1. Introduction

The purpose of this Review is to consider the steps New Zealand is currently taking to manage the human-health risks of bovine spongiform encephalopathy (BSE) in imported foods and, if appropriate, to propose changes to the current BSE Measure.[1]

The Terms of Reference for this Review are set out in Appendix 6.

BSE is a neurological disease of cattle that can lead to the fatal variant Creutzfelt Jacob disease (vCJD) in humans.

Since 1996, New Zealand has taken steps to manage the potential human-health risks of the BSE agent in imported food. In January 2002 new import procedures[2] were introduced requiring that bovine meat products can only be imported into New Zealand when certified to a level commensurate with the exporting country's BSE status.

As a trading nation New Zealand needs to adopt measures that are consistent with international standards and our trade obligations. The current New Zealand BSE Measure closely follows the now out-of-date recommendations of the 2002 edition of the Terrestrial Animal Health Code of the OIE, the World Organisation for Animal Health.

The Code was revised significantly in May 2005 in light of new scientific information, and accordingly it is now appropriate to reconsider New Zealand's BSE Measure.

The OIE's Terrestrial Animal Health Standards Commission has proposed further changes to the Code's BSE chapter and appendix, which are expected to be adopted over the next two or three years. For this reason, the review team has based its proposals on the science-based negotiating position of the New Zealand Government for further revisions to the Code. Where the review team's proposals go beyond the current (2005) Code, these are noted in the text of this Review.

An independently chaired committee of officials (see Appendix 4 for membership) has conducted this Review with independent advice from an interdepartmental advisory group (IDAG), whose terms of reference are in Appendix 7 of this report.

No attempt has been made to consult with wider stakeholder groups. Such consultation will be the responsibility of the New Zealand Food Safety Authority (NZFSA) once it has considered its response to the recommendations in this report.

2. Scientific background

BSE is a member of a family of diseases known as transmissible spongiform encephalopathies (TSEs). It is a fatal, feed-borne, neurological disease of cattle, which originated through, and has been amplified by, the feeding to cattle of meat-and-bone meal contaminated with an agent related to, and perhaps originating from, the agent that causes scrapie in sheep.

In 1996 human cases of a new TSE known as variant Creutzfelt Jacob disease (vCJD) were reported. The disease is always fatal in humans. These vCJD cases were soon shown to be caused by human infection with the BSE agent.

Because of this risk to human health, many precautionary measures were implemented around the world to reduce the potential for BSE to be transmitted to humans via food products derived from cattle.

However, in the intervening years much has been learned about BSE and the risk to human health, and in many countries some of the precautionary measures put in place after 1996 are being reviewed.

2.3 Infectivity of agent

TSEs are generally considered to be caused by infection with a proteinaceous agent known as a "prion".

The dose of this agent needed to infect cattle is very small. This was a source of major concern in 1996 when the first cases of vCJD occurred but it is now known that this infectious agent does not easily cross the species barrier into humans. Thus the development of vCJD from exposure to the BSE agent is much more rare than was thought likely in 1996. Even with the massive exposure to BSE agent in the United Kingdom before infective tissues were removed from the food chain, vCJD cases have been much fewer than expected and the vCJD epidemic is now declining (see Figure 3).

2.4 Presence of infective agent

Since 1996 the specific tissues that are likely to contain the BSE agent, and the time that they become infectious, have become better defined. It is now known that detectable infectivity is restricted to only a few bovine tissues; over 40 bovine tissues have been tested, have not been shown to contain the BSE agent, and are thus regarded as safe. Moreover, it is relatively simple to remove potentially infected tissues from the human food chain. All countries with BSE require these tissues to be removed from all animals slaughtered for food, and that these tissues then be destroyed.

1 New Zealand's BSE control measures are codified in "Measure to Provide Ongoing Management of the Human Health Risks Associated with Imported Food Products Potentially Containing the Bovine Spongiform Encephalopathy Agent" (New Zealand Ministry of Health, December 2001), and are enabled by Section 11D of the Food Act 1981.

2 This review considers only imports of bovine food products. BSE export requirements for such products are set by the importing country and are administered in New Zealand by the Ministry of Agriculture and Forestry.

3 http://www.oie.int/eng/info/en_esbru.htm

2.5 Preventing infection of cattle

The infectious agent is transmitted between cattle only through ingestion of contaminated tissues, and it is relatively easy to remove potentially infected tissues from the animal feed chain. The ruminant-to-ruminant feed ban imposed after 1996 has been rigorously observed and has effectively broken the cycle of infection in cattle, with BSE rates globally dropping significantly over the past three years.

Nevertheless, while the incidence of BSE in cattle has fallen significantly in the UK and the European Union, sporadic cases are still seen occasionally in countries in which contaminated stockfeed was fed in the past.

The effect of the initial feed ban in the United Kingdom is shown in Figure 1. From 1993 on, BSE incidence in the UK declined steadily, with only 338 cases occurring in 2004.[3]

2.6 BSE and vCJD

In early 1996 the first cases of variant Creutzfeldt Jakob disease (vCJD) were reported in the United Kingdom. Biochemical studies and inoculation of laboratory animals provided very strong evidence that vCJD was caused by the same infectious agent that caused bovine spongiform encephalopathy (BSE), a progressive neurological disease which, by 1996, had killed over 158,560 British cattle.[4]

Since 1996 around 157 people in the UK have died from vCJD, and a small number of cases have been reported from other countries (nine in France, and one each in Canada, Ireland, Italy, the United States, Hong Kong and Japan[5]). The vCJD cases outside the European Union are all believed to have been acquired while the people were staying in the UK.

In 1996, when the British government announced that vCJD was most probably caused through humans becoming infected with the same agent that caused BSE in cattle, it was assumed that infection had been acquired through eating BSE-contaminated beef (that is, cuts of meat from cattle infected with BSE).

In 1996, not a lot was known about BSE and even less about vCJD. Thousands of BSE cases were still occurring each year and it was feared, with some reason, that a vCJD epidemic in humans of similar proportions to the cattle epidemic of BSE could be about to unfold. Fortunately, a lot has been learned since, and it is now clear that these fears are not going to be realised.

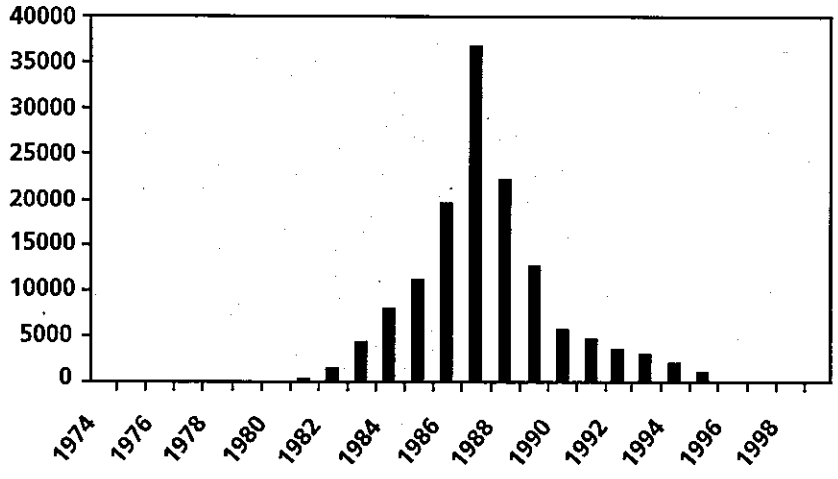
2.7 BSE infectivity in meat

A large number of studies, known as 'bioassays', have been carried out to determine which tissues in BSE-infected cattle carry the BSE agent.

Table 1 shows the very broad range of tissues that have been collected from cattle showing clinical BSE and injected into mice without producing signs of TSE. Similar bioassays conducted by inoculation of tissues into cattle have since failed to detect BSE infectivity in a similar range of tissues (muscle, sciatic/radial nerves, salivary gland, liver, spleen, thymus, lymph nodes, white blood cells, bone marrow, skin and urine)[6].

It is significant that BSE infectivity has not been detected in any of the tissues that are commonly eaten (the muscles, or 'meat', and milk) or traded internationally (semen and embryos).

Figure 1: BSE cases in the United Kingdom, by year of animal's birth



4 http://www.defra.gov.uk/animalh/bse/statistics/bse/monthlystats.pdf
5 http://www.promedmail.org/pls/promed/f?p=2400:1000
6 Dr Danny Matthews. Veterinary Laboratories Agency. United Kingdom. Personal communication with Stuart C MacDiarmid, October 2004.

Table 1: Tissues from confirmed, naturally-occurring cases of BSE in cattle in which no infectivity was detected by bioassay in mice injected both intracerebrally and intraperitoneally [7]

Nervous tissues	Lymphoreticular tissues
Cerebrospinal fluid	Spleen
Cauda equina	Tonsil*
Peripheral nerves:	Lymph nodes
- sciaticus	- prefemoral
- tibialis	- mesenteric
- splanchnic	- retropharyngeal
Alimentary tract	**Reproductive tissues**
Oesophagus	Testis
Reticulum	Prostate
Rumen (pillar)	Epididymis
Rumen (oesophageal groove)	Seminal vesicle
Omasum	Semen
Abomasum	Ovary
Proximal small intestine**	Uterine caruncle
Distal small intestine	Placental cotyledon
Proximal colon	Placental fluids :
Distal colon	- amniotic fluid
Rectum	- allantoic fluid
	Udder
	Milk
Other tissues	
Blood :	Liver
- buffy coat	Lung
- clotted	Muscle
- foetal calf	- semitendinous
- serum	- diaphragma
Bone marrow	- longissimus
Fat (midrum)	- masseter
Heart	Pancreas
Kidney	Skin
	Trachea

* Tonsil was found positive in the cattle bioassay.

** Infectivity has been detected in the distal ileum of cattle *experimentally* infected with a large oral dose of infected brain.

It can be seen, then, that BSE infectivity is not found in the tissues that people commonly regard as 'beef' and eat. How, then, did people become infected with the BSE agent? Pathogenicity experiments in mice and cattle have shown that infectivity in cattle is largely confined to the central nervous system: brain, spinal cord, eye, and associated ganglia, with a small amount sometimes detectable in tonsils and terminal ileum (see Table 2). Mice bioassays have been shown to be a very sensitive method for detecting the BSE agent.

7 http://europa.eu.int./comm/food/fs/sc/ssc/out296_

Table 2: Distribution of BSE infectivity in the tissues of a clinically affected cow[8]

Tissue	ID50 per case	% Total infectivity
Brain	25,000	60.2%
Spinal cord	10,000	24.1%
Dorsal root ganglia	1,500	3.6%
Trigeminal ganglia	1,000	2.4%
Distal ileum	4,000	9.6%
Tonsil	0.25	< 0.1%

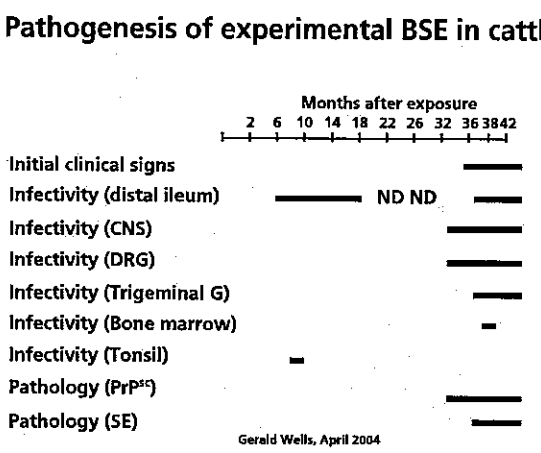
BSE infectivity is not detectable in any of these tissues until relatively late in the course of the disease in cattle – nor is the accumulation of the abnormal form of the prion protein PrP^{SC}, which is associated with this family of diseases, nor lesions in the brain (See Figure 2).

It can be seen that, with the exception of distal ileum (part of the small intestine) and tonsil (a single experimental result only), infectivity is not detectable until around 32 months after inoculation. Cattle are usually slaughtered for beef at less than this age.

Since tissues from the central nervous system were not a feature of the British diet, it remained unclear how humans had become exposed until 'mechanically recovered meat' came under the spotlight. Mechanically recovered meat is recovered from bones (such as the vertebral column) of cattle by high pressure techniques. The resulting product, a meat paste, was commonly used in burgers, sausages, pies, baby food and similar processed products.

Spinal cord was removed before vertebral columns were processed to harvest this meat, but each segment of the backbone includes two dorsal root ganglia. These were being collected along with the meat paste, and therefore as much as 2% of the resulting product could be central nervous system tissue. That is, a 100 gram sausage might contain two grams of infectious material, and the infectious oral dose of BSE for a sheep had been shown to be only 0.5 grams. It is now considered probable that it was the dorsal root ganglia in mechanically recovered meat that exposed British consumers to BSE infectivity in their diet.[10,11]

Figure 2: The pathogenesis of experimental BSE in cattle showing the times after inoculation when infectivity, abnormal prion protein and lesions become detectable[9]



2.8 Gelatine

Originally there were fears that the BSE prion might be present in gelatine prepared from bovine tissues, and this led to precautionary measures to protect consumers in New Zealand and overseas. The scientific basis of this risk has recently been reviewed by NZFSA, whose analysis was also subjected to peer review. The full analysis is attached in Appendix 2.

Recent experimental studies have confirmed that the chemical processes used in the manufacture of gelatine (see Appendix 2) are sufficient to inactivate any BSE infectivity that might have been present in the raw material, even under worst-case conditions. The experimental studies were designed to insure that they accurately represented the "lowest common denominator" of current industrial processes. That is, the times, temperatures and alkaline pH were the lowest found in industrial gelatine production.[12]

Gelatine produced by modern industrial processes can thus be considered to pose no BSE risk to consumers, regardless of the source country from which it is derived.

8 Adapted from the European Commission's Scientific Steering Committee

9 Based on data in http://europa.eu.int./comm/food/fs/sc/ssc/outcome_en.html . Dr Gerald Wells. Veterinary Laboratories Agency. United Kingdom. Personal communication with Stuart C MacDiarmid, April 2004. Since published; Wells GAH, Spiropoulos J, Hawkins SAC, Ryder SJ (2005) Pathogenesis of experimental bovine encephalopathy: preclinical infectivity in tonsil and observations on the distribution of lingual tonsil in slaughtered cattle. Veterinary Record 156: 401-407.

10 Chadeau-Hyam M, Tard A, Bird S, Le Guennec S, Bemrah N, Volatier J-L, Alperovitch A. Estimation of the exposure of the French population to the BSE agent: comparison of the 1980-95 consumption of beef products containing mechanically recovered meat in France and the UK, by birth cohort and gender. Statistical Methods in Medical Research. 2003. 12:247-260.

11 Cooper JD, Bird SM. UK dietary exposure to BSE in beef mechanically recovered meat: by birth cohort and gender. Journal of Cancer Epidemiology and Prevention. 2002. 7: 59-70.

12 Dr. Uwe Seybold, DGF STOESS AG, Eberbach, Germany. Personal communication with Stuart C MacDiarmid, 30 May 2005.