BSE and the results of that surveillance.

In addition to an assessment of BSE risk, the OIE status categorization for BSE includes evaluation of some of the measures in place in the country. According to the OIE Code, factors evaluated in the establishment of BSE status should include:

- the outcome of a risk assessment (as described above)
- disease awareness programmes to encourage reporting of all cattle showing clinical signs consistent with BSE;

[2] In 2006, the OIE BSE chapter was modified so that only BSE, and not other TSEs, is included in the exposure assessment.

- compulsory notification and investigation of all cattle showing clinical signs consistent with BSE;
- examination in an approved laboratory of brain samples from the surveillance and monitoring system

## 7.2. The geographical BSE risk assessment

The geographical BSE risk assessment (GBR) is a BSE risk assessment tool developed by the Scientific Steering Committee of the European Commission and based on OIE assessment criteria. The GBR is a qualitative indicator of the likelihood of the presence of one or more cattle being infected with BSE, at a given point in time in a country, and has been applied to a number of countries throughout the world. The method is a qualitative risk assessment, which uses information on risk factors that contribute either to the potential for introduction of BSE into a country or region or to the opportunity for recycling of the BSE agent in a country or region. The following questions, related to release and exposure, are answered through the GBR:

- Was the agent introduced into the country by import of potentially infected cattle or feed (MBM), and if so to what extent?
- What would happen if the agent were introduced into the animal production system, i.e. would it be amplified or eliminated?

Before the detection of the first cases in many "BSE-free" countries, the GBR showed that a risk could be present. This confirmed the concept that a serious, comprehensive risk assessment must be carried out to estimate the extent of the BSE problem in countries.

Thus, decisions on preventive measures should be based on such a detailed risk assessment, whether it is the GBR or another science-based assessment based on OIE recommendations. No country should wait until the first case occurs before taking preventive measures. There remain many countries with an unknown BSE risk. In order to minimize import risks from these countries, further risk assessments are needed to evaluate the real BSE distribution worldwide.

Risk assessment for TSEs is covered in depth in the *Capacity Building for Surveillance and Prevention of BSE and Other Zoonotic Diseases* project course manual entitled *Epidemiology, surveillance, and risk assessment for transmissible spongiform encephalopathies* (FAO, 2007).

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# OVERVIEW: IMPLEMENTATION OF TRANSMISSIBLE SPONGIFORM ENCEPHALOPATHIES MEASURES IN MEAT PRODUCTION

## 1. GENERAL CONCEPTS

The goal of a national BSE control programme is to minimize exposure of humans and animals to the BSE agent. Experience in Europe and elsewhere has shown that a complementary system of integrated measures must be effectively implemented to ensure that this goal is met (Heim and Kihm, 2003). Exactly which measures are implemented in a country should depend primarily on national BSE risk as determined by a comprehensive national BSE risk assessment, as well as economics, trade and capacity available to enforce the measures effectively (Heim and Mumford, 2005). In some cases, more restrictive measures may be more simple to enforce, and therefore may be more economically justifiable, but all measures ultimately aim to prevent the exposure of humans and animals to the BSE agent.

Measures must be applied from feed production and the feeding of animals on the farm, to the identification of all potentially ill animals, to safe slaughtering and meat processing practices; i.e. "from stable to table." Moreover, restrictions on imports must be considered, to prevent entry or re-entry of infective material in exposed animals, feeds for animals and foods for humans. Because risk is not limited to exporting countries that have reported BSE cases, importing countries must not only evaluate their domestic risk, but also the risk posed by any imports of potentially risky products. In order to be effective at reducing risk, all implemented measures must be controlled and enforced through a system of self-regulation, controls and audits integrated at multiple steps along the production chain. Finally, education and disease awareness must be promoted in order to promote compliance with the measures along the feed production chain, including at the farm level.

## 2. CONTROL ON THE FARM

It is well accepted that cattle can be exposed to the BSE agent through the ingestion of contaminated feed. Generally, this is feed containing meat and bone meal (MBM) derived from ruminants. Therefore, a key measure in preventing the spread and recycling of the BSE agent is to prevent ruminant-derived material from being fed to ruminants through implementation and enforcement of a feed ban. This control must begin with the appropriate rendering of animal by-products and manufacturing of feeds, and must continue through the farm level to ensure that the national feed ban is complied with. Measures associated with feed manufacturing are covered in depth in the *Capacity Building for Surveillance and Prevention of BSE and Other Zoonotic Diseases* project course manual entitled *Management of transmissible spongiform encephalopathies in livestock feeds and feeding* (FAO, 2007).

The possibility of identifying individual animals and tracking them through slaughter and processing is important not only to control of TSEs but for food safety in general. The farm of birth (or origination) is the logical place for identification to be initiated.

Optimally, a national system would exist for unique identification of all animals.

In addition, it is important that animals ill with TSEs and other diseases be recognized and removed prior to going to slaughter. Optimally, this occurs at the farm level, which requires good disease awareness and education of both animal owners and veterinarians. The animal owners must also be willing to report TSE suspects. The willingness to report is directly related to the consequences of reporting. If the official TSE control programme is seen as unfair or too restrictive or is not adequately communicated to the animal owners, or if compensation for culled animals is inadequate, the disease will not be reported.

## 3. CONTROL AT THE SLAUGHTERHOUSE AND PROCESSING PLANT

Control measures for TSEs in the production of meat and meat products must specifically address the following points at the slaughter and processing levels:

*Slaughter level:*

- Pre-slaughter inspection
- Appropriate stunning procedures
- Appropriate hide and head removal procedures
- Proper removal and handling of specified risk materials (SRM) (including carcass inspection)
- Control of cross contamination

*Processing level:*

- Traceability
- Control of SRM in further processing

Specified risk materials (SRM) are those animal tissues most likely to contain TSE infectivity, including bovine fallen stock. Therefore, SRM should be excluded not only from the human food chain, but also from the feed chain (at minimum for ruminant species). Rendering of SRM, even at the standard processing parameters of 133 ºC and 3 bars of pressure for 20 minutes, does not entirely inactivate the agent (Taylor and Woodgate, 2003). Therefore separation and subsequent destruction of all SRM at slaughter is the most effective method for minimizing the recycling of BSE infectivity and thereby substantially reducing the risk of intentional or inadvertent exposure of ruminants. Controls at the slaughterhouse (as well as at the rendering plant in the case of fallen stock) must be in place to ensure the appropriate separation and disposal of the risk material.

The possibility of tracing products back to the slaughterhouse, or optimally, to the farm of origin, is an important concept for assuring food safety.

## 4. CONTROL OF CATTLE NOT FIT FOR NORMAL SLAUGHTER

After clinical BSE suspects, cattle showing non-specific signs of disease (signs for which no clear diagnosis is possible) are the most likely to be BSE positive. Therefore, removal and disposal of these cattle prior to entering the slaughter line reduces the risk of contamination of the slaughterhouse and, as above, minimizes the recycling of BSE infectivity, thereby reducing the risk of intentional or inadvertent exposure of ruminants. As for suspects, identification of these risk animals at the farm, during sale or transport and at the slaughterhouse requires good disease awareness as well as a programme of reasonable measures for compensation.

These basic concepts are developed in further detail in the following course manual

chapters, in parallel with current general practices for management of animals from the farm through the slaughterhouse, and of bovine products through processing.

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# REGULATIONS AND STANDARDS FOR THE MEAT INDUSTRY

## 1. GENERAL CONCEPTS

The appearance of TSEs has presented new public and animal health challenges to countries throughout the world. International recommendations and regulations have been developed both to improve public and animal health and facilitate fair trade through the standardization of measures to control and prevent TSEs, and BSE in particular, across countries and regions. The World Trade Organization (WTO) considers the standards set and recommendations made by two international bodies, the Codex Alimentarius Commission (of the World Health Organization [WHO] and FAO) for feeds and food and the World Organisation for Animal Health (OIE) for animal health and zoonoses, to be the official international standards (WTO, 1994).

Many countries have implemented some national measures, based on the international standards, in order both to protect domestic public and animal health and maintain trade in animals and animal products. Standards and requirements are also set by groups of countries (e.g. the European Union/[EU]), independent standard setting organizations, and international regional, and national industry groups and partnerships.

To help countries and individual agricultural operations effectively implement the various standards in place, practice guidelines and codes of practice have been developed. For example, good manufacturing practices (GMPs) are given by the Codex Alimentarius for slaughter and processing.

## 2. THE PLAYERS: WHO SETS THE STANDARDS?

### 2.1. International standards

Officially, according to WTO, standards for animal import and for management from the farm to the slaughterhouse have been the responsibility of OIE and standards within the slaughterhouse through retail foods (including import of foods) have been the responsibility of FAO. Recently, OIE and FAO have also begun to work jointly on food safety issues within the "stable to table" concept. All international standards are based on the recommendation that measures be applied based on the outcome of a national BSE risk assessment (OIE, 2005a, WTO, 1994). Countries then develop their own legislation based on these guidelines and their own risk, needs and goals.

#### The Codex Alimentarius

In 1963, the Codex Alimentarius Commission was created by WHO and FAO to develop food standards, guidelines and related texts such as codes of practice. The main purposes are to protect the health of consumers, to ensure fair trade practices in the food industry and to promote coordination of all food standards work undertaken by international governmental and non-governmental organizations. The output from the Codex Commission is called the *Codex Alimentarius* (hereafter referred to as "Codex"), which comprehensively describes basic principles of food hygiene (www.codexalimentarius.

net). Codex is the internationally recognized minimum standard for food production and products (Codex Alimentarius, 2006).

In addition to providing technical standards for products, the Codex also provides recommended codes of practice. These are recommendations for "good manufacturing practices" and safe food production. General principles of food hygiene are given in CAC/RCP 1, which includes the globally recognized recommendation for the set-up and implementation of HACCP systems (HACCP is described in the "Quality control concepts, hygiene and HACCP in the meat industry" chapter of this course manual). The recommended international code of hygiene practice for fresh meat is given in CAC/RCP 011, which applies to fresh meat intended for human consumption. This Code contains minimum requirements of meat hygiene up to and including the transport of meat, including recommendations and principles for:

- hygienic practices during animal production and transport of animals to slaughter;
- availability of information on hazards that may be present in slaughter animals;
- hygienic facilities and equipment for holding, slaughter, dressing and further processing, storage and distribution;
- hygienic practices during holding, slaughter, processing, storage and distribution;
- provision of adequate facilities for inspection activities.

Requirements for ante mortem and post mortem inspection of slaughter animals and for ante mortem and post mortem judgement of slaughter animals are given in CAC/RCP 041, which should be considered in conjunction with CAC/RCP 011.

Requirements provided by the Codex are continually being updated for each commodity category. The most recent official versions are published on the Web site.

### *Terrestrial Animal Health Code* of the World Organisation for Animal Health

OIE, (www.oie.int) is an intergovernmental organization representing 167 member countries. The OIE collects, analyses and makes available the latest scientific information on animal diseases and disease control throughout the world. Scientific standards are then developed based on this information. The standards are prepared by elected specialist commissions and working groups comprised of internationally-renowned scientists, most of whom are experts from within the network of 156 OIE collaborating centres and reference laboratories that also contribute towards the scientific objectives of the OIE. After adoption, the standards are made available as the *Terrestrial Animal Health Code* (OIE Code; OIE, 2005b) and the Manual of diagnostic tests and vaccines for terrestrial animals (OIE, 2005c). Similar standards are available for aquatic species.

The OIE sets standards for animal health issues and zoonoses, and provides specific information on BSE (OIE, 2005d), as well as recommendations on what products are safe to trade under what conditions (OIE, 2005a). An overriding concept in the OIE Code is that measures must be applied based on the outcome of a risk assessment.

### International Organization for Standardization

The International Organization for Standardization (ISO; www.iso.org) is an non governmental organization made up of a representative of the national standards institutes in each of 153 countries and a coordinating Secretariat in Geneva, Switzerland. The ISO delegates are not representatives of the governments but may represent national governmental organizations or the private sector. Thus, the ISO can align requirements of all stakeholders including suppliers, users, government, industry and consumers in an

effort to promote the concepts of the WTO Technical Barriers to Trade (TBT) Agreement. The ISO holds observer status in the WTO, and publishes a directory of all standardizing bodies in the world that have accepted the WTO TBT Standards Code (ISO, 2006) on behalf of the WTO. It has collaborative relationships with several UN organizations, including the Codex Commission.

The ISO develops uniform criteria to be applied to all areas of production of a variety of products, including food products. Standards are developed by consensus. The standards are widely applied and are in some cases accepted by official standard setting organizations such as national governments.

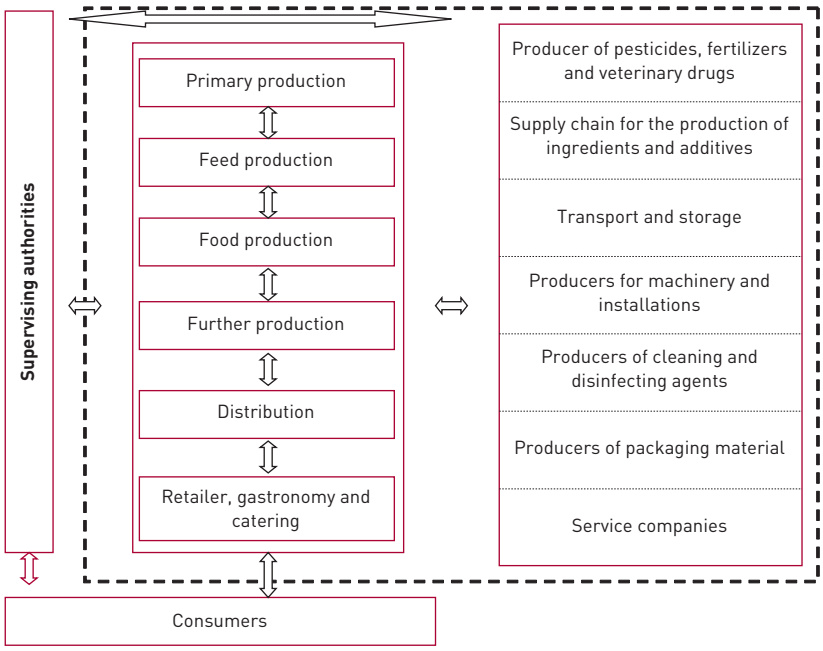
The latest standards for control of safe foods are given in ISO 22000:2005, developed by working groups specialized in food safety. This standard is for certification of food safety systems and covers the whole supply chain from stable to table (Figure 1). It also covers all peripheral aspects of the food supply chain such as feed, veterinary drugs, packaging and transport.

## European Committee for Standardization

The European Committee for Standardization (CEN, www.cenorm.be) is a non-governmental organization that is the European counterpart to ISO. It includes all the regional

FIGURE 1

**The scope of the ISO 22000:2005 includes the entire food supply chain**




The scope of the ISO 22000:2005 includes the entire food supply chain (within the dotted line in the figure). Communication throughout the food chain, including consumers, third party suppliers and supervising authorities, is emphasized to ensure identification and control of all food safety hazards. The scheme shows the interaction between the many steps of the supply chain, including other products and institutions that are not directly considered food or do not produce food, but which may have an impact on the safety of food.
*Source:* Modified from ISO 22000, available at http://www.iso.org/iso/en/commcentre/pressreleases/archives/2005/Ref966.html

standardization bodies of Europe, who send balanced delegations to the CEN policy making bodies, technical committees and working groups. Other interested stakeholders (associate members, counsellors, European trade federations and international organizations) may take part in developing standards, depending on the specific terms of reference of the work. The CEN also works with other European bodies and international bodies.

Standards are adopted according to a weighted majority vote of the CEN National Members. The standards are binding to all member countries, which must implement the standards at national level and withdraw any conflicting standards.

## 2.2. National standards

National standards are those set by individual governments of countries or groups of countries, which bilateral trading partners are required to meet in order to trade. Because of the variability in and frequent modifications to national standards, it is important that exporters understand the most current regulations in the country of destination of their food products. These can often be found on the Web site of the responsible department, but all the current requirements for a specific commodity may be difficult to determine.

In terms of global impact on trade, there are two main regulatory blocks (the EU and the USA), each having their own standards. Within Europe, the European Committee for Standardization also provides standards. Both the EU and USA try to maintain extremely high national sanitary security through strict regulations of imported goods. Thus, the standards set by the EU and the USA, as well as those of other trading partners, can have major impacts on countries wishing to export.

However, in order to protect national animal and human health while optimizing the ability of countries to trade, the WTO requires that all national standards (including those of the EU and USA) be based on the outcome of a risk assessment, if they are more strict than the international standards. The risk assessment must be scientifically based, and take into account the disease status in the country and the actual risk of importing a disease through trade.

### Regulations of the European Union

The 25 countries (member states) of the EU are united under a uniform system of regulations and laws, as well as a common single market, a single currency (adopted by 12 out of 25 member states), and a single agricultural policy.

Within the EU, comprehensive regulations have been put in place to provide for the control and eventual eradication of BSE. Specific regulations can be found on the EU Web site (EU, 2006a). These regulations affect not only the member countries, but also affect third countries (countries outside the EU) in their actions and trade with the EU. Individual EU states may have their own rules for implementation, but all must ultimately comply with the EU regulations.

In addition, the EU regulations must be considered by countries looking towards EU accession or wishing to expand their opportunities for trade. The EU regulations are therefore being adopted, as a whole or in principle, by many other countries throughout the world. Consequently, bans and other measures implemented by the EU continue to influence the world market in animals and animal products.

The EU regulations are continually being updated, and it can be difficult to extract

the most current and relevant information. Many specific decisions are no longer in force, and the relevant regulations have been incorporated into other current legislation. However, updated summaries of new information on BSE topics are available, and current legislation on food hygiene and hygiene of food of animal origin including slaughtering, boning and further processing as well as inspection and official control is available. Updates on general questions of food safety and consumer health can be obtained on the food safety Web site of the Directorate-General Health and Consumer Protection (EU, 2006b).

The EU has consolidated most of their animal by-products legislation into the text of Regulation 1774/2002 (EU, 2002), which categorizes animal by-products (animal carcases, parts of animal carcases and products of animal origin that are not intended for human consumption) according to risk, and controls their use and disposal. This regulation is discussed in detail in the "Rendering of animal by-products" chapter in the *Capacity Building for Surveillance and Prevention of BSE and Other Zoonotic Diseases* project course manual entitled Management of transmissible spongiform encephalopathies in livestock feeds and feeding (FAO, 2007).

Animal welfare (important in the context of meat production and slaughtering) is a subject of concern for European consumers, and is also covered by EU regulations. The EU animal welfare regulations (EU, 2006c) are based upon the European Convention for the Protection of Animals. The purpose of this Convention, signed under the auspices of the Council of Europe, is to lay down minimum common standards for the protection of animals kept for farming purposes. The standards require member states to ensure that the owners or keepers of animals look after the welfare of their animals and see that they are not caused any unnecessary pain, suffering or injury. The standards are developed based on past experience and present scientific knowledge.

The EU also has rules for the protection of animals during transport, which safeguard animal welfare during transport to the market and to the slaughterhouse. These rules identify all the parties involved in transport and set out their respective responsibilities, strengthen monitoring, and provide for stricter regulation of long journeys and the vehicles used.

The European Convention also applies to the movement, lairaging, restraint, stunning (restraint and stunning are compulsory without exception) and actual slaughter, including in the case of ritual slaughter, of domestic solipeds, ruminants, pigs, rabbits and poultry bred and kept for the production of meat, skin, fur or other products, with the aim of sparing animals suffering and stress. The design, construction and facilities of slaughterhouses and their operation must comply and/or facilitate compliance with the rules laid down in the Convention.

### Regulations of the United States of America

There are several different agencies responsible for setting and enforcing standards for animal products in the USA, including the US Department of Agriculture, Food Safety Inspection Services (USDA FSIS) and US Department of Health and Human Services, Food and Drug Administration (HHS FDA). The US Department of Agriculture, Animal and Plant Health Inspection Service (USDA APHIS) is responsible for setting standards regarding live animals.

The USDA FSIS (http://www.fsis.usda.gov) is responsible for the safety of meat, poultry, and egg products. Legislation and other information are available on the Regula-

tions Web pages (USDA FSIS, 2006a-c), and specific information for countries wishing to export can be found on the International affairs Web site (USDA FSIS, 2006d). Also, the FSIS publishes a list of approved facilities in second countries and the products they are eligible to export into the USA (USDA FSIS, 2006e).

The United States Government's Department of Health and Human Services (HHS; www.hhs.gov) is the principal agency for protecting the health of Americans. The HHS includes more than 300 programmes, covering a wide spectrum of activities. In addition to assuring food and drug safety (under the Food Drug and Cosmetic Act), the HHS is also responsible for health and social science research, preventing disease (including immunization services) and contributing to health information technology.

Within the HHS, the FDA (www.fda.gov) assures the safety of foods and cosmetics, and the safety and efficacy of pharmaceuticals, biological products and medical devices. The FDA provides information regarding policies and diseases, including BSE (US FDA, 2006a). Within FDA, the Center for Food Safety and Applied Nutrition (CFSAN) is responsible for assuring that FDA-regulated food products (plant and dairy foods and beverages, eggs, food and colour additives, seafood, infant formula and dietary supplements) are safe, and provides guidance on exporting these products into the USA (US FDA, 2006b). Prior to export, FSIS investigators inspect facilities in other countries to ensure that products imported into the USA are manufactured correctly and labelled truthfully, and are not adulterated or misbranded.

As with the EU, the most current applicable US regulations for a particular commodity may be difficult to determine. Therefore, it is important to initiate direct bilateral communication with the appropriate agency (FSIS for meat, poultry and egg products, or FDA for other food products) to determine requirements for trade.

## 2.3. Industry guidelines and standards

Retailers and distributors use food safety standards as basic criteria when sourcing products from primary producers and other suppliers, both domestically and internationally. More and more, these criteria are being confirmed through supplier audits, which may be conducted by the purchaser or by a third party. Producers and suppliers that supply more than one purchaser may therefore be confronted with many different sets of criteria, which are sometimes conflicting, and with many audits per year. Especially for producers in developing countries, meeting all the various criteria can be difficult.

Standards for food safety have been developed by the British Retail Consortium (BRC), resulting in the BRC Global Standard Food (www.brc.org.uk), which is accepted by the majority of retailers in the UK and some European retailers. Retailers in the USA and elsewhere have adopted a standard called Safe Quality Food (www.sqfi.com; SQF, 2000, which originated in Australia and is now owned by the Food Marketing Institute (FMI). The SQF criteria are meant to manage both safety and quality of foods, and are based on both Codex and HACCP guidelines. According to the SQF Web site, these guidelines are being used by over 5 000 companies operating in the Asia–Pacific region, the Near East, the United States, Europe and South America. In Germany in 2002, a retailers' working group developed the International Food Standard (IFS; www.food-care.info) to help reduce the number of standards in use. The IFS was adopted by the French retailers' association 2003. The IFS is also based on HACCP principles.

### EurepGAP

In 1997, retailers belonging to the Euro-Retailer Produce Working Group (EUREP) developed EurepGAP (www.eurep.org), with the goal of establishing widely accepted standards and procedures for the global certification of good agricultural practices (GAP) at the level of the primary producer (EurepGAP, 2006). These standards aim to promote the concepts of food safety, the environment, workers' welfare and the welfare of animals.

EurepGAP has now evolved into an equal partnership of primary producers and their retail customers, with all committees made up of 50% retailer and 50% producer representation from all aspects of the food chain internationally. The representatives participate in developing normative documents to be included within internationally recognized certification criteria such as ISO. Other stakeholders, including consumer and environmental organizations and governments, provide their views. The committees also have a mandate to review emerging issues with sector experts, carry out risk assessments (following the principles of HACCP), and revise and update the protocols.

The protocols are used by producers to achieve compliance with standards for GAPs. Because EurepGAP's scope is limited to the primary producer, once products leave the farm they come under the control of other standards for food packing and processing described in this chapter. The EurepGAP standards are available in simple tabular format and individual criteria are prioritized (e.g. recommended, major must, minor must). The standards are published and freely accessible on the Web site (EurepGAP, 2006).

In order to decrease redundancy with other standards, EurepGAP allows for achieving equivalence through benchmarking. EurepGAP also accredits organizations to be able to conduct certification audits, and publishes a list of certification bodies on their Web site. In most cases, costs for audits are borne by the primary producer or producer cooperative.

### Global Food Safety Initiative

In order to establish standards globally, the Global Food Safety Initiative (GFSI) Benchmark Project was initiated by the Food Business Forum in 2000 (www.ciesnet.com; CIES, 2006). The GFSI is governed by an advisory group and supported by a task force representing over 70% of food retail revenue worldwide. The goals of the GFSI are to:

- implement and maintain a scheme to recognize food safety standards worldwide;
- facilitate better communication, cooperation and transparency between standard owners;
- work towards worldwide integrity and quality in the certification of standards and the accreditation of certifying bodies (CIES, 2006).

The GFSI does not produce new food safety standards. Instead, it has developed a benchmark model, outlining key criteria for food safety standards, against which any food safety or farm assurance standard can be benchmarked. These key elements are:

- a food safety management system (e.g. based on the ISO 9000 series);
- good manufacturing (or agricultural) practices;
- HACCP-based system.

The GFSI developed its requirements based on existing food safety standards (including Codex, ISO standards and related Codes of Practice), taking into account consumer

health and safety concerns. Thus, it aims to combine theory and practice for audits and provide a high level of protection for the consumer.

Once a food safety standard has been benchmarked successfully by GFSI, the standard becomes recognized. For example, the BRC, IFS and SQF standards (mentioned above), among others, are recognized by the GFSI. The recognized standards can then be applied by food suppliers and retailers as they agree on sourcing contracts for products. The specific application of standards will vary depending on the product, as well as company policies, general regulatory requirements and other product liability and due diligence regulations.

The GFSI standards differ from ISO standards in that GFSI certifies products rather than the system itself. The GFSI standards are also restricted to certification of safe food handling. The GFSI standards differ from EurepGAP standards, as neither accreditation nor certification are part of the GFSI activities. GFSI encourages the use of third party audits using the benchmarked standards.

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# TRANSMISSIBLE SPONGIFORM ENCEPHALOPATHIES MANAGEMENT AT THE FARM LEVEL

## 1. GENERAL CONCEPTS

Prevention and control of BSE at the farm level is conceptually different from that of most other infectious diseases of animals. Because the BSE agent cannot be transmitted directly from one cow to another, traditional measures such as quarantine and hygiene are not effective. The two measures that can be applied on the farm are:

- control of livestock feeds and feeding;
- identification and proper notification of suspect (and other risk) animals.

## 2. LIVESTOCK FEEDS AND FEEDING

Because cattle are exposed to the BSE agent through the ingestion of contaminated feed (notably feed containing meat and bone meal/[MBM] derived from ruminants), preventing ruminant-derived material from being fed to ruminants is crucial to preventing exposure to the BSE agent. This control must begin with the appropriate rendering of animal by-products and manufacturing of feeds, but must continue through the farm level. Measures associated with feed manufacturing are covered in depth in the *Capacity Building for Surveillance and Prevention of BSE and Other Zoonotic Diseases* project course manual entitled Management of transmissible spongiform encephalopathies in livestock feeds and feeding (FAO, 2007 a).

Many countries have feed bans in place, but these bans differ in scope among countries. Depending on the specific ban, feeds or feed components containing ruminant-derived protein may be available for poultry, fish, pigs or pets. Farms purchasing components for on-farm mixing of feeds intended for ruminants should understand exactly what is in the components, and purchase only components approved for feeding to ruminants. Farms housing multiple species may be purchasing feeds or feed components not approved for ruminants, and thus care must be taken to avoid cross contamination of feeds or feed components for ruminants with those for non-ruminants during transport, storage, mixing and feeding.

## 3. IDENTIFICATION AND NOTIFICATION OF SUSPECT CASES

The second farm-level measure for BSE control is the identification and official notification of BSE suspects or risk cattle by the animal owner or farm veterinarian. These animals should then be tested, and the carcasses appropriately disposed of in order to minimize the risk that any BSE-infected animals will enter the food or feed chain.

In most countries, BSE is, at least legally, a reportable disease (FAO, 2007b). In these countries, BSE suspects must be reported when identified. It has been noted in Europe that identification of the subtle changes associated with early clinical BSE is best done by the farmer. However, recognition that any identified changes may indicate BSE requires good disease awareness and education of both animal owners and veterinarians.

The animal owners and veterinarians must also be willing to report suspects to the officials, which is directly related to the consequences of reporting. If the official control

programme is seen as unfair or too restrictive or is not adequately communicated to the animal owners, or if compensation for culled animals is inadequate, the disease will not be reported.

Once suspect animals are identified and reported, the official control programme mandates the next steps. In effective official control programmes the suspect animal is killed and its brain removed for testing by an approved laboratory. Sampling may be the responsibility of official government veterinarians, or accredited private veterinarians. At minimum, the obex region of the brain stem is removed and tested (FAO, 2007c). The carcass of a suspect animal should not enter the food or feed chain.

Depending on the country, other categories of ill cattle may be part of a national surveillance system for TSEs, and must also be notified and sampled.

The government must develop and distribute easily understandable information about the official notification, sampling and disposal process to all people involved in identification of BSE at the farm level.

### 3.1. Clinical signs

Owing to the difficulties in recognizing clinical signs associated with BSE, Dr. U. Braun and his staff at the University of Zurich, Switzerland, developed a special scheme for examination of potentially BSE infected animals (Braun *et al.*, 1997). Animals of this group include all cows over 30 months, all animals with a disturbed behaviour, and all sick or insured animals. The test is simple and contains five points to check:

1. Swaying and unsafe action, bending at knees, falling;
2. Fear of passageways, thresholds, channels and other obstacles on the ground;
3. Hypersensitivity to noise, to sudden light, to touching in head and neck region;
4. Extremely nervous, frightened, aggressive, e.g., flinging head;
5. Sneering, dental crunching, drooling.

These signs might be very subtle, especially early in the disease. As well, all signs do not appear in all cases. Additional information on clinical signs is available in the 'Introduction to TSEs and BSE' chapter of this manual.

## 4. INDUSTRY STANDARDS

Industry standards (such as EurepGAP described in the previous chapter), as well as standards for legally regulated production schemes such as "organic production" or "integrated production" exist for management of animals at the farm level. However, these standards currently do not make any reference to measures to control or prevent BSE.

## 5. TRANSPORT

For all cattle, transport should be as short and as careful as possible to maintain should be good meat quality. No ill or injured animals should be transported or their transport minimized. Transportation causes stress to any animal and therefore transportation is an important issue for both welfare and meat quality.

A veterinarian should inspect animals prior to loading. Optimally, the inspection takes place immediately prior to loading, or within 6 to 12 hours of loading. No animals with signs of any neurological disease should be loaded for transport, or they should undergo a complete veterinary examination prior to loading. BSE suspect animals should not

be loaded and, after veterinary inspection, should be officially notified. In some cases, transport of cattle showing subtle BSE signs will worsen the signs, and thus these animals might be more easily recognized at unloading.

Legal requirements for transportation of cattle to slaughter must be determined and respected. The OIE code chapters 3.7 on animal welfare gives the international standard for transport by land, sea, and air (OIE, 2005). Other regulations and recommendations also exist (as described in the previous chapter of this course manual).

## 6. ANIMAL IDENTIFICATION AND DOCUMENTATION

Animal identification and traceability are required for effective national control of many diseases, including BSE. The identification system must begin on the farm, and must continue throughout the life of the animal. There are many different systems in use, but all systems must guarantee that a unique identifier exists for each animal. If an animal is never moved from one place to another, the identification system can be site-specific. But as soon as animals move, such a system is no longer useful.

Many countries have decentralized systems where identification is given through a programme (such as a dairy cattle improvement programme) or an entity such as a breed organization. There may be many databases in existence, but identified animals have documents that can be checked before leaving one place and on arrival. In decentralized systems, each organization is responsible for control at their own point. Animals can only be traced through their lifetimes by checking back stepwise through each relevant database.

In centralized systems, national or even international identification systems give unique identifiers (numbers, letters and/or combinations) to each newborn animal or, at minimum, to each animal at the time when it leaves its place of birth. Decentralized systems may be modified so that documentation and data are controlled centrally, even though documents may be issued and filled out by decentralized institutions or even individually by the farmer. The central system has to be informed each time the animal is moved, giving both the place of origin and arrived at point.

In "animal passport" systems, each animal is issued a "passport" at birth specifying all individual markings and other information. The passport follows the animal and is handed over with the animal when ownership is transferred. Registration can take place either only when the passport is issued and when the animal dies or is slaughtered, or at every change of location. Passport systems can work with either decentralized or centralized systems.

The EU runs a new centralized system for import and exports among and between EU states and other countries, called "TRACES" (TRAde Control and Expert System; EU, 2006) to track all movements of animals and to allow rapid response to disease outbreaks.

## 7. REFERENCES

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