

ATYPICAL SCRAPIE IN SMALL RUMINANTS

POSITION STATEMENT ON CONTINGENCY PLANNING

1 EXECUTIVE SUMMARY

1.1 Background

1.1.1 Cattle, sheep and goats suffer from a group of neurological diseases known as transmissible spongiform encephalopathies (TSEs), which include BSE and scrapie. Sheep have been known for hundreds of years to suffer from scrapie, with no apparent association with any human disease. More recently, scientific tests have identified another TSE disease in sheep called atypical scrapie. Atypical scrapie is not BSE, and there is an absence of scientific evidence that it can be transmitted to humans or that it is any risk to humans. However such a risk cannot be ruled out.

1.1.2 The Agency Board has been kept informed about atypical scrapie and has discussed it on several occasions. In June 2006 the Board considered the possible risk from atypical scrapie in relation to the controls in place to protect consumers from the possible risk from BSE in sheep and concluded that no additional measures were needed at that time. However, the Board requested that a contingency plan, for any developments that change the assessment of the risk from atypical scrapie, be put in the public domain. The Board also asked the Agency to issue information to keep consumers and stakeholders up to date with what is known about atypical scrapie.

1.2 FSA advice on atypical scrapie

1.2.1 Further information, including a full statement of the Agency's advice on atypical scrapie, can be found on the Agency's website at <http://www.food.gov.uk/bse/what/atypicalscrapie>.

1.3 SEAC

1.3.1 In May 2007 the Spongiform Encephalopathy Advisory Committee (SEAC) discussed the background to the FSA contingency plan and considered possible results from research or surveillance that would be likely to produce a significant change in their understanding of the risk to humans from atypical scrapie. The Committee's key conclusions were:

- it is not possible to assess the human health risk from atypical scrapie, or changes in risk, in the absence of hard scientific data;
- no single data set is likely to be definitive and it would be essential to have the results from a number of comparable experiments, rather than data from single studies in isolation;

- studies comparing the properties of atypical scrapie and other TSE agents using the same animal model, especially humanised mice or non-human primates, would be the most informative in the short term;
- surveillance data to assess any association between forms of CJD and atypical scrapie prevalence would be most persuasive, but are unlikely to become available in the short term;
- SEAC would have to review the experimental methods and results in detail, before any conclusion of a change to the risk to human health from atypical scrapie could be made.

1.4 *Timescale*

- 1.4.1 Atypical scrapie is not restricted to the UK. In 2006, cases were detected in 12 of the 25 EU countries. As a result, key experiments are underway in a number of laboratories in both the UK and other countries. However it is not possible to give a definitive timeline for results to become available. Some of the key results will be from experiments that test if atypical scrapie can be transmitted to non-human primates or to mice that express a human prion protein instead of the mouse protein. These experiments are underway but are likely to take anything from 2 to 5 years (particularly if atypical scrapie does not produce disease in these species). However, results from the analysis of archived UK TSE samples from sheep and goats dating back to 1964, which will indicate whether the disease predates the findings in the current surveillance program, should be available by autumn 2008.
- 1.4.2 The key point in relation to the timeframe is that results would be needed from a number of comparable experiments, which could take several years, before any robust conclusion that the risk has changed could be reached.
- 1.4.3 It is also extremely difficult to predict the time that would be needed to complete the work to establish a link between any new human TSE (should one be found) and atypical scrapie.

1.5 *Action*

- 1.5.1 When experimental results or any significant new surveillance data become available, they will be presented to SEAC for consideration. The Committee will be asked whether their opinion on the potential risk from atypical scrapie in the UK has changed. SEAC will also be asked to make clear the uncertainties associated with any conclusion.
- 1.5.2 If significant results emerge it is likely that the European Commission (EC) will ask the European Food Safety Authority (EFSA) for their view of the risk to the EU population.

- 1.5.3 The Board will be informed should either SEAC or EFSA conclude that their risk assessment has changed. If a major health risk is identified then an emergency Board meeting may need to be called and key stakeholders will be consulted. Otherwise the views of stakeholders will be sought prior to the Board's discussion. If sufficient data is available, the Agency will also consider commissioning a more quantitative risk assessment, which would be reviewed by SEAC.
- 1.5.4 The Board will then have the opportunity to consider if their policy advice on the appropriate risk management measures should be amended. At this time it is not possible to recommend any specific action that should be taken since there are too many unknowns. Possible options for risk management (which may change as the science develops) are:
- (i) keeping sheep over a certain age out of the food chain;
 - (ii) TSE testing all sheep over a certain age and allowing only those that test negative into the food supply;
 - (iii) increasing the range of tissues classified as specified risk material (SRM)¹;
 - (iv) providing consumers with advice on any risk and the associated uncertainties to allow better-informed consumer choice.
- 1.5.5 Depending on the results available at the time, decisions may have to be made by the Board when there is still a high level of uncertainty.
- 1.5.6 The Agency would then advise Government on the risk from atypical scrapie and the measures needed to manage that risk. This advice would also inform the UK's input to discussions at EU level on any changes to EC TSE legislation.
- 1.5.7 Alternatively, if SEAC were by then more confident that atypical scrapie was not a risk, then an update would be provided for Board members. Under these circumstances a policy discussion would be needed only if a reduction in current controls were being considered.
- 1.5.8 In the meantime consumers would be kept informed through amendments to the information on atypical scrapie on the Agency website, ensuring that informed consumer choice is maintained.

¹ SRM must be removed and destroyed and is not allowed into the food supply. The tissues in sheep/goats which are currently SRM are spleen and ileum of animals all ages and skull (including brain and eyes), spinal cord and tonsils of animals aged over 12 months (or with one permanent incisor erupted).

2 BACKGROUND

2.1 *Atypical scrapie*

2.1.1 Cattle, sheep and goats are known to suffer from a group of neurological diseases known as transmissible spongiform encephalopathies (TSEs). The best known of these is bovine spongiform encephalopathy (BSE) in cattle. Sheep can suffer from scrapie, a related disease which is not known to be harmful to humans. Scientific tests have identified another member of this family of diseases in sheep called atypical scrapie. Atypical scrapie is not BSE, and there is an absence of scientific evidence that it can be transmitted to humans or that it is any risk to humans. However, such a risk cannot be ruled out. Further information on atypical scrapie is on the FSA website at: <http://www.food.gov.uk/bse/what/atypicalscrapie>.

2.2 *FSA advice to consumers*

2.2.1 The Agency's advice to consumers in relation to atypical scrapie, in summary, is that the Agency is not advising people to change their eating habits with regard to lamb or mutton (sheep meat) and goat meat or products derived from these animals. However, if there were any risk to humans from sheep being infected with atypical scrapie it would be greater in older animals. It has also been calculated that in sheep with scrapie (and in sheep with BSE, when they are infected experimentally with the disease) it would be impossible to remove all traces of the infectivity from the animals' intestines when the intestines are made into sausage casings. This may also apply in the case of atypical scrapie. While there may be no risk to humans from atypical scrapie, anyone wishing to take extra precautionary measures might decide to stop eating meat from older sheep (mutton) or sausages covered in wet skins (casings) made from sheep intestines.

2.3 *FSA Board discussions*

2.3.1 The Agency Board has been kept fully informed about atypical scrapie and has discussed it in detail on several occasions.

2.3.2 In February 2006 the sheep subgroup of SEAC (the Government's independent advisory committee on TSEs) produced a position statement on atypical scrapie. This reported on what was known and what was not known at that time about the disease. It concluded that there were insufficient data to make reliable risk assessments for human health or animal health and identified specific areas where rigorous studies were needed to provide better risk assessments and inform policy.

- 2.3.3. This statement was discussed by the FSA Board². The Board noted that there was still a great deal of uncertainty about atypical scrapie, including the potential implications, if any, for human health. The Board agreed that there should be no immediate change in the Agency's advice that it is not advising people to stop eating lamb or mutton (sheep meat) and goat meat or products derived from these animals.
- 2.3.4 The Agency held discussions with stakeholder groups on the precautionary measures in place to protect consumers from the possible risks from TSEs in sheep and goats and whether additional measures should be considered in the light of the uncertainty about the risks from atypical scrapie. The consensus was that it would not be proportionate to introduce additional measures at that time, but that the Agency should focus on providing information and advice for consumers.
- 2.3.5 To ensure that consumer views were adequately represented, a series of focus groups was held to explore consumer views on the risk and their understanding of, and response to, the Agency's advice on atypical scrapie and BSE in sheep. In general this cross-section of consumers were not greatly concerned about the risk and felt that the Agency should provide information about the risk and the surrounding uncertainty, but leave consumers to choose what to eat. They also indicated that they would be likely to react to a food-related issue only if there were a major trigger (e.g. intense media coverage or withdrawal of products).
- 2.3.6 These discussions were reported to the Board in June 2006³. The Board considered the current precautionary measures, the views of stakeholders and the proportionality of any additional measures that might be recommended and concluded that the measures in place were sufficient. The Board also agreed that the Agency's advice to consumers and recommendations on precautionary measures should be kept under review and brought back to the Board if the understanding of the risk were to change significantly and that a contingency plan should be put in the public domain.

3 SEAC

3.1 Discussion

² paper FSA 06/03/06 (<http://www.food.gov.uk/multimedia/pdfs/fsa060306.pdf>)

³ paper FSA 06/06/03 (<http://www.food.gov.uk/multimedia/pdfs/fsa060603.pdf>)

3.1.1 An important aspect of a contingency plan is determining the point at which action may need to be considered. In May 2007 SEAC discussed the background to the FSA contingency plan and considered possible research or surveillance results that would be likely to produce a significant change in their understanding of the risk to humans from atypical scrapie. The SEAC paper⁴ updated the Committee on the research being undertaken on atypical scrapie and discussed, in broad terms, what information this research might provide in the future. SEAC emphasised that the Committee would need to consider the detail of the experimental method and the actual results when they became available before any definite conclusions that the risk had changed could be reached. The Committee's conclusions have been published in a position statement.⁵

3.2 Prevalence

3.2.1 A number of findings in terms of the past and future prevalence and/or epidemiology could influence SEAC's view of the risk. The first case of atypical scrapie was reported in 2003, having been found in Norway in 1998. More historic scrapie samples (currently known to be available back to 1964 in Great Britain) are being analysed to see if any conform to the definition of atypical scrapie. Future surveillance and epidemiological studies, both in the UK and elsewhere, will provide data on whether the prevalence is changing with time and whether or not atypical scrapie has been detected in countries previously thought to be free from classical and atypical scrapie.

3.2.2 SEAC considered that such data would be significant from a public health perspective and that it was important to continue to assess the prevalence of atypical scrapie and for archived sheep samples to be analysed for the presence of the disease. If the results indicate that atypical scrapie had been present for many years and was not increasing in prevalence then, by analogy with classical scrapie, the human health risk would be considered low. However, if atypical scrapie were found to be spreading rapidly, this would imply that it is a new disease and any human health risk would be more uncertain.

3.2.3 Human TSE diseases including Creutzfeldt-Jakob Disease (CJD) are monitored in many countries. Whilst changes in atypical scrapie prevalence might increase the uncertainty about the possibility of a risk to human health, SEAC's view was that a human health risk would be confirmed only by analogous changes in the prevalence of new types of CJD. Because of the long incubation periods of prion diseases, such data might not become apparent for many years. Atypical scrapie has

⁴ paper 97/3 (<http://www.seac.gov.uk/papers/97-3.pdf>)

⁵ [SEAC Statement - Food Standards Agency atypical scrapie contingency plan](#)

however been identified in a UK sheep from 1989, implying that humans may have been exposed to atypical scrapie via the dietary route for a number of years.

3.3 *Transmission studies*

- 3.3.1 SEAC discussed how far experiments in which other species are inoculated with the disease would provide information on the potential for atypical scrapie to transmit to humans.
- 3.3.2 They concluded that results from studies in which non-human primates are infected by the oral route would strongly inform the understanding of human health risk. It is known that the immune and lymphoreticular systems of non-human primates are closely related to those of humans and that the peripheral pathogenesis of TSEs in non-human primates mimics that in humans. However, non-human primates provide data relating only to one human prion genotype, MM, which comprises about 37% of the UK population. Assessment of the level of risk would require comparison with results from transmissions of other TSEs in the same models, in particular BSE, some of which are already available.
- 3.3.3 Mice that have been adapted to express the human prion gene (and therefore produce a human prion protein instead of the mouse protein) can provide data on the potential for transmission of TSEs to all three human prion protein genotypes. SEAC was of the view that these mice are a good model for human disease, but that it would be critical to compare the behaviour of atypical scrapie with other TSEs, especially classical scrapie and BSE, in the same model. They also concluded that strong evidence of the level of risk could be achieved only if similar results were obtained from a number of comparative studies.
- 3.3.4 SEAC noted that it is important to be aware of the possibility that such mice may not show any clinical sign of infection after primary transmission of atypical scrapie, yet a secondary transmission from these animals to others might result in clinical disease due to loss of the interspecies transmission barrier.
- 3.3.5 The barrier to transmission of atypical scrapie between animal and human can be tested by measuring the ability of abnormal animal prion to convert the human protein to the abnormal form in cell-free conversion assays. However, care is needed in interpreting the significance of such experiments as data obtained without the use of whole animals do not always correlate well with live animal studies. SEAC concluded that such experiments could provide data on whether conversion of the normal prion protein in humans to the abnormal form

by the atypical scrapie prion is or is not possible, particularly when confirmed by results from the mouse transmissions.

3.4 Tissue Distribution

3.4.1 Little is known about the distribution of abnormal prion protein (PrP^{Sc}) – a marker for TSE - and infectivity, or how these increase during the incubation period, in the tissues of sheep with atypical scrapie. If atypical scrapie were found to be a health risk to humans, SEAC considered that data from studies to assess the tissue distribution of PrP^{Sc} and infectivity would be essential to allow an assessment of the risk under specific control measures.

3.5 Human Health

3.5.1 Establishing a definitive link between an animal and a human TSE is extremely difficult. SEAC considered that the animal model data would be only indicative of a risk, and not definitive proof. However they considered that if the animal experiments were carried out appropriately they would provide a strong indication of the human health risk.

3.5.2 In the same way that the link between BSE and vCJD has been established, the emergence of a new type of CJD which showed the same transmission characteristics as atypical scrapie in non-human primates and humanised mice would provide a strong indication that transmission to humans had occurred through the consumption of infected material.

3.6 Decreased risk

3.6.1 SEAC also considered the question of what data would allow them to conclude that it was unlikely that atypical scrapie is a risk to humans. They noted that it is always difficult to provide proof of absence and to draw conclusions from negative experimental or surveillance results. However, negative results from current and retrospective surveillance and transmission studies, over a significant period of time to allow for possibly long incubation periods, would imply a negligible human health risk.

3.7 Key Conclusions

- It is not possible to assess the human health risk from atypical scrapie, or changes in risk, in the absence of hard scientific data.

- No single data set is likely to be definitive and it would be essential to have the results from a number of comparable experiments, rather than data from single studies in isolation.
- Studies comparing the properties of atypical scrapie and other TSE agents using the same animal model, especially humanised mice or non-human primates, would be the most informative in the short term.
- Surveillance data to assess any association between forms of CJD and atypical scrapie prevalence would be most persuasive, but are unlikely to become available in the short term.
- SEAC would have to review the experimental methods and results in detail, before any conclusion of a change to the risk to human health from atypical scrapie could be made.

4 TIMESCALE

Experiments are underway in a number of laboratories both in the UK and in other countries with atypical scrapie, but it is not possible to give a definitive timeline for results to become available.

4.1 *Prevalence calculations*

4.1.1 Surveillance is ongoing, but changes in prevalence of either atypical scrapie or CJD can be detected only over a number of years. Results of the analysis of archived UK TSE samples should be available by autumn 2008. Monitoring and analysis of human CJD cases is ongoing, but, as indicated above, a robust link between human disease and atypical scrapie could be obtained only after extensive research. In the meantime the Agency would seek advice from SEAC on any results from human surveillance that suggest a food-borne infection.

4.2 *Transmission studies*

4.2.1 In transmission studies mice can show clinical signs of disease at any time. The shortest incubation periods will typically be when the TSE does not have to overcome a PrP species barrier⁶. However, mice that do not develop any signs of disease will normally be left two years before being culled. If the first transmission does not produce disease then most experiments will include a further transmission of brain material from mouse to mouse to test for sub-clinical infection. The total time to get a result (particularly one demonstrating a lack of transmission) can therefore be about five years.

⁶ e.g. vCJD into a mouse with the human 129MM genotype

- 4.2.2 The timeframe for transmissions to non-human primates will typically be greater than for mice. For example, intra-cerebral transmission of vCJD to cynomolgous macaques produces clinical disease in 2-3 years, whereas oral transmission of BSE gave incubation periods of 5 years. However animals will be left for at least six years to ensure that disease does not develop.
- 4.2.3 Individual cell-free conversion assays can be carried out in shorter timeframes, but will provide only an indication of whether transmission is likely.
- 4.2.4 The key point in relation to the timeframe is that results would be needed from a number of comparable experiments, which could take several years, before any robust conclusion that the risk has changed could be reached.

4.3 Human Health

- 4.3.1 It is difficult to associate any timescale with the emergence of a new human TSE. The link between vCJD and BSE was established through transmission studies. The time required to undertake the necessary studies comparing atypical scrapie and a human TSE could be several years, but the first indicative results from the most susceptible mice (or voles) would be likely to be available within months.

5 ACTION TO BE TAKEN WHEN RESULTS BECOME AVAILABLE

See diagram on page 13.

- 5.1.1 The European surveillance data for 2006 published by the EC (see Appendix 1) show that atypical scrapie cases were detected in 12 of the 25 EU countries (including the UK) plus Norway. The percentage of scrapie cases that are atypical ranges from 100% in 4 countries to less than 5%, with 90% of the total number of EU scrapie cases being classified as classical and 10% as atypical.
- 5.1.2 It is clear that this is not an issue unique to the UK and therefore any proposals would have to be considered in a European forum.
- 5.1.3 When experimental results or any significant new surveillance data become available they would be presented to SEAC for their consideration. After considering all the available data and how it should be interpreted, SEAC would be asked whether this has changed their opinion on the potential risk from atypical scrapie in the UK. As

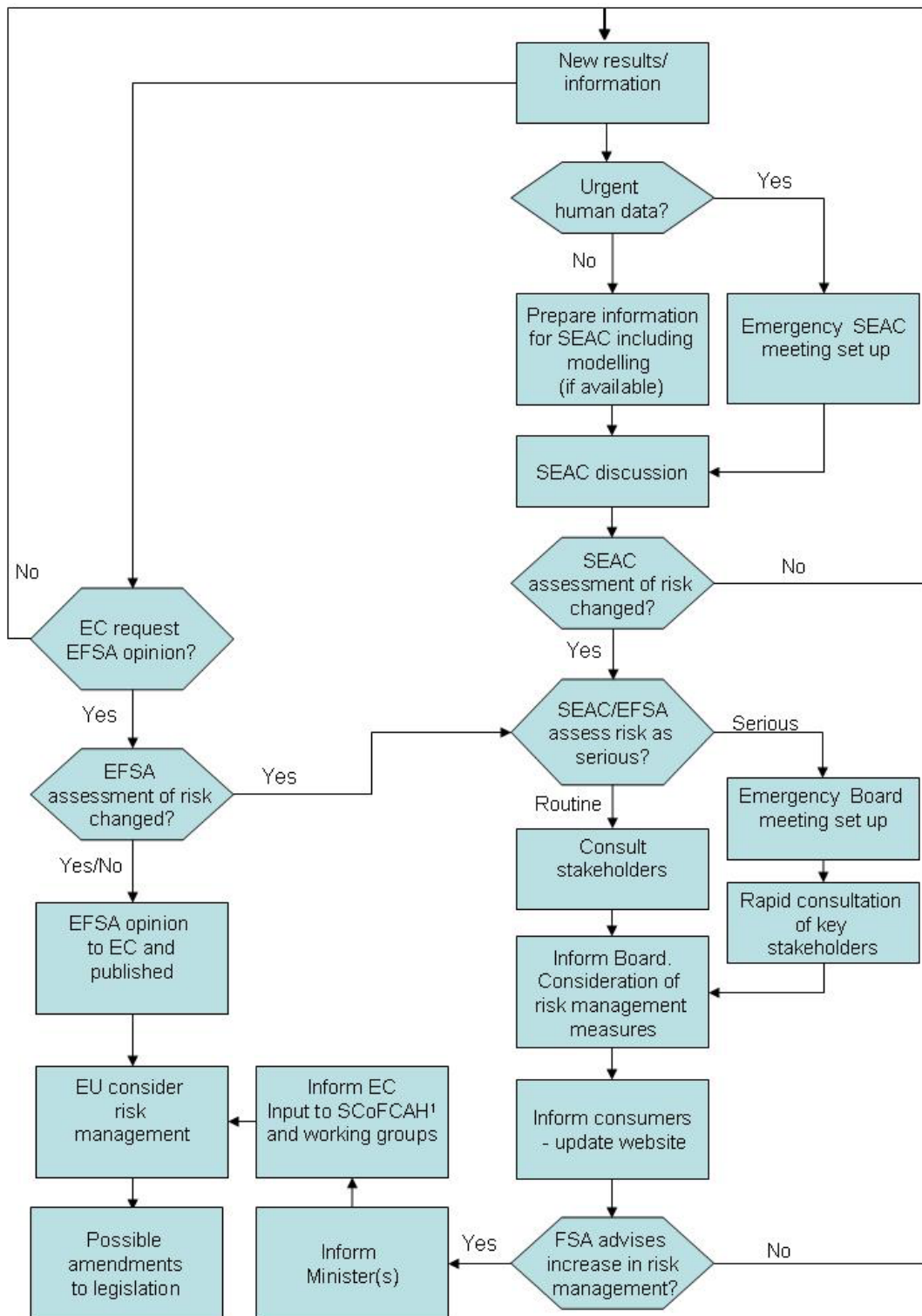
has been noted above, it is unlikely that SEAC would come to such a conclusion until confirmatory evidence had accumulated from a number of experiments and/or surveillance data. SEAC would also be asked to make clear the uncertainties associated with any conclusion.

5.1.4 It is clear that, unlike the early years of the BSE crisis, atypical scrapie is not just a UK issue and research is being undertaken in many affected countries. If significant results emerge it is likely that the EC would ask EFSA to assess the risk to the EU population. The EFSA Biohazards Committee has already noted that “currently several projects are under way to estimate the extent of the human species barrier to animal-derived TSEs, using transgenic models as surrogates for humans. The outcome of such experiments is to date unpredictable, and results could be difficult to interpret.”⁷

5.1.5 The FSA Board would be informed should either advisory body conclude that their assessment of the risk has changed. If a major health risk is identified then an emergency Board meeting may need to be called and key stakeholders (see Appendix 2) consulted.

5.1.6 Otherwise, as with previous consideration of possible risk management measures for atypical scrapie, the views of stakeholders on proportionality will provide important input to the Board’s discussion. Both industry representatives and consumers will be consulted and asked to consider the latest information on the risk and the options for risk management. If sufficient data were available the Agency would also consider commissioning a more quantitative risk assessment, which would be reviewed by SEAC. This would be available to inform both stakeholder and Board discussions.

⁷ in their ‘Opinion on certain aspects related to the risk of Transmissible Spongiform Encephalopathies (TSEs) in ovine and caprine animals’ (published 08-03-07)
[http://www.efsa.europa.eu/EFSA/Scientific Opinion/biohaz_op_ej466_tse_ovine_caprine_en.pdf](http://www.efsa.europa.eu/EFSA/Scientific%20Opinion/biohaz_op_ej466_tse_ovine_caprine_en.pdf)



¹ Standing Committee on Food Chain and Animal Health – European Commission Regulatory Committee responsible for food safety.

5.1.7 The Board would then have the opportunity to consider if their policy advice on the appropriate risk management measures should be amended. At this time it is not possible to recommend any specific action that should be taken since there are too many unknowns. Possible options for risk management (detailed below) are essentially those considered by the Board in June 2006⁸. However these may change as the science develops.

(i) Keeping animals over a certain age out of the food chain

Considerations:

- not yet known at what age atypical scrapie infectivity starts to accumulate
- practical difficulties in accurately aging sheep and therefore selecting route for slaughter
- costs dependent on age limit applied, but could be high

(ii) TSE testing all animals over a certain age and releasing only those that test negative into the food supply

Considerations:

- likely to result in major increase in number of animals to be tested each year in the UK, e.g. from the current 20,000 to almost 2 million for an 18 month age limit
- not yet known at what age animals with atypical scrapie would test positive
- practical difficulties in accurately aging sheep
- costs dependent on age limit applied, but could be high

(iii) Increasing the range of tissues classified as specified risk material (SRM)⁹

Considerations:

- currently very limited information on tissue distribution of atypical scrapie infectivity, but could be much more restricted than classic scrapie. If so, current rules may be adequate.

(iv) Providing consumers with advice on any risk and the associated uncertainties to allow better informed consumer choice.

Considerations:

⁸ see FSA Board paper <http://www.food.gov.uk/multimedia/pdfs/fsa060603.pdf>

⁹ SRM must be removed and destroyed and is not allowed into the food supply. Currently the following tissues in sheep/goats are SRM: spleen and the ileum of animals all ages and the skull (including the brain and eyes), spinal cord and tonsils of animals aged over 12 months (or with one permanent incisor erupted)

- if risk is greater than previously thought it will be important to ensure that advice reaches consumers, particularly those groups with higher than average consumption of sheep and goat meat.
- 5.1.8 Depending on the results available at the time, there may still be a high level of uncertainty and decisions may have to be made with only limited knowledge of the distribution of infectivity in sheep and goat tissues and how this varies within the incubation period.
- 5.1.9 Following the Board's discussion, the Agency would advise Government on the risk from atypical scrapie and any measures needed to manage that risk. This advice would also inform the UK's input to discussions at EU level on any changes to EC TSE legislation.
- 5.1.10 Alternatively, if SEAC were to conclude that the results indicate that the uncertainty concerning a potential human risk had decreased and that they could by then be more confident that atypical scrapie was not a risk, then an update would be provided for Board members. Under these circumstances a policy discussion would be needed only if a reduction in current controls were being considered.
- 5.1.11 In the meantime consumers would be kept informed through amendments to the information on atypical scrapie on the Agency website, ensuring that informed consumer choice is maintained.

EC surveillance data for small ruminants for 2006¹⁰ (as at 31/07/07)

Sheep

	Total tested	Total scrapie cases	Of which atypical	%age cases atypical	Atypical cases per 10,000 tests
UK	82,701	313	68	22	8.2
Belgium	10,248	3	3	100	2.9
Cyprus	6,108	1,327	0	0	0
Denmark	8,067	3	3	100	3.7
Finland	3,834	2	2	100	5.2
Germany	44,123	24	0	0	0
Greece	11,031	296	2	1	1.8
France	507,887	747	188	25	3.7
Ireland	59,025	123	0	0	0
Italy	60,530	320	19	6	3.1
Hungary	12,759	7	5	71	3.9
Netherlands	37,030	84	0	0	0
Portugal	63,711	65	48	74	7.5
Slovakia	7,532	10	1	10	1.3
Slovenia	2,040	40	0	0	0
Spain	94,057	135	18	13	1.9
Sweden	8,786	8	8	100	9.1
EU 25	1,035,065	3,507	365	10	3.5
Norway	15,356	15	8	53	5.2
Romania	14,867	9	0	0	0

Goats

	Total tested	Total scrapie cases	Of which atypical	%age cases atypical	Atypical cases per 10,000 tests
UK	5,034	13	0	0	0
Cyprus	6,025	713	0	0	0
France	162,822	15	1	7	0.1
Greece	7,081	22	0	0	0
Italy	27,916	17	6	35	2.1
Spain	56,899	11	4	36	0.7
EU 25	309,246	791	11	1	0.4
Norway	5,699	1	1	100	1.8

Note: Only those countries reporting positive results from TSE testing of sheep or goats are listed in the tables above.

¹⁰ http://ec.europa.eu/food/food/biosafety/bse/annual_report_tse2006_en.pdf

Key stakeholders

Consumer groups
Groups representing those affected by CJD
Farmers' organisations
Meat industry representatives
Retail industry representatives
SEAC
Veterinary associations

Government:
DARD
Defra
Department of Health
European Commission
Scottish Government
Welsh Assembly Government