



SEAC SHEEP SUBGROUP POSITION STATEMENT

In view of SEAC's commitment to keep the scientific evidence underpinning the strategy of the National Scrapie Plan (NSP) under review¹, and in light of rapidly emerging scientific findings relating to atypical scrapie, the opinion of the sheep subgroup was sought by SEAC in consultation with Defra. A meeting of the SEAC sheep subgroup was held on January 24th 2006, with the following aims:

- To give the best interpretation of the current data on atypical scrapie and of the potential risks for a) animal health and b) human health. To consider whether new data change the risk basis underpinning the NSP, flock control, or relevant sections of the TSE roadmap.
- To consider what additional information is necessary in order to improve assessment of the risk for animal and human health.
- To produce a statement for consideration at SEAC 91

The meeting brought together European experts on atypical scrapie, as well as UK experts and officials from the relevant Government Departments. The subgroup considered a body of unpublished data as well as published information and ongoing studies.

Background

Atypical scrapie

In 2002 the European Union launched a Europe-wide TSE surveillance programme to establish the prevalence of TSEs (scrapie and potentially BSE) in small ruminants in Member States. In the UK since January

¹ SEAC sheep subgroup statement 13 October 2004
http://www.seac.gov.uk/publicats/sheepsubgrp_statement.htm

2004 this has required the testing of 10,000 sheep slaughtered for human consumption and 10,000 fallen sheep per annum.

This TSE testing has involved screening by the Veterinary Laboratories Agency of the obex using the BioRad rapid ELISA method. Any positive result by ELISA was further tested using Office International des Epizooties (OIE) approved methods, which in the UK is western blotting and/or immunohistochemistry (IHC). Atypical scrapie first came to light as cases which were ELISA positive but could not be confirmed as scrapie by either western blotting or IHC. An expert group² met in September 2003 at the request of the Food Standards Agency and Defra to discuss data from the first 28 cases of atypical scrapie. In November 2003³ SEAC endorsed the expert group's opinion that it was not possible given the available data to comment on the significance of these preliminary results for the NSP and that further research including infectivity studies in mice using the unclassifiable samples was of high priority.

In 2003, researchers in Norway also announced that they had detected a form of scrapie, designated Nor98⁴, with strikingly unusual features, and in 2004 the same was reported for France and Germany⁵. Numerous other European countries have also now reported atypical scrapie cases in both sheep and goats although, as procedures for sampling and confirmation vary, data are not always directly comparable.

Sheep PrP genotypes

Sheep are relatively heterogeneous in their prion protein (PrP) gene. Three codons, in particular, appear to influence susceptibility to classical scrapie infection and the distribution of proteinase K resistant PrP (PrP^{res}) deposition in the brain. The VRQ allele confers greatest sensitivity and the ARR allele greatest resistance. For simplicity, in the NSP five groups of genotypes (including heterozygotes) are defined as increasingly-resistant to classical scrapie infection.

² <http://www.seac.gov.uk/statements/expertgroupstatement.pdf>

³ <http://www.seac.gov.uk/minutes/final80.pdf>

⁴ Benestad S.L., Sarradin P., Thu B., Schonheit J., Tranulis M.A. and Bratberg B. (2003). Cases of scrapie with unusual features in Norway and designation of a new type, Nor98. *Vet Rec* (153), 202-208

⁵ Buschmann A., Biacabe A., Ziegler U., Bencsik A., Madec J.-Y., Erhardt G., Lühken G., Baron T. und Groschup M.H. (2004). Atypical scrapie cases in Germany and France are identified by discrepant reaction patterns in BSE rapid tests. *J. Virol. Meth.* 117: 27-36.

A striking observation about atypical scrapie is the sheep genotypes in which it is found. Most infections are associated with sheep PrP alleles that are considered to be relatively resistant to classical scrapie, including ARR homozygotes. In addition, few atypical scrapie infections are associated with the VRQ allele which is highly susceptible to classical scrapie.

BSE in sheep

It is known that sheep can be infected experimentally with BSE, both intracerebrally and orally. Since sheep were exposed to BSE-infected meat and bone meal (MBM) in the 1980s, it seems likely that the UK flock was exposed to BSE infection prior to the MBM ban. Until recently it was not possible to distinguish between BSE and scrapie in sheep using rapid biochemical tests. It was therefore possible that BSE infection in sheep was being masked by scrapie. However, more recent biochemical tests have enabled BSE and scrapie to be distinguished with some confidence. Despite extensive surveillance, BSE has not yet been detected in sheep. The extensive surveillance undertaken enables the prevalence of BSE in sheep, if it ever entered the British sheep flock, to be estimated at 0.54% (upper 95% confidence limit) of the total TSE cases in sheep, based on samples tested up to 30th November 2005 (2483 cases from 556 flocks)⁶.

If BSE entered the sheep flock it may have been eliminated if the rate of transmission of infection from one sheep to another is insufficiently great to engender a sustainable epidemic. Indeed, one case of BSE in a goat born in March 2000, has been identified in France⁷, probably infected by feeding the animal infected MBM prior to the European feed ban of 2001. There is no evidence of transmission to the remainder of the herd.

European Food Safety Authority (EFSA) opinion

An EFSA Opinion, adopted on 26 October 2005⁸, concluded that an operational definition of atypical scrapie in small ruminants was possible, in juxtaposition with definitions for classical scrapie and BSE in small ruminants. EFSA concluded that it was premature to try to subcategorise classical or atypical scrapies.

⁶ SEAC 84 open meeting minutes page 10
<http://www.seac.gov.uk/minutes/final84.pdf>

⁷ Eloit M., Adjou K., Culpier M., Fontaine J.J., Hamel R., Lilin T., Messiaen S., Androletti O., Baron T., Bencsik A., Biacabe A.G., Beringue V., Laude H., Le Dur A., Vilotte J.L., Comoy E., Deslys J.P., Grassi J., Simon S., Lantier F. and Sarradin P.(2005) BSE agent signatures in a goat. *Vet. Rec.* 156, 523-524.

⁸ http://www.efsa.eu.int/science/biohaz/biohaz_opinions/1216/biohaz_op_ej_276_atypicalscrapiedefinition_en_vf1.pdf

EFSA concluded that the implications of atypical scrapie for animal health were difficult to quantify due to insufficient data, and that it was essential that statistically-valid surveillance should continue. EFSA recommended the use of appropriate combinations of tests on brain stem and cerebellum, and the collection of whole carcasses, to enable the biological characterisation of isolates, transmission experiments in the natural hosts, and preparation of reference material.

Measures to control and eradicate scrapie

National Scrapie Plan (NSP)

The NSP for Great Britain⁹ is a strategic, long-term breeding programme aimed at increasing the number of sheep that are genetically resistant to classical scrapie and, potentially, BSE if it ever enters the sheep flock. It implements a recommendation from SEAC's 'Report on Research and Surveillance for Transmissible Spongiform Encephalopathies in Sheep' for a long-term control and eradication programme for scrapie¹⁰. It is based on the finding that sheep with the VRQ and ARQ PrP alleles are most sensitive to scrapie while sheep with the ARR allele are relatively resistant. Its primary aims are two-fold: to protect animal health by reducing, and eventually eradicating, scrapie; and to protect public health from the theoretical risk of BSE if it is present in sheep and is masked by scrapie. SEAC recommended that the NSP should be kept under review as new scientific information emerged¹¹.

TSE roadmap

On 15th July 2005 the EC published a Roadmap¹² on the TSE control strategy in the short, medium and long term with strategic goals relevant to small ruminants:

- *To ensure and maintain the current level of consumer protection by continuing to assure the safe removal of SRM but modify list/age based on new & evolving scientific opinion.*
- *A relaxation of certain measures of the current total feed ban when certain conditions are met.*

⁹ <http://www.defra.gov.uk/animalh/bse/othertses/scrapie/nsp/index.html>

¹⁰ <http://www.seac.gov.uk/publicats/sub-rep.pdf>

¹¹ SEAC sheep subgroup statement 13 October 2004

http://www.seac.gov.uk/publicats/sheepsubgrp_statement.htm

¹² http://europa.eu.int/comm/food/food/biosafety/bse/roadmap_en.pdf

- *To reduce the numbers of tests of bovine animals and at the same time continue to measure the effectiveness of the measures in place with a better targeting of the surveillance activity. With respect to small ruminants, future monitoring depends on the estimated prevalence of BSE in such animals.*
- *Review and relaxation of the eradication measures for small ruminants taking into account the new diagnostic tools available but ensuring the current level of consumer protection.*

Flock culling

The Compulsory Scrapie Flocks Scheme (CSFS) implements EU legislation (latest Commission Regulation is 1492/2004¹³) and came into force from 20 July 2004 in England and Scotland, 4 October 2004 in Northern Ireland and in November 2004 in Wales. Under the Scheme when a case of classical scrapie is confirmed on a holding, either:-

- The flock is genotyped and the susceptible animals are culled, leaving only Type 1 (ARR/ARR) rams and Type 1 and 2 ewes (ARR/xxx with no VRQ).
- The whole flock is culled and restocking must be with only Type 1 rams and Type 1 and 2 ewes

Movement restrictions apply to the holding, with only certain animals allowed on and off the holding and into the food chain. These restrictions apply for 3 years from when the flock has reached the status of NSP Type 1 males and NSP Type 1 or 2 ewes. During this 3 year period, fallen stock over 18 months old and some annual cull animals have to be tested for the presence of TSEs. Derogations are available in some circumstances for certain flocks or breeds with low levels of ARR alleles or at risk of in-breeding.

The SEAC Sheep subgroup considered a number of key issues:

1. The nature and classification of atypical TSE cases in small ruminants

The subgroup considered western blot, proteinase K-sensitivity and IHC information from British, Norwegian, French and German atypical scrapie cases and controls, primarily in sheep but also in a few cases in goats. The subgroup:

¹³ http://europa.eu.int/eur-lex/pri/en/oj/dat/2004/l_274/l_27420040824en00030008.pdf

- Concluded that, on the basis of a number of characteristics, atypical scrapie could reliably be distinguished both from classical scrapie and from experimental BSE in sheep. The subgroup therefore concurred with the EFSA opinion that “an operational definition of atypical scrapie in small ruminants was possible, in juxtaposition with definitions for classical scrapie and experimental BSE in small ruminants”.
- Noted that the phenotypes of an atypical scrapie infection may differ depending on sheep genotype, particularly with respect to immunohistochemical distribution of PrP^{res}, but that data are currently limited.
- Noted that, although some variation has been reported between atypical scrapie cases from around Europe, as more data are obtained increasing similarities are being noted. Atypical scrapie cases from around Europe form a subset of TSE cases in sheep which are more closely related to each other and distinct from classical scrapie. The subgroup agreed with the EFSA opinion that it was premature to sub-classify atypical scrapie cases, if indeed that will ever be possible.
- Agreed with the EFSA opinion that “samples of brain tissue should include brain stem and cerebellum as a minimum, and collection of whole carcasses should be encouraged” to enable further characterisation of atypical scrapie isolates and their prevalence.
- Concluded that, on the basis of emerging data, it may be more appropriate to consider atypical scrapie as a distinct TSE of small ruminants, and not simply a variant of what is now called classical scrapie.

2. Epidemiology of atypical scrapie and prevalence of atypical and classical scrapie

The subgroup considered evidence from active surveillance, scrapie notifications and the compulsory scrapie flocks scheme. In the UK in 2005 up to 2nd December, 168 clinical classical scrapie cases and 3 clinical atypical scrapie cases have been confirmed. Three additional atypical scrapie cases have been detected in a snapshot retrospective analysis. In contrast, an abattoir survey indicates that there are similar numbers of sheep infected with atypical scrapie as with classical scrapie (see below). Thus, clinical cases of atypical scrapie may be disproportionately low amongst the total scrapie (classical plus atypical) infections. This might be because the incubation period for clinical signs to appear is longer for atypical scrapie than it is for classical scrapie. Alternatively, differences in presentation of clinical signs in atypical cases may mean they are not readily recognised as a TSE. Consistent with this latter hypothesis are data which indicate that the prevalence of

atypical scrapie is of the same order of magnitude as that for classical scrapie in 'dead in transit' animals and amongst fallen stock¹⁴. The subgroup agreed that, although data are limited:

- Atypical scrapie, which was originally distinguished from classical scrapie by biochemical tests, can cause clinical disease in sheep. There may be phenotypic differences between classical and atypical scrapie, but, given the wide variation in clinical signs and effects of sheep genotype, the two cannot currently be distinguished reliably on clinical signs alone.
- Clinical atypical scrapie tends to be found in older animals compared with classical scrapie. It is likely that many cases of atypical scrapie in the past were not diagnosed, either because cases may have exhibited clinical signs distinct from classical scrapie and so were not considered candidates for TSE testing, or because the confirmatory histopathological tests used until recently would not have detected cases of atypical scrapie and so putative clinical cases would have gone undetected.
- Data from active surveillance show that the frequency of atypical scrapie infections in the British sheep flock is similar to that of classical scrapie, and may be slightly higher. Modelling of the abattoir survey results for the Great British sheep population over 18 months old (14 million sheep) shows that around 56 000 sheep could be infected with classical scrapie and around 82 000 infected with atypical scrapie¹⁵. These numbers are considerably greater than the number of known clinical cases, in part because many infected animals may be sent to the abattoir at an age before clinical signs appear, but it may also reflect a degree of under-reporting¹⁶.
- Atypical scrapie has been identified in many European countries and in at least some may also be of similar or higher prevalence than classical scrapie. For instance, Portugal has only notified atypical scrapie cases so far from active surveillance¹⁷, with no classical scrapie cases.
- That there are generally smaller numbers of atypicals per infected flock compared with classical scrapie. One interpretation is that atypical scrapie may be less readily

¹⁴ paper SS/Jan 06/5 tables 1 and 2 for the sheep subgroup meeting 24 January 2006

¹⁵ modelled data from active surveillance (abattoir survey) provided by Professor John Wilesmith post meeting.

¹⁶ Sivam S.K., Baylis M., Gravenor M.B., Gubbins S. and Wilesmith J.W. (2003) Results of a postal survey in 2002 into the occurrence of scrapie in Great Britain. *Vet. Rec.* 153, 782-783

¹⁷ http://www.efsa.eu.int/science/biohaz/biohaz_opinions/1216/biohaz_op_ej_276_atypicalscrapiedefinition_en_vf1.pdf

transmitted naturally between sheep within a flock than is classical scrapie.

- Atypical and classical scrapie can occur together in the same flock but do not always do so. There is no evidence for a direct link between the occurrence of classical scrapie and atypical scrapie, consistent with the view that classical scrapie and atypical scrapie should be considered as independent TSEs.

The subgroup agreed that it was critical to know whether or not the prevalence of atypical scrapie in the UK (and other European) flocks is increasing. This knowledge will inform the question of whether atypical scrapie is likely to pose a human health risk. The subgroup agreed that:

- Biochemical tests able to discriminate atypical and classical scrapie have only been available for a few years. The limited data available from the last 4 years only, do not suggest a significant change in prevalence over that period. Nevertheless, on the basis of current data it is not possible to ascertain whether atypical scrapie is an old or new disease of sheep, or whether the prevalence of atypical scrapie is changing over time.
- A retrospective analysis of historical samples might help ascertain whether atypical scrapie is a new disease and whether or not its prevalence is changing. It was acknowledged that only limited samples may be available from the last 40 years, and some may not be suitable for analysis.
- Continued surveillance using an appropriate combination of tests is essential to ensure that atypical cases continue to be identified.
- Proactive approaches should be taken to monitor any change in the prevalence of atypical scrapie in UK flocks with some urgency. It should be noted that the changing sheep PrP genotype ratios resulting from the NSP implementation may be a confounding factor which should be taken into account in analysing any possible changes in prevalence of atypical scrapie.

3. Role of sheep genotype

The sheep subgroup noted that the prevalence of atypical scrapie with respect to sheep PrP genotype differs significantly from that of classical scrapie.

The sheep subgroup agreed that:

- Most critical is that atypical scrapie shows higher prevalence in so-called resistant ARR homozygote and heterozygote genotypes, compared with classical scrapie.
- Atypical scrapie has not been found naturally in VRQ/VRQ sheep, although such sheep can be infected artificially. VRQ sheep are, in contrast, highly susceptible to classical scrapie. In the UK, one case of atypical scrapie has been found in VRQ heterozygote (AF¹⁴¹RQ/VRQ) sheep. It is important to ascertain whether or not VRQ-carrying sheep are significantly resistant to infection with atypical scrapie or whether the data might result from a failure to detect PrP^{res} in atypical scrapie due to a different pattern of PrP distribution in tissues.
- Increased incidence of atypical scrapie in sheep with PrP alleles carrying the variant phenylalanine (F) at position 141 (leucine(L)/phenylalanine) has also been observed compared with classical scrapie.
- It will be important to clarify the genotype effect, particularly in relation to ARR and L141F in transmission studies.
- In classical scrapie, there is clear evidence for a PrP genotype effect on tissue distribution patterns of PrP^{res}. This might also be true for atypical scrapie although the data are less complete.

4. Transmission of atypical scrapie

It has recently¹⁸ been demonstrated that atypical scrapie is experimentally transmissible to mice and sheep, primarily through intracerebral injection. There are some data suggesting that it may also be transmissible orally to sheep of different genotypes. The subgroup noted that challenge experiments with atypical scrapie in sheep were underway in the UK, with one successful intracerebral challenge to date. The subgroup was informed that positive transmission of infectivity from atypical scrapie isolated from sheep with a range of genotypes had been observed in mice. This included ovinised transgenic mice over-expressing the VRQ allele. Nor98 atypical scrapie had also transmitted to ARR ovinised mice, with transmission experiments in AF¹⁴¹RQ ovinised mice planned. Biochemical features of the isolates were maintained after transmission, and were distinct from BSE and classical scrapie. High infectivity titres were observed in brain tissue from atypical scrapie, including from ARR/ARR sheep. Brain transmission experiments in mice carrying the human PrP gene were at an early stage.

¹⁸ Le Dur A., Béringue V., Andréoletti O., Reine F., Lai T.H., Baron T., Bratberg B., Vilotte J.-L., Sarradin P., Benestad S.L. and Laude H. (2005) A newly identified type of scrapie agent can naturally infect sheep with resistant PrP genotypes. *PNAS* 102, 16031-16036

The subgroup agreed that:

- The species barrier from atypical scrapie in sheep to VRQ ovinised mice appeared low since atypical scrapie could be transmitted relatively easily to VRQ ovinised mice. However general information on the species barriers is currently limited. As atypical scrapie is experimentally transmissible the possibility that it may be transmissible to humans must be considered. It was noted that BSE may be transmitted to humans while there is no evidence that scrapie can cross this species barrier. Further studies on the effect of route of transmission (oral or intracerebral) on the pathogenesis of atypical scrapie will inform on the potential risk to human and animal health.
- The available evidence suggests that, unlike experimental BSE in sheep, atypical scrapie may be absent from the lymphoreticular system. Thus, assuming Specified Risk Material (SRM) regulations remain in place, if atypical scrapie can be transmitted to humans, it may pose a relatively lower health risk than BSE if it ever enters the sheep flock. However, one study using oral delivery to a VRQ sheep suggests that PrP^{res} may be present in the LRS. It is urgent to clarify this issue.
- Transmission experiments between sheep of the same and different genotypes will be very informative. The results of experimental transmission of atypical scrapie to transgenic mice expressing the human forms of PrP might indicate its relative transmissibility to humans and thus inform on the potential risk to human health of exposure to atypical scrapie.

5. Environmental persistence of TSEs and maternal transmission

The subgroup noted that transmission of classical scrapie can occur in the absence of lambing and in the absence of direct contact with infected sheep. Infectivity survives on pasture left fallow for at least 2 months (from ongoing VLA studies) after removal of an infected flock. It has been speculated that this is a consequence of the widespread distribution of classical scrapie in the body. This is in contrast to BSE in cattle which is restricted primarily to neural tissues and does not appear to be shed into the environment. However, BSE experimentally introduced into genetically susceptible sheep, like classical scrapie, appears to have a wide distribution in the body¹⁹, and it was recently

¹⁹ Bellworthy S.J., Hawkins S.A.C., Green R.B., Blamire I., Dexter G., Dexter I., Lockey R., Jeffrey, M., Ryder S., Berthelin-Baker C. and Simmons M.M. (2005) Tissue distribution of bovine spongiform encephalopathy infectivity in Romney sheep up to the onset of clinical disease after oral challenge. *Vet. Rec.* 156, 197-202

demonstrated that a BSE infection can be maintained within a sheep flock by spreading the disease from infected ewes to their lambs²⁰. The detailed pathway of the infectious agent from ewe to lamb still needs to be elucidated.

It is not known how atypical scrapie is transmitted between animals. The possibility that it has spread through feed cannot be excluded. The environmental persistence of atypical scrapie is unknown. The fact that more than one case may be found in a flock may reflect a level of environmental transmission, or a common alternative route of exposure. It is clearly important to assess its possible route of transmission if control measures are to be effective.

6. Current TSE control measures

Current CSFS policies were introduced when less information was available about ovine BSE and before tests were introduced to distinguish BSE in sheep from scrapie. The EU TSE roadmap proposes a relaxation in flock culling policy where BSE can be excluded, with increased testing within infected flocks, and slaughter for human consumption if negative by rapid testing.

The subgroup concluded:

- As further surveillance data are now available, an update of the estimate for the maximum prevalence of BSE in the UK flock would be informative.
- While the theoretical risk of BSE in sheep may now be lower than previously calculated, a risk that BSE may be found in sheep cannot be excluded. However the maximum prevalence would be very low.
- Emerging knowledge of atypical scrapie, which is present in the UK and European flocks, should be taken into account when reviewing the CSFS policy.

The NSP has been implemented to reduce the risk to human health through selective breeding to reduce classical scrapie and BSE susceptible genotypes, and increase resistant genotypes. The theoretical risk of atypical scrapie to human health and the fact that it affects sheep with genotypes (ARR) resistant to classical scrapie and BSE has potential implications for the NSP. Although the current information on atypicals is insufficient to alter the risk basis of the NSP,

²⁰ Bellworthy S. J., Dexter G., Stack M., Chaplin M., Hawkins S. A. C. and Simmons, M. (2005). Natural transmission of BSE between sheep within an experimental flock. *Vet. Rec.* 157, 206.

emerging findings on atypical scrapie should be kept under constant review.

Summary

Atypical scrapie has recently been identified, through new rapid testing procedures, as a distinct TSE of small ruminants. It is relatively widespread in sheep flocks in Europe: there are estimated to be around 82 000 infected sheep in the UK compared with 56 000 infected with classical scrapie. This compares with BSE in sheep which, despite extensive surveillance, has not been detected and a maximum prevalence of 728 cases estimated from 2003 abattoir survey data²¹. Atypical scrapie is experimentally transmissible to sheep and mice. There is no evidence, to date that atypical scrapie can infect humans, although a theoretical risk cannot be excluded.

There are insufficient data, as yet, to make reliable risk assessments for human health or animal health and welfare. In the view of the subgroup, in order to provide better risk assessments and inform policy, rigorous studies are critical and urgent, addressing the following questions.

1. *Prevalence.* Is the prevalence of atypical scrapie increasing or decreasing? Has it been in the national flock for many years or is it relatively new? Careful analysis of historical samples, and well designed and proactive surveillance, is critical.
2. *Transmission.* How is atypical scrapie transmitted? Is it naturally transmissible between sheep maternally or through the environment? If it is naturally transmissible, is the widespread distribution throughout Europe the result of a single or relatively few introductions, and if so, how has spread occurred? Alternatively, is its spread principally feed-borne? Is there evidence that atypical scrapie cases are clustered?
3. *Tissue distribution.* For atypical scrapie, what is PrP^{res} and infectivity distribution within sheep of different genotypes, particularly with respect to SRM removal? For classical scrapie and experimental BSE in sheep, tissue distribution of infectivity is widespread. Thus, even with SRM controls in place, an infected sheep poses around 1000 times the risk to human health than does an infected cow²². Does the distribution depend on whether infection is by the oral or

²¹ Gubbins S. Prevalence of BSE in sheep: interpreting the results of retrospective and prospective testing of sheep TSE cases. SEAC 84 open meeting

²² paper presented to Food Standards Agency board on 9 December 2004.

<http://www.foodstandards.gov.uk/multimedia/pdfs/fsa041204.pdf>

Also see paper SEAC/84/2 Annex 2: McLean, A.

- intracerebral route? Are some VRQ sheep carriers with no neurological symptoms?
4. *Genotype*. Atypical scrapie infects sheep with genotypes considered relatively resistant to classical scrapie and BSE in sheep. Further information on the genotype distribution of field cases of atypical scrapie is necessary. What is the effect of sheep genotype on susceptibility to oral and intracerebral infection? Sheep and ovinised mouse infectivity studies will be critical.
 5. *Human Health Risk*. There is no evidence of a risk to human health, but a theoretical risk cannot be excluded. Comparative transmission studies with humanised mice and other species (including primates) are urgently needed to inform on the potential risk to human health.
 6. *Animal Health*. Even if atypical scrapie proves not to be a risk to human health, there is still a need to know the real incidence of clinical disease in small ruminants. Although atypical scrapie can cause clinical disease in sheep and goats, the similarities and differences from classical scrapie remain unclear. Is it a significant animal health and welfare problem or relatively benign with low morbidity and mortality? There is an urgency for clear observation of clinical signs during surveillance and in future transmission experiments.
 7. *NSP*. This subgroup reconfirms that the scientific basis upon which the NSP was based was sound, given the evidence available at its inception. It was SEAC's recommendation that the NSP should be reviewed as new scientific data became available. The new data, and identification of atypical scrapie, while of concern, are insufficient to justify immediate changes to the NSP. Nevertheless, the subgroup strongly recommends that the NSP should be kept under continuous review as new findings emerge.

SEAC Sheep Subgroup
February 2006