Appendix 1: OIE Code Safeguards

When considering whether to permit the importation of foods from countries where BSE has been shown to be present, or where the BSE status has not been determined, the OIE's 2005 edition of the Terrestrial Animal Health Code recommends the following measures to protect the consumer:

1) That the cattle from which the fresh meat and meat products originate:

a) are not suspect or confirmed BSE *cases*;

b) have not been fed meat-and-bone meal or greaves;

c) were subjected to ante-mortem and post-mortem inspections; and

d) were not subjected to a stunning process, prior to slaughter, with a device injecting compressed air or gas into the cranial cavity, or to a pithing process.

2) That ante-mortem and post-mortem inspections were carried out on all cattle from which the fresh meat and meat products originate.

3) That cattle from which the fresh meat and meat products destined for export originate were not subjected to a stunning process, prior to slaughter, with a device injecting compressed air or gas into the cranial cavity, or to a pithing.

4) That the fresh meat and meat products do not contain:

a) the tissues listed in Table 5 (in body of report)

b) mechanically separated meat from the skull and vertebral column from cattle over 30 months of age, *or*

c) nervous and lymphatic tissues exposed during the de-boning process

and that all of these have been completely removed in a manner to avoid contamination with these tissues.

BSE infectivity has not been detected in skin (see Table 1 in body of report), and for this reason no BSE-specific safeguards are required for gelatine prepared solely from hides and skins. However, gelatine is also manufactured from bones and so, if such gelatine were to be imported from a country where BSE is present, or where the BSE status has not been determined, the OIE's 2005 edition of the Terrestrial Animal Health Code recommends the following measures to protect the consumer:

a) skulls and vertebrae (except tail vertebrae) have been excluded

b) the bones have been subjected to a process which includes all the following steps:

i) pressure washing (degreasing)

ii) acid demineralisation

iii) prolonged alkaline treatment

iv) filtration,

v) sterilisation at $\geqslant$138°C for a minimum of 4 seconds, *or* to an equivalent process in terms of infectivity reduction.

Appendix 2: European Union's Geographical BSE Risk-Assessment System

Introduction

The main task of the agency completing the geographical BSE risk assessment (GBR) assessment (namely, the Scientific Steering Committee (SSC) of the European Union and, since 2003, the European Food Safety Authority as defined and amended by the SSC) is to assess whether the presence of one or more infected cattle in a given country is:

- highly unlikely (GBR I)
- unlikely, but not excluded (GBR II)
- likely, but not confirmed or confirmed at a lower level (GBR III)
- confirmed at higher level (GBR IV)

The following should be noted when considering the GBR assessment process within its five-category system:

- In making the GBR assessment, a reasonable worst-case (i.e. conservative) position has been taken every time data were insufficient.
- The SSC has stated that it is aware that the borderline between GBR levels III and IV has to remain arbitrary, as no clear scientific justification can be provided for this differentiation. GBRs adopt the OIE threshold, i.e. an incidence of more than 100 confirmed BSE cases per million within the cattle population over 24 months of age in the country or zone, calculated over the past 12 months.
- The SSC also agrees with the OIE that, under certain circumstances, countries with an observed domestic incidence between 1 and 100 BSE-cases per million adult cattle calculated over the past 12 months should be put into the highest risk level – if, for example, there are clear indications that the true clinical incidence is in fact higher than 100 per million adult cattle calculated over the past 12 months.
- The SSC believes that decisions aimed at managing the BSE risk are the responsibility of the authorities in charge, and might need to take into account other aspects than those covered by this risk assessment.
- The GBR of a country has no direct bearing on human exposure to BSE. The SSC has stated that, at a given GBR, the risk that food is contaminated with the BSE agent depends on three main factors:

b. the likelihood that infected bovines are processed (i.e. whether systems exist to detecting and exclude at-risk animals from processing)

c. the amount and distribution of infectivity in BSE-infected cattle at slaughter (killing methods, age of animals)

d. the ways in which the various tissues that contain infectivity are processed (SRMs, mechanically recovered meat, advanced meat recovery).

The GBR levels, New Zealand's BSE categories, and the current and recently accepted OIE code categories roughly align in the following way:

GBR levels	NZ Current BSE Measure categories	Current OIE Code recommendations	Future OIE Code recommendations & proposed NZ BSE Measure (key differences discussed next section)	
I Highly unlikely	Category 1: Country or region free of indigenous BSE	BSE-free country or zone	Negligible BSE risk (Some fall into next category, "controlled BSE risk".)	
II Unlikely but not excluded	Category 2: Provisionally free country or region where no indigenous case has been reported	Provisionally BSE-free country or zone	Controlled BSE risk (Can include countries previously categorised in the NZ system as 1-5)	Undetermined BSE risk (Can include countries previously categorised in the NZ system as 2-5)
III Likely but not confirmed or confirmed at a lower level (incidence <100)	Category 3: Provisionally free country or region where at least one indigenous case has been reported Incidence: <1/m(E4x12)	Country or zone with a minimal BSE risk Incidence: <2/m(E4x12) *		
	Category 4: Country or region with low incidence of BSE Incidence: 1/m≤ι≤100/m(12)§	Country or zone with a moderate BSE risk Incidence: 2/m(<4x(E4x12)†		
IV Confirmed at a higher level (incidence 100)	Category 5: Country or region with high incidence of BSE Incidence: I>100/m(12) ¥	Country or zone with a high BSE risk ‡		

Key to incidence rates:

* Less than two indigenous BSE cases per million during each of the last four consecutive 12-month periods within the cattle population over 24 months of age.

† Less than two indigenous BSE cases per million for less than four consecutive 12-month periods

‡ Unable to demonstrate whether it meets requirements of other OIE categories

Ð Less than one indigenous case per million during each of the last four consecutive 12-month periods within the bovine population over 24 months of age

§ Less than one indigenous case per million within bovine population over 24 months of age

¥ Greater than 100 cases per million within the bovine population over 24 months of age

GBR assessments are based on the current OIE Code recommendations for risk analysis. The categories align with those recommended by the OIE, even though there are four GBR categories and five OIE Code categories.

The new three-category system to be adopted by the OIE is a significant change and sets the 'bar' at a very high level for entry to the 'Negligible BSE risk' category. New Zealand has had to enhance its surveillance programme to meet the new requirements. If the GBRs align with the OIE 3 category system in future, then we will need to consider the effects of this on our imported food Measure.

The criteria for defining the OIE Code's three categories are very different than those used to define the previous five categories. The OIE has moved away from the categories being based on the BSE incidence for the country being categorised, to recognition of risk assessments and measures in place to effectively manage the risk of BSE. New Zealand's proposed BSE Measure reflects this shift. Key differences between New Zealand's proposed Measure and the OIE Code recommendations are outlined in the section below.

The OIE is recognised by the SPS Agreement as the relevant international organization that develops the sanitary measures required to manage human and animal health risks associated with BSE. As a signatory, New Zealand is obliged to base its measures on the relevant international standards where they exist, and otherwise to be judged scientifically.

Since 1989, the European Commission, in close co-operation with the Member States, has taken a series of measures to manage the risk of BSE in the European Union. Regulation (EC) No 999/2001 of the European Parliament and of the Council of 22 May 2001 brings all existing BSE measures as adopted over the years through more than 60 Commission Decisions into a single, comprehensive framework, consolidating and updating them in view of scientific advice and international standards. In addition, it introduced a number of new instruments to manage the risk of BSE and other similar diseases such as scrapie in all animal species and relevant products.

Currently, 66 countries have been assessed and have a GBR categorisation. The adoption of the GBR country categorisation system would increase New Zealand's international trade and alleviate resource difficulties, whilst being confident that the methodology to assess a country's GBR is sound and based on the OIE BSE Chapter (as detailed below).

It should be noted that the GBR is based on animal health, and has no direct bearing on human exposure to BSE. GBR would, however, provide New Zealand with a base categorisation system (indicating a country's BSE-risk status) enabling human-health standards to be applied by New Zealand in a manner appropriate to that country's BSE-risk status.

Methodology for GBR Determination

The final opinion of the SSC on the GBR (adopted 6 July 2000) describes the transparent and qualitative nature of this methodology. In addition, it also states that its limitations should be understood in the context of present scientific knowledge on BSE, and of the availability and quality of data. Therefore, as both knowledge and data evolve, and with the advancement of new diagnostic methods, the SSC states that the methodology may need to be revised and/or its application to particular countries be repeated (i.e. a reassessment).

This statement ensures that a country's GBR is kept up to date with any changes (either science-based or specific to a country) – a requirement that creates difficulties for New Zealand, due to the resources required.

The last update was released on 11 January 2002, and the methodology detailed below is based on the latest "Update of the Opinion of the SSC on the GBR".

Basically, the GBR methodology tries to answer two questions:

1. Is there a risk that the BSE agent was imported into the country under consideration?
2. If the BSE agent was introduced into a country, would it have been recycled and amplified, or was the BSE/cattle system of that country able to eliminate the agent?

Basic Assumptions

Origin and transmission

The assessment of the GBR is based on the assumption that BSE originated from the United Kingdom (UK) and that the agent was transmitted through the recycling of bovine tissues into animal feed.

Thus for countries other than UK, the importation of contaminated feed or infected animals is the only possible initial source of BSE that is considered. No other sources or transmission routes are considered, as they have not been scientifically confirmed

Geographical Limitation

Present GBR risk assessments only address entire countries and national herds due to limited regional data. Therefore it should be noted that free trade zones are not considered.

Information Factors

Eight factors are used for assessing the GBR:

1. Structure and dynamics of the cattle, sheep and goat populations
2. Surveillance of BSE
3. BSE-related culling
4. Import of cattle and meat and bone meal (MBM)
5. Feeding
6. Bans on meat-and-bone meal (MBM)
7. Bans on risk materials (SRMs)
8. Rendering.

A qualitative model of the BSE/cattle system details the interaction between these factors. Factors can activate or prevent the activation of the loop, or slow down or reverse the building up of BSE infectivity within the system.

External Challenge

The initial sources of BSE must come from outside the relevant country. Two possible outside sources are considered in the model: import of infected cattle, or import of contaminated MBM (factor 4). These are referred to as an external challenge.

The term "external challenge" refers to both the likelihood and the amount of the BSE agent entering a defined geographical area in a given time period, through infected cattle or MBM.

The following basic guidelines for assessing the external challenge are:

1. The external challenge is regarded independent from the size of the challenged BSE/cattle system, and in particular the size and structure of the cattle population.
2. The assumed challenge resulting from imports from the UK during the peak of the BSE-epidemic in the UK is the point of reference.
3. The challenge resulting from imports during other periods and from other BSE-affected countries is established in relation to this baseline.

It should be noted that imports from all countries with a BSE risk are considered when assessing the external challenge of an individual country. This is in light of scientific knowledge that active surveillance (testing of cattle that are not notified as BSE suspects, but belong to risk sub-populations) detects BSE cases that would have remained undetected by passive surveillance, which targets cattle with neurological symptoms.

Stability

The ability of a BSE/cattle system to prevent the introduction of the BSE agent and to reduce the spread of the BSE agent within its borders is referred to as the stability of the system. Therefore, feeding of MBM to cattle (factor 5), rendering (factor 8) and SRM bans (factor 7) are the main stability factors which could either eliminate BSE over time ("stable" system) or amplify it ("unstable system").

Surveillance (factor 2) activities (both active and passive) that ensure the detection, isolation and destruction of BSE cases and cattle at risk of being infected would also enhance the stability of a system. In combination with appropriate culling (factor 3); both these factors would improve the stability by supporting the exclusion of BSE-infectivity from the system.

Internal Challenge

The likelihood of, and the amount of the BSE-agent being present and moving in a specific geographical area in a given period of time, are known as the "internal challenge". Therefore, the overall challenge is the combination of external and internal challenges being present in a BSE/cattle system at a given point of time.

Interaction of Overall Challenge and Stability over Time

Four basic combinations of stability and challenge are:

1. A "stable" system is not or only slightly "challenged"
   This is the best situation.
2. A "stable" system is significantly "challenged"

This is still rather good, because the system will be able to cope with the challenge, even if this might need some time.

3. An "unstable" system is not or only slightly "challenged"
   As long as BSE is not entering the system, the situation is good. However, even a small challenge could spark the amplification of the BSE problem.
4. An "unstable" system is "challenged"

This is an unfortunate situation. The BSE infectivity will be amplified and an epidemic can develop.

Procedure for Assessing the GBR

1. Appraisal of the quality of the available data'
2. Assessment of the Stability of the BSE/cattle system (over time)
   - 2.1 Ability to identify BSE-cases and to eliminate animals at risk of being infected before they are processed (Factors 1, 2 and 3). The quality of the surveillance (factor 2) is of critical importance for this aspect of stability.
   - 2.2 Ability to avoid recycling BSE-infectivity, should it enter processing (Factors 5, 6, 7, and 8)
   - 2.3 Overall assessment of the stability (over time)
3. Assessment of the challenges to the system (over time)
   - 3.1 External challenge resulting from importing BSE (factor 4)
   - 3.2 Internal challenge resulting from domestic infected animals
   - 3.3 Overall assessment of the challenges (over time)
4. Conclusion on the resulting risks (over time)
   - 4.1 Interaction of stability and challenge (over time)
   - 4.2 Risk that BSE-infectivity enters processing (over time)
   - 4.3 Risk that BSE-infectivity is recycled and the disease propagated (over time)
5. Conclusion on the Geographical BSE-Risk
   - 5.1 The current GBR as function of the past stability and challenge
   - 5.2 The expected development of the GBR as a function of the past and present stability and challenge
   - 5.3 Recommendations to influence the expected development of the GBR

GBR Updates – Process for Review

New scientific knowledge and data which may arise trigger an update to the GBR methodology, including re-apply it to countries that were assessed previously. Therefore, the GBR report/opinion is subject to change as more scientific evidence becomes available.

New evidence or knowledge may relate to the source of BSE, to the diagnosis and transmissibility of BSE, or to the infective dose for humans. In addition, developments in surveillance and management techniques or new tests to assess the prevalence of sub-clinical BSE conducted in a country may also lead to the need for a selective re-assessment of a particular GBR.

However, the SSC's experience in assessing changes in the challenges and stability of countries suggests that trends in incidence figures may allow new conclusions to be drawn only after three to five years. In any case, the current assessments have to be updated from time to time.

With the proposed adoption of the GBR country categorisation system, New Zealand would have to decide whether this level of process review is adequate or whether to develop its own criteria for review.

GBR's relationship with the OIE Code on BSE

As mentioned previously, the method for assessment of the GBR is comparable to the OIE guidance on risk analysis, and in particular to the chapter on risk assessment. Each proposes very similar factors that are to be taken into account.

The SSC method also involves an external review of the GBR on the basis of information provided by countries. Considering the long incubation period of the disease and its initially slow progress, it tries to cover the last 20 years.

The latest updates to the OIE BSE chapter must also be considered when adopting the GBR system. New Zealand must ensure that the GBR methodology is still in line with OIE requirements. The latest measure in relation to country categorisation adopted by the OIE is the change from a five-category system to a three-category system, namely: negligible BSE Risk, controlled BSE risk and undetermined BSE risk.

This change in the number of categories does not change the method of categorisation, but rather the outcome of the assessment.

The GBR methodology for country categorisation remains in line with OIE requirements and New Zealand's adoption of the GBR system would align it with the European Union (EU) BSE country categorisation and the OIE BSE chapter.

Appendix 3: Exempting processed foods containing minimal bovine ingredients from the BSE Measure

An exemption is the preferred option for the reasons outlined below. Other options were considered and the arguments for and against each are noted.

Problem: Bovine-derived ingredients are often a minor component of imported ingredients used to make products. For some products, this trail can involve more than three countries' competent authorities. Importers are currently required to obtain a trail of competent authority certification back to the country in which the bovine animal used in the ingredient was born, reared and slaughtered. Obtaining this certification for some products has proved to be very difficult or impossible for New Zealand importers.

Option One: Exemption of processed food

Remove the requirement for certification for processed products containing a small percentage of bovine material when consumed.

Exempting processed products containing negligible bovine meat content is consistent with the Canadian Meat Inspection Regulations, which states:

- "Processed foods such as bouillon, soups, and stock cubes that contain negligible meat content (i.e. less than 2% of rendered fat and meat extract in the ready-to-serve product after added water) are exempt from the Meat Inspection Regulations.
- Other products such as salad dressing, dairy-base dip, flavouring, seasoning preparations and cheeses containing 3% or less of meat ingredients are not considered meat products for the purpose of the Meat Inspection Regulations.
- These products are not subject to CFIA meat import controls and can be imported from any country."

It is recommended that the threshold be set at three percent to reflect the reality of the beef content in many processed products. These products pose negligible risk but are captured by current measures. Setting one threshold also prevents confusion, for example around deciding whether a product is flavouring (at the Canadian three percent or less) or whether it is a stock cube (at less than two percent).

While an informal survey has been carried out to ascertain the beef content in many processed foods, it is recommended that a more detailed survey be completed to determine if three percent is a realistic cut-off point and what proportion of processed foods would fall into the category of three percent or less. If the survey shows that a significant amount of processed foods contain less that two percent beef, or four percent or less, the limit should be adjusted.

It is suggested that the Manufactured Food Database may be a useful resource for such a survey. The database collects information from food manufacturers, 20% of which are based in Australia with the remainder in New Zealand; all foods are sold in New Zealand. The labelling survey that was completed in $2004_{[H1]}$ could be used to collect information on foods from other countries and to ascertain if there are significant differences in manufacturing practices.

This information may then be used to categorise foods so they can easily be identified at the border as falling into the exempted categories e.g. all noodle packs with meat flavour sachets may be exempted as all those surveyed contained less than two percent beef. A review of the tariff codes will be necessary when establishing a new standard and the exempted foods should be kept in mind during this process as eliminating tariff codes that target exempted processed foods would be the ideal option.

A database of exempted and non-exempted products should be developed and built upon over time for use by Health Protection Officers. Health Protection Officers should be given training to ensure they understand criteria for exempted products and can investigate new products and refer them to be approved for adding to the database.

Background

When BSE was first discovered most countries responded with conservative measures to reflect the unknown level of risk of BSE and the severe consequences to public health. Since the last New Zealand measure was implemented in 2001, significantly more is known about the disease. Production and processing controls have dramatically reduced the incidence of BSE and products have been exempted from measures as the evidence has shown these products to pose negligible or non-existent risk.

The major source of human exposure to the BSE agent was meat recovered mechanically (MRM) from bovine vertebral columns.[25]

Mechanical recovery of meat from vertebral columns is now prohibited in the European Union.

The source of BSE infectivity in MRM was from fragments of spinal cord remaining after incomplete removal, and from dorsal root ganglia (DRG).

It was concern over the presence of DRG in T-bone steaks which led to a British ban on bone-in beef. However, it has been estimated that an individual consuming one DRG from a BSE-infected carcass would ingest only between 0.015 and 0.5 of a human oral ID50 (infectious dose 50%).[26]

25 Gale, P. (1998) Quantitative BSE risk assessment: relating exposure to risk. Letters in Applied Microbiology. 17. 239-242.

26 Cooper, JD, Bird, SM. (2002) UK dietary exposure to BSE in beef mechanically recovered meat: by birth cohort and gender. Journal of Cancer Epidemiology and Prevention. 7 (2). 59-70.

In 1995, the last year in which MRM was harvested in the UK, it has been estimated that the BSE infectivity present in beef MRM was 12.8 ($CL_{95\%}$ 10.6 – 14.9) bovine ID_{50} **per tonne.**[27]

One human ID_{50} is approximately 10 bovine ID50.28 This means that BSE contamination of beef MRM in 1995 would have been about 1.28 human ID_{50} per tonne. That is, a person would need to consume a tonne of MRM to have a 50% chance of becoming infected.

A product containing 3% of beef, if made from British MRM in 1995, would contain no more than about 0.04 human ID50 per tonne. That is, for a consumer to have a 50% chance of becoming infected with BSE, they would need to consume 25 tonnes of the product. This is, however, a worst-case scenario, as harvesting of MRM from vertebral columns was banned in the UK in 1995, and the incidence of BSE in the UK has dropped from 14,562 cases in that year to 151 cases in 2005.29 That is, the incidence of BSE in the UK, the worst affected country, has declined nearly a hundredfold since 1995.

While the BSE risk cannot be precisely quantified, the science clearly illustrates there is an extremely low level of risk of BSE from such products. As a result, the high degree of scrutiny required to monitor such products cannot be justified by the risk posed.

Consistency with International Standards

Under the WTO Sanitary and Phytosanitary Agreement, member countries should only apply measures that are necessary to protect human, animal or plant health. The Agreement provides for more conservative measures where there is uncertainty as was the situation when BSE first emerged. There is now a better understanding of the disease and the source of the risk so that, although the risk may not be quantitatively measured in any meaningful way, it can be qualitatively assessed against the probability of 'entry, establishment or spread'[30] of the disease.

International standards have taken a broad approach to defining meat with the OIE and the EU defining meat as 'all edible parts of an animal' and Codex defining it as 'all parts of the animal that are intended for, or have been judged as safe and suitable for, human consumption'. The preferred method of avoiding inadvertent capture of products posing negligible or non-existent BSE risk is to exempt by commodity.

Exempting processed products containing three percent or less of bovine meat will be consistent with international practice in terms of risk assessment and through the use of exemptions.

Option Two: Status Quo

Require all processed products containing bovine derived ingredients to be accompanied by competent authority certification.

Argument for:

It may be perceived that the status quo is a belts and braces approach to food safety and if it results in the saving of one life (although it would not be possible to attribute any saving to such a measure) it will have been worth the cost and administrative difficulties.

Argument against:

The Code of Good Regulatory Practice notes that regulatory benefits should outweigh the costs and regulation should be to the minimum extent necessary.

Beef content in processed foods is often sourced from different countries depending on availability and market price. Continuing with the status quo will require substantially more resource from regulators (to monitor) and from importers. There is no evidence to suggest that the costs of this regulation will measurably increase New Zealand's level of protection from vCJD.

Option Three: Case-by-case assessment

Decide exemptions product by product following individual risk assessments.

Argument for: Science-based, consistent with SPS Agreement

Argument against: Expensive exercise and not likely to be taken up by importers as the need for a new risk assessment may arise each time the supply is changed.

The costs would not outweigh the benefits.

27 Grist, EPM. (2005) Transmissible spongiform encephalopathy risk assessment: the UK experience. Risk Analysis. 25 (3). 519-532.

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

29 Definition of risk assessment, SPS Agreement, Annex A, par 4 found at http://www.wto.org/english/tratop_e/sps_e/spsagr_e.htm

30 http://www.geafiltration.com/html/library/gelatin/gelatin_world_production.htm

31 Based on figures cited in Schrieber R, Seybold U (1993) Gelatine production, the six steps to maximum safety. In Transmissible Spongiform Encephalopathies – Impact on Animal and Human Health. Edited by F Brown. Developments in Biological Standardization. Volume 80. Karger, Basel: 195- 198.

32 Grobben AH, Steele PJ, Somerville RA, Taylor DM (2004). Inactivation of the bovine spongiform encephalopathy (BSE) agent by the acid and alkaline processes used in the manufacture of bone gelatine. Biotechnology and Applied Biochemistry, 39. 329-338.

33 Schrieber R, Seybold U (1993) Gelatine production, the six steps to maximum safety. In Transmissible Spongiform Encephalopathies – Impact on Animal and Human Health. Edited by F Brown. Developments in Biological Standardization. Volume 80. Karger, Basel: 195- 198.

34 http://europa.eu.int./comm/food/fs/sc/ssc/out296_en.pdf

Appendix 4: Does gelatine pose a BSE risk to consumers?

Stuart C MacDiarmid, Principal Adviser, Zoonoses and Animal Health, New Zealand Food Safety Authority

BSE is a member of a family of diseases known as transmissible spongiform encephalopathies (TSEs). These are generally considered to be caused by infection with proteinaceous agents known as a "prions".

In 1996, human cases of a new TSE known as variant Creutzfeldt-Jakob disease (vCJD) were reported in the United Kingdom and were soon shown to be caused by human infection with the BSE agent. Because of this BSE risk to human health, many precautionary measures were implemented around the world at that time. Because of fears that the BSE prion might be present in foods prepared from bovine tissues, including gelatine, precautionary measures to protect consumers were implemented in New Zealand and overseas.

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

Total world production of gelatine in 2003 was 278,300 tonnes.[31] Probably around 65% of this was produced from bovine materials.[32] Gelatine is made either from hides or bones and although there are differences in the processes, both involve a series of chemical steps which have some capacity to inactivate the BSE agent.[33, 34]

Raw materials

Gelatine is produced either from skin or bones of cattle and pigs. BSE is not a disease of pigs, so gelatine produced from porcine raw materials has never been of concern.

Hides are considered a safe source of raw material because BSE infectivity has not been found in skin, even in advanced clinical cases.[35] More gelatine is produced globally from skins than from bone.[36] BSE infectivity has been found in the bone marrow in advanced disease in a single experimentally-infected animal[37], but has not been detected in bone marrow of infected cattle before they show clinical signs.

The global BSE epidemic is in decline, although occasional cases are still detected in countries with a history of feeding cattle on meat and bone meal containing the BSE agent, and occasional cases may also be expected, in future, in countries hitherto considered BSE free.

The first step in processing the bones for gelatine manufacture is to grind them into pieces. Hides and skins are also chopped into small pieces. Hides may arrive at the gelatine plant in the form of 'hide splits', a by-product of the tanning industry. Hide splits are the lower part of the cutis or corium.[38] The upper part of the cutis is used for leather production.

Gelatine is produced either from bone or from skin. The two raw materials are not mixed.

Dilution

As with all infections, with BSE there is a minimum level of infectivity necessary to transmit the infection. In the case of transmission to humans, there is also a species barrier to be surmounted.

Should an animal infected with BSE pass ante-mortem inspection and contribute raw materials to gelatine manufacture, its tissues would be diluted by those from a large number of normal, uninfected animals. The average weight of raw material used from one animal, depending on age, will be approximately 10-15 kg.[39] (In New Zealand, where gelatine is manufactured from head skins, the average weight is 3 kg.40) The normal batch size used in the industrial production of gelatine varies from around 20,000 to 100,000 kg. (In New Zealand, the normal batch size is 28,000 kg.)

This means that the dilution factor of raw material from one animal into an industrial batch is between $10^{3.5}$ and 10^{5}. So, regardless of any further treatment, in theory only in advanced clinical disease would there be detectable infectivity in the final product.[41]

In the country with the highest incidence of BSE, the UK, there were 338 cases of the disease in 2004. That is, the annual BSE incidence rate is 68 per million cattle over 24 months of age.[42] This is the highest rate in the world.

Using the data given above for average weight of raw material per animal and average industrial batch size, it can be calculated that the average number of animals contributing to a single batch is 4,800 (SD 1,880).[43] From these data and the annual incidence of BSE in the United Kingdom in 2004, it can be calculated using the software programme @Risk[44] that the mean number of BSE cases which could contribute to a batch of gelatine, assuming that they were to escape detection, would be 0.33 animals per batch (upper 95 percentile, 0.66 animals).

I developed an @Risk simulation model to estimate the likely BSE contamination of gelatine produced in the UK from bones including the vertebral column (vertebral column is actually banned from all food uses in the UK and so is not, in reality, used in gelatine production). If vertebral column of cattle were used in the production of gelatine, BSE infectivity could be present in remnants of spinal cord and associated dorsal root ganglia (DRG). It has been estimated that the weight of DRG in a typical carcass is 30 g and the weight of spinal cord is 200g.[45] The simulation model assumed that something between 0 and 100% of the spinal cord might remain in vertebral column used in gelatine production, but that the most likely quantity was 10%. The model further assumed that all the DRG material would be included.

35 http://www.geafiltration.com/html/library/gelatin/gelatin_world_production.htm

36 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.

In an assessment of the risk to human health from inclusion of DRG in foods such as 'T bone' steaks, Comer assumed that the best estimate of the oral infectivity for humans of spinal cord and DRG derived from cases of BSE is 1 human oral ID_{50} /g,[46] with a confidence range of 0.0001 to 10.[47]

Using the data outlined above, the @Risk model estimated that the mean BSE contamination of raw material containing vertebral column of UK origin (an extremely unrealistic scenario) would be 9.8×10^{-7} human oral ID_{50} /Kg (upper 95% 3.03×10^{-6}).

It can be expected, on the basis of experimental studies described below, that this quantity of BSE infectivity is likely to be eliminated entirely by the processes used to manufacture gelatine.

Removal of hair

After skin has been chopped into small pieces, hair is removed by tumbling in drums containing a mixture of sodium sulphide and lime.[48] This process not only removes the hair, but would also be expected to remove any surface contamination with tissues (such as brain) which might contain BSE agent. Hide splits, which are a by-product of the tanning industry, do not have hair.

Bone degreasing

Bone itself is free from BSE infectivity, but infectivity has been detected in bone marrow in a single advanced clinical case in an experimentally-infected animal. Infectivity is, of course, present in high concentration in spinal cord and dorsal root ganglia, both of which can be expected to contaminate vertebral column used to produce the degreased chipped bone (DCB) used in the manufacture of gelatine.

Before bone can be used to manufacture gelatine, fat must be removed. This is done by crushing the bones to a particle size of less than 12 mm and then washing and degreasing the resulting chips with hot water to remove residues of fat, marrow and other soft tissues such as spinal cord and dorsal root ganglia. (In Europe, where BSE is present, vertebral columns are classified as 'specified risk material' (SRM) and are not used in gelatine production.)

Studies conducted on the ability of the degreasing process to remove nervous tissue proteins from bones demonstrated that degreasing eliminated 98% to 99% of such proteins.[49] It has been estimated that the degreasing process alone would reduce any BSE contamination of bone by a factor of approximately 10^{2}.[50]

Acid treatment

Before bone chips can be used to produce gelatine, the minerals calcium and phosphorus must be removed. This is achieved by immersion of the DCB in hydrochloric acid (approximately 4%, <pH 1.5) for a period of at least 2 days. This intensive acid treatment changes the internal structure of the collagen protein, from which gelatine is extracted, as well as the structure of the BSE prion protein. On the basis of previous studies[51], this acid treatment would be expected to reduce the titre of any BSE infectivity which might be present. The demineralized bone is known as ossein.

Alkaline treatment

The next step in the production of gelatine is to soak the materials (pieces of skin or ossein) in a saturated lime solution, >ph 12.5, for a period of between 20 and 50 days[52,53] (40 in New Zealand.[54])

A treatment sometimes used with a raw material known as hidesplits (split form of skin) is to soak the material in 0.3n sodium hydroxide (caustic soda) for around 14 days.

As with the acid treatment referred to above, this alkaline treatment changes the internal structure of the collagen protein, as well as the structure of the BSE prion protein. On the basis of studies conducted into the destruction of TSE agents[55], it has long been expected that the time, temperature and concentration of these alkaline treatments would significantly reduce the titres of any BSE infectivity present in the raw materials.[56]

Further acid treatment

Some gelatine is also produced from ossein (demineralized bone) by an acid process, rather than by an alkaline one. In this acid process, the ossein is immersed for 12-24 hours in dilute acid at pH2-3.5.

Extraction of gelatine

After the skin or ossein has been subjected to alkaline or acid treatment, gelatine is extracted by a series of hot water steps. The gelatine extract is purified by filtration through diatomaceous earth and cellulose filter plates, and this process removes suspended particles.[57,58]

The purified gelatine solution is concentrated by evaporation in partial vacuum and the concentrated solution is sterilized by UHT treatment of at least 138°C for at least four seconds.[59] It is likely that the filtration and sterilization processes also remove some BSE infectivity, in the unlikely event that any should be present by this stage of production.

37 Dr. Uwe Seybold, DGF STOESS AG, Eberbach, Germany. Personal communication with Stuart C MacDiarmid, 8 June 2005.

38 Schrieber R, Seybold U (1993) Gelatine production, the six steps to maximum safety. In Transmissible Spongiform Encephalopathies – Impact on Animal and Human Health. Edited by F Brown. Developments in Biological Standardization. Volume 80. Karger, Basel; 195- 198.

39 Mr. Steve Ford, Purchasing Manager, Gelita New Zealand Ltd. Personal communication with Stuart MacDiarmid, 5 April 2005.

40 Schrieber R, Seybold U (1993) Gelatine production, the six steps to maximum safety. In Transmissible Spongiform Encephalopathies – Impact on Animal and Human Health. Edited by F Brown. Developments in Biological Standardization. Volume 80. Karger, Basel; 195- 198.

41 http://www.oie.int/eng/info/en_esb.htm

42 Terry Ryan, Senior Adviser (Epidemiology & Public Health), New Zealand Food safety Authority. Personal communication with Stuart MacDiarmid 22 April 2005.

Experimental studies

Relatively recently, the results of experimental studies have been published confirming risk assessments made earlier. An accurately scaled down laboratory process was developed to measure the effect of gelatine manufacturing processes on BSE infectivity. The experiment used crushed bones and intact calf vertebral columns. The crushed bone was smeared ("spiked") with mouse brain infected with the 310V strain of mouse-passaged BSE. The same brain was injected into the spinal cord of the vertebral columns. The 301V strain of BSE was selected because it has a high infectivity titre and is one of the most heat-resistant TSE strains.[60]

The BSE infectivity of the spiked starting material was $10^{8.4}$ mouse intracerebral ID_{50} /Kg. Clearance factors of $10^{2.6}$ and $10^{3.7}$ ID_{50} were demonstrated for the first stage of the acid and alkaline processes (see above) respectively. The complete acid and alkaline processes both reduced infectivity to undetectable levels, giving clearance factors of $\geqslant 10^{4.8}$ ID_{50} for the acid process and $\geqslant 10^{4.9}$ ID_{50} for the alkaline.[61]

The level of infectivity used in the experiments reflect worst-case conditions. The experiment did not take into account the very large effect of dilution of raw materials referred to above. Even if a BSE-infected animal contributed a vertebral column to an industrial batch of raw material, the concentration of BSE prion in the batch would not be as great as achieved by the "spiking" described in the experimental study.

Conclusions

In the years since the public health risk posed by BSE was first recognized, much has been learned about the disease. It is now clear that humans are relatively difficult to infect by mouth and that the BSE epidemic is largely under control internationally. This means that any batch of raw material used to produce gelatine is highly unlikely to contain sufficient BSE to be able to infect humans consuming products made from it. Further, recent experimental studies have confirmed what was long suspected; namely, the described chemical processes used in the manufacture of gelatine are sufficient to inactivate any BSE infectivity which might have been present in the raw material from which the gelatine is made, even under "worst case" conditions.

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.

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43 @Risk, Palisade Corporation, Newfield, NY USA.

44 Source: http://europa.eu.int/comm/food/fs/sc/ssc/out13_en.html

45 ID50: this means "the dose which will infect 50% of recipients".

46 Comer, PJ (1997) Assessment of risk from possible BSE infectivity in dorsal root ganglia. Risk assessment for the Ministry of Agriculture, Fisheries and Food and the Spongiform Encephalopathy Advisory Committee. Det Norske Veritas , Technical Consultancy Services, London. 16 pages.

47 Mr Steve Ford, Purchasing Manager, Gelita New Zealand Ltd. Personal communication with Stuart MacDiarmid, 5 April 2005.

48 Manzke U, Schlaf G, Poethke R, Felgenhauer K, Mäder M (1996) On the removal of nervous proteins from materials used for gelatine manufacturing during processing. Pharmazeutische Industrie, 58 (9). 837-841.

Appendix 5: Membership of Review Team

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Appendix 6: Terms of Reference

Project purpose

To review new scientific knowledge and experience concerning BSE and the risks to human health, and propose modifications to the New Zealand BSE Measure as appropriate.

Project strategy

The review will be carried out by a project team made up of NZFSA, Ministry of Health and Ministry of Foreign Affairs and Trade staff with relevant technical, operational, trade and policy skills and knowledge. The project team will be lead by an independent person who has a sound knowledge of relevant national and international issues.

The project team will:

- Review new scientific knowledge and experience with BSE concerning the risks to human health and document its findings,
- Make recommendations on appropriate changes to the current New Zealand BSE Country Categorisation Measure to take account of the new scientific knowledge and experience with BSE, that are consistent with developments occurring in review of the OIE *Terrestrial Animal Health* Code BSE Chapter,
- Consult with appropriate experts within New Zealand, and
- Provide a report to NZFSA which documents the review team's findings and recommendations.

Stakeholders will be informed of and update on progress of the review.

Benefits

New Zealanders effectively protected from exposure to the BSE agent in imported bovine food products for human consumption through the application of sanitary measures that are necessary and appropriate.

Project objectives

1. New scientific knowledge and experience with BSE concerning the risks to human health documented.
2. Changes to the current New Zealand BSE Country Categorisation Measure to take account of the new scientific knowledge and experience with BSE, that are consistent with developments occurring in review of the OIE *Terrestrial Animal Health* Code BSE chapter recommended.
3. Recommendations and proposed modifications to the New Zealand BSE Country Categorisation Measure have science community support.

Final Deliverables

1. Documented review of new scientific knowledge and experience.
2. Report recommending proposed changes to the NZ BSE Measure.
3. Support of New Zealand BSE expert scientific group community.
4. Support of other stakeholders – specifically MoH and MFAT.

Inclusions

- Communication about the project

Exclusions

- Animal health issues associated with BSE
- Development, consultation and implementation of a modified New Zealand BSE Country Categorisation Measure

49 Pharmaceutical Research & Manufacturers of America BSE Committee (1998) Assessment of the risk of bovine spongiform encephalopathy in pharmaceutical products. BioPharm, 11 (3). 18-30.

50 Brown P, Rohwer RG, Gajdusek DC (1986) Newer data on the inactivation of scrapie virus or Creutzfeldt-Jakob disease virus in brain tissue. Journal of Infectious Diseases, 153. 1145-1148.

51 Grobben AH, Steele PJ, Somerville RA, Taylor DM (2004). Inactivation of the bovine spongiform encephalopathy (BSE) agent by the acid and alkaline processes used in the manufacture of bone gelatine. Biotechnology and Applied Biochemistry, 39. 329-338.

52 Schrieber R, Seybold U (1993) Gelatine production, the six steps to maximum safety. In Transmissible Spongiform Encephalopathies – Impact on Animal and Human Health. Edited by F Brown. Developments in Biological Standardization. Volume 80. Karger, Basel: 195-198.

53 Mr Steve Ford, Purchasing Manager, Gelita New Zealand Ltd. Personal communication with Stuart MacDiarmid, 5 April 2005.