TSE Roadmap 2005 – The Evidence Base

1. Specified Risk Material

Strategic goal:
To ensure and maintain the current level of consumer protection by continuing to assure safe removal of SRM but modify list/age based on new & evolving scientific opinion

1.1. General

Removal of Specified Risk Material (SRM) is estimated to remove over 99% of any infectivity that might be present, and is the main public health control for BSE.

The following factors could influence modification of SRM rules:

- Knowing which tissues definitely/ possibly/ never/ contain infectivity
- Knowing when is the earliest stage in the incubation period/earliest age that tissues could contain infectivity
- Knowing the sensitivity and specificity of the test for infectivity
- Knowing when the exposure window was – for BSE in cattle this may be assessed by the date of effective enforcement of the feed ban, and monitored by surveillance e.g. minimum and mean age of cases, prevalence in animals born after the feed ban and recent cohorts. [The BSE incidence and the historical application of BSE controls (feed ban, SRM removal) and surveillance (passive and active) vary between Member States.]
- New diagnostic tests which can reliably detect pre-clinical disease, or further data on current tests.

The current list of bovine, ovine and caprine SRM [see Appendix 2[1]] is based on a precautionary interpretation of various pathogenesis studies. The pathogenesis studies have provided evidence for establishing age limits for SRM removal.

In BSE in cattle there is early infection of the ileum and tonsils, followed by later infection of the CNS, dorsal root ganglia and trigeminal ganglia. Emerging Japanese data suggests that there may be infectivity in peripheral nerves in clinical BSE.

The distribution of infectivity for scrapie in sheep and goats differs from that for BSE in cattle with early infection of the lymph nodes, spleen, tonsil, and bowel, and later infection of the CNS. Other tissues and organs are also infective.

The distribution of infectivity of experimental BSE in sheep and goats is diffuse. In 2005 BSE was confirmed in a single French goat which died in 2002 and was born in

[1] http://www.food.gov.uk/bse/beef/controls

2000 (before the 2001 EU feed ban). Further tests are determining whether or not a Scottish goat which was diagnosed with scrapie in 1990, actually had BSE. There is no evidence of widespread BSE in EU goats. There is no evidence of BSE in EU sheep.

The distribution of infectivity in Chronic Wasting Disease in cervids is diffuse. There is no evidence of CWD in EU deer, but further surveillance is required. Although it is unknown whether CWD presents a risk to other domestic livestock or humans, a 2005 study suggests that the incubation period for orally transmitted CWD in cattle could be long (5 years) and require a high dose of infection. Research in progress has so far failed to transmit BSE to red deer.

The mean incubation period for BSE is 60 months (range 2-14 years). The vast majority of clinical cases are aged 4-6 years at clinical onset. The ongoing Veterinary Laboratories Agency (VLA) cattle pathogenesis studies indicate that the incubation period is dose dependent. The peak susceptibility is at about 6 months of age, and adult cattle are less susceptible to infection[2] .

The VLA cattle pathogenesis studies indicate that there is a greater than 99% probability of detecting BSE infectivity in the CNS at 3 months before the onset of clinical disease, falling to a 50% probability at 8 months before the onset of clinical disease[3]. Results of an ongoing Health Canada study will provide further data on detection of infectivity.

The April 2005 European Food Safety Authority (EFSA) opinion on the assessment of the age limit in cattle for the removal of SRM concludes that infectivity of the CNS in cattle occurs at ¾ of the incubation period. The opinion indicates that the minimum age for BSE cases in the EU has increased from 28 months in 2001 to 42 months in 2004. [In 2005, Poland confirmed BSE in a 33-month old animal[4]; the UK confirmed BSE in 36-month old and a 39-month old animal; Spain confirmed BSE in $\leq$ 40 month old animal.] EFSA concluded that a 21-month age limit for SRM removal (excluding tonsils and intestines) would cover even the youngest bovine animal observed since 2001 (28 months), whereas a 30-month age limit would not.

The current EU age limit for vertebral column removal is 12 months. The UK removes vertebral column at 30 months under derogation. In 2005, the UK Spongiform Encephalopathy Advisory Committee (SEAC) concluded that reducing the limit to 12 months would make a small to negligible difference in risk. In 2002 the EU Scientific Steering Committee (SSC) advised that vertebral column/dorsal root ganglia risk assessments depend on the country-specific BSE incidence and beef consumption patterns.

1.2. Tallow – see 2.3

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[2] Arnold et al. 2004, Estimation of the age-dependent risk of infection to BSE of dairy cattle in Great Britain. Prev.Vet.Med.66:35-47 & Supervie et al.2004 The unrecognised French BSE epidemic. Vet.Res.35:349-362

[3] European Food Safety Authority (EFSA) Opinion on the Assessment of the Age Limit in Cattle for the Removal of SRM, 2005

[4] Bovine Spongiform Encephalopathy in Poland, Polak and Zmudzinski 2005,Vet.Rec. 157, 56-58

1.3. Collagen

In 2005, EFSA opined on a hydrolysis-based process that can achieve a TSE inactivation capacity of 5-logs.

1.4. Gelatine

The three major factors affecting the risk of gelatine are source material, the effectiveness of the inactivation process and the end use. In 2002, the SSC reported on methods for processing gelatine, which could reduce the TSE risk of the end product to almost zero.

A recently published study[5] investigated whether the autoclaving process used in the industrial manufacture of gelatine (3 bar, 133°C, 20 minutes) inactivates the BSE agent. Crushed bovine bones and vertebral column spiked with the brains of mice infected with the 301V strain of BSE, were subjected to a simulated industrial gelatine-extraction process. No infectivity was detected by intracerebral inoculation of mice with the extracted gelatine. The process was calculated to reduce infectivity by at least 10 E6.5 ID50.

A new European Food Safety Authority (EFSA) opinion on gelatine is expected in 2005.

2. Feed Ban

Strategic goal:
A relaxation of certain measures of the current total feed ban when certain conditions are met

2.1 Environmental Contamination of Beet Pulp

The environmental contamination of German beet pulp by historic bone fragments in soil is not believed to present a BSE risk. Genetic analysis indicates that the bone fragments detected do not derive from ruminants.

2.2 Fish meal/Lifting Feed Ban Provisions

There is no evidence that a natural TSE exists in fish, and there are no indications of replication of scrapie or BSE agent in experimental transmission studies in fish.

There is no evidence that inclusion of fish meal in animal feed presents an animal or human health risk. Cross contamination of fish meal with mammalian meat and bone meal (MMBM) is unlikely with short supply chains. In 2001, the Advisory Committee on Animal Feedingstuffs recommended that fish meal should be traceable and existing rules on meat and bone meal (MBM), fully enforced.

[5] Grobben et al. 2005 Inactivation of the BSE agent by the heat and pressure process for manufacturing gelatine. Vet.Rec. 157, 277-281

UK and French studies suggest that cross-contamination of cattle feed with MMBM continued after the bans on feeding ruminant MBM to ruminants. MMBM was still permitted in pig and poultry feed and the risk of BSE increased in the pig-dense regions. The 2001 EU total feed ban (on feeding MBM to farmed livestock) addressed this weakness.

There is no evidence of naturally occurring TSEs in farmed pigs or poultry. There is evidence that pigs are susceptible to intra-cerebral infection with BSE, but not to oral infection. There is no convincing evidence of poultry susceptibility to TSEs.

In 2000, the Scientific Steering Committee (SSC) opined that cross contamination of animal feed with MMBM is not acceptable. The Microscopy Analysis Test (MAT), approved by the EU, is currently unable to reliably detect 0.1% MMBM in the presence of 0.5% fish meal in feed.

Although adopted as the only appropriate method for producing MBM for inclusion in animal feed, the 133°C, 3 bar, 20 minute rendering method (Method 1)[6] might not be robust under worst-case conditions. (see 2.3)

Recent evidence indicates that extremely low levels (1mg) of raw infective material can transmit BSE. The ongoing pathogenesis studies indicate that the incubation period of BSE is dose dependent.

Recycling animal by-products in feed (and particularly intra-species recycling) increases the risk of propagating detectable or undetectable TSE infections.

2.3 Tallow

Historically, tallow has not been considered a significant BSE risk. Epidemiological studies failed to find any association between tallow consumption and BSE in UK. (The tallow historically used in milk replacer was typically imported and derived from human consumption grade raw material. There is currently a voluntary UK manufacturers' agreement not to use tallow in calf milk replacers).

The quality and safety of tallow depends upon the source and type of the raw material, the rendering extraction process, and the level of protein impurities. Recent unpublished experimental data indicates that BSE infectivity can survive in pressure-rendered tallow recovered by centrifugation or solvent extraction.

In 2005, the European Food Safety Authority (EFSA) assessed the validity of the outcome of a quantitative risk assessment (QRA) of the residual BSE risk in tallow. The QRA supports the general conclusions of the 2001 SSC Opinion and Report on the safety of tallow.

EFSA concluded that estimates of risk for tallow production and use, as specified in the 2001 Opinion, are low, and in general the calculated exposure levels can be regarded as minimal.

2.4 Dicalcium Phosphate (DCP) & Tricalcium Phosphate (TCP)

[6] Regulation (EC) No.1774/2002, Annex V, Chapter III

The 2003 EU Scientific Steering Committee opinion on the safety of DCP and TCP from bovine bones used as a feed additive or fertiliser, suggests the BSE risk of feeding DCP and TCP is very low providing appropriate safeguards are taking with regard to sourcing, removal of high-risk materials and use of a validated process.

3. Monitoring programmes

Strategic goal:
To reduce the numbers of tests of bovine animals and at the same time continue to measure the effectiveness of the measures in place with a better targeting of the surveillance activity

The current TSE surveillance requirements of Regulation (EC) 999/2001 for cattle, sheep and goats are summarised in the TSE Roadmap document. Surveillance is key to targeting and modifying TSE controls (e.g. SRM) effectively. However SRM controls, rather than surveillance, are the main public health control.

EFSA has supported the use of the BSurvE model, and the surveillance requirements of the 2005 OIE Code are based on this model.

As the BSE epidemic declines, there may be scope for reducing BSE surveillance in historic cohorts of cattle, concentrating resources on establishing the disease prevalence in recent cohorts. However, the BSE incidence and the historical application of BSE controls (feed ban, SRM removal) and surveillance (passive and active) vary between Member States. Consequently future surveillance requirements may vary between Member States.

Further surveillance is required for CWD in deer.

In 2004, EFSA recommended further surveillance for TSEs in small ruminants. This is particularly important in relation to determining the presence or absence of BSE in these populations.

4. The categorisation of countries according their BSE risk.

Strategic goal:
Simplification of the categorisation criteria and conclude the categorisation of the countries before 1 July 2007.

The new “Three Category” classification for countries according to their BSE risk was considered in detail during the negotiation of the 2005 OIE Code – adopted May 2005.

The European Commission is proposing to categorise countries as Negligible BSE Risk, Controlled BSE Risk or Undetermined BSE Risk, if the OIE does not succeed in categorising countries in this way before 1 July 2007.

Categorisation is based on a risk assessment, and if appropriate an exposure assessment covering presence or absence of TSE, and prevalence based on surveillance; use of MBM; import of cattle; import of feed; import of products of

ruminant origin; recycling of BSE agent; use of ruminant carcases in animal feed; feeding ruminants with MBM and level of surveillance. Other factors include awareness of passive surveillance, compulsory notification of TSE, use of approved laboratories, feed ban monitoring, restriction of cohorts and offspring. There are two tiers of surveillance.

The EU Scientific Steering Committee, and now the European Food Safety Authority has categorised countries by Geographical Risk of Bovine Spongiform Encephalopathy (GBR).

GBR is a qualitative indicator of the likelihood of the presence of one or more cattle being infected with BSE, pre-clinically as well as clinically, at a given point in time, in a country. Where the presence of BSE is confirmed, the GBR gives an indication of the level of infection. There are four levels: I – highly unlikely; II-unlikely but not excluded; III-likely but not confirmed or confirmed, at a lower level; IV-confirmed at a higher level.

The assessment is based on 8 factors – structure and dynamics of cattle population; BSE surveillance; BSE related culling; import of cattle and MBM; feeding; MBM-bans; SRM-bans; rendering.

5. Review of culling policy with regard to TSEs in small ruminants

Strategic goal:
Review and relaxation of the eradication measures for small ruminants taking into account the new diagnostic tools available but ensuring the current level of consumer protection

The small ruminant culling policy aims to breed TSE-resistant sheep genotypes. There is evidence that TSE resistance in the most resistant ARR/ARR sheep genotype is not absolute. There is no evidence of resistant genotypes in goats.

In 2005 BSE was confirmed in a single French goat which died in 2002 and was born in 2000 (before the 2001 EU feed ban). Further tests are determining whether or not a Scottish goat which was diagnosed with scrapie in 1990, actually had BSE. A recent experimental study indicates that experimental BSE in susceptible sheep can transmit either *in utero* or perinatally[7]. There is no evidence of widespread BSE in EU goats. There is no evidence of BSE in EU sheep.

Since EFSA's 2003 opinion, the TSE Regulation (999/2001) was amended in January 2005 requiring discriminatory testing of all positive scrapie samples, to determine the presence or absence of BSE.

There is no evidence that scrapie (in contrast to BSE) presents a human health risk. There is circumstantial evidence that scrapie does not pose a risk to human health. Scrapie has been known for over 300 years and is endemic in the UK. There is no evidence of transmission of scrapie from sheep to man, and no increased incidence

[7] Bellworthy et al. 2005 Natural transmission of BSE between sheep within an experimental flock Vet.Rec. 157:7 p.206

of CJD in countries with scrapie compared to those without (e.g. UK and Australia).[8] No cases of BSE or vCJD (linked to BSE) have been reported in Australia. vCJD was first reported in UK in 1996, and the vast majority of cases have been confined to UK.

6. Cohort culling in bovine animals

Strategic goal: To stop the immediate culling of the cohort

6.1 Cohort Cull

The cull of cattle that have been exposed to the same infected feed as a BSE case eliminates pre-clinical cases and prevents further clinical cases of BSE.
Cohort culling was originally proposed as an animal health measure to reduce the observed incidence of BSE. Culling of birth cohorts (the group of bovine animals born in the same herd as the index case within 12 months before or after the birth of the affected animal) has a similar effect to herd whole herd culling, but is more cost effective.

There is no evidence of horizontal transmission of BSE.

In 2004, EFSA concluded that the prevalence of BSE in cohort animals was ten times higher than the prevalence in the overall healthy population.

The risk to cohorts may decrease as the feedbourne risk decreases, and levels of feed contamination decrease.

6.2 Offspring Cull

The current estimate of the BSE risk of maternal transmission is less than 1% across the entire UK epidemic (for calves born in the last 6 months of incubation of disease in the dam). The risk is believed to have declined as the feedbourne risk decreased.

This low level of maternal transmission alone, would be insufficient to maintain a BSE epidemic.

7. UK restrictions

Strategic goal: To discuss the lifting of the additional restrictions on exports of beef and beef products from the UK if the preset conditions are complied with.

Available evidence indicates that the UK's current BSE status is equivalent to that in certain other Member States which have BSE and are permitted to trade in beef and beef products.

[8] http://www.cjd.ed.ac.uk/intro.htm

Appendices

Appendix 1 – Consolidated Scientific Evidence and Opinion

Appendix 2 – Specified Risk Material from November 2004

Appendix 3 – Summary of Scientific Opinions from the EC Scientific Steering Committee (SCC) and European Food Safety Authority (EFSA) and other Scientific Data

Appendix 4 – Summary of Scientific Opinions from the Spongiform Encephalopathy Advisory Committee (SEAC)