



DEFRA OR FSA FUNDED RESEARCH ON ATYPICAL SCRAPIE

1. An Expert Panel was convened by SEAC on 17th September 2003 to discuss the unusual results arising from the introduction of rapid testing methods into the scrapie surveillance programme in Great Britain. This panel recommended research that should be undertaken to investigate the nature and biology of atypical scrapie.
2. In response to these recommendations, Defra has funded several research studies on atypical scrapie. The studies, which are all in progress, include:
 - Intracerebral and oral challenges in sheep of various genotypes (SE1847¹)
 - Intracerebral challenges of conventional and transgenic mice carrying sheep VRQ and ARQ PrP genes (SE1850)
 - Biochemical characterisation of the prion protein (SE1789)
 - Full sequencing of the PrP gene in sheep with atypical scrapie (SE0240)
 - Estimation of the prevalence of infection (part of SE0243)
 - Investigations on the flocks of origin (funded by Defra's Sheep TSEs Policy Group)
3. The Expert Panel also recommended that the rapid diagnostic tests should be applied to samples from sheep of genotypes associated with atypical scrapie from a source guaranteed to be scrapie free. This has not been carried out because the scrapie-free flock in the UK is too small to design a meaningful study².
4. Defra has set up a programme of studies to investigate the relative transmissibility of atypical scrapie across species by challenges in transgenic mice carrying human and bovine PrP genes. In addition, the Food Standards Agency has requested applications to develop or apply relevant experimental models to assess the risk to humans from other TSEs,

¹ SE1847 is the Defra code for the research project. This code can be used to find further details of the project on Defra's public web-site (http://www2.defra.gov.uk/research/project_data/Default.asp).

² It should be noted that the negative controls in the 2004 evaluation of rapid tests for TSEs in small ruminants were 1000 sheep samples sourced from New Zealand, which is free from classical scrapie.

UP-DATE ON ATYPICAL SCRAPIE FOR SEAC MEETING ON 28th APRIL 2006

including atypical scrapie, relative to BSE in cattle. Proposals have been received and are currently being appraised.

5. Research on atypical scrapie throughout Europe has been limited by the availability of material for study. Nevertheless, there is an increased understanding of atypical scrapie, which is now recognised as a distinct TSE of small ruminants that occurs in sheep that are relatively resistant to classical scrapie. Atypical scrapie has been experimentally transmitted to sheep and ovinised transgenic mice by the intracerebral route.
6. Information from the Defra-funded research programme and from other European laboratories was presented at the SEAC Sheep Subgroup Workshop on 24th January 2006 and summarised in a position statement³.
7. The Sheep Subgroup recommended that further information about atypical scrapie was needed, including:
 - the historical prevalence
 - the route(s) of natural transmission
 - the distribution of infectivity within sheep of different genotypes
 - comparative transmission studies with other species
 - the incidence and nature of clinical disease
8. To investigate the past prevalence of atypical scrapie in sheep in GB, Defra is determining the availability of suitable archived material from sheep collected since the 1960's to which current tests for the differentiation of atypical scrapie can be applied.
9. Comparative transmission studies in humanised transgenic mice are planned for the immediate future and studies in different sheep genotypes have been put in place previously (2 and 4 above). The latter will also provide information on the tissue distribution of infectivity and possibly the potential for a carrier state. These studies will be programmed or expanded as enough suitable atypical scrapie material becomes available for further challenges. Knowledge of the tissue distribution is obviously fundamental to ensuring that effective risk reduction measures, such as the SRM controls are in place. The FSA plans to call for proposals for further work in this area. However the shortage of infected material to use as inocula for these experiments may necessitate a preliminary experiment primarily aimed at generating infected tissue. Ideally this would be subject to joint funding since tissue also needs to be archived for use in test evaluation.
10. A small number of natural cases of atypical scrapie known to have expressed clinical disease have been found. Monitoring for further clinical

³ <http://www.seac.gov.uk/pdf/positionstatement-sheep-subgroup.pdf>

UP-DATE ON ATYPICAL SCRAPIE FOR SEAC MEETING ON 28th APRIL 2006

cases and the experimental challenges in sheep will provide a profile of the disease phenotype over time.

11. Natural transmission and the behaviour of atypical scrapie in sheep populations will be further investigated in an epidemiological case control study on farms which have had cases detected by abattoir surveillance.
12. The FSA and Defra are also funding projects that, whilst not specifically targeted at atypical scrapie, are working on improved diagnostics, with potential for tests that can be applied to live animals or improved strain differentiation.
13. Annex 1 provides a time-line for research studies on atypical scrapie that are in progress or planned.