Annex 1: ATYPICAL SCRAPIE IN THE VLA SCRAPIE-FREE FLOCK (PROJECT SE1931)

Update on investigations into the origin of the case.

Introduction

1. SEAC has previously been briefed following the diagnosis of a case of atypical scrapie in the VLA flock of New Zealand-derived sheep, maintained as a scrapie-free resource for research into prion diseases of sheep. This note summarises the initial events, and describes progress in investigating the possible origin of the case, with a view to enabling decisions to be taken in relation to the future of the flock.

Preliminary Action

2. Animal G320 (AFRQ/AFRQ), born May 2000, was confirmed as having been affected by "atypical scrapie" in November 2006. This result has been re-confirmed by Dr Sylvie Benestad of the Norwegian National Reference Laboratory. It conformed with the diagnostic phenotype of over 100 atypical cases already identified through surveillance programmes in the United Kingdom.

3. Animal G320 was born to a surrogate dam (C105) imported from New Zealand in 1998. Its natural mother (D301, ARQ/ARQ) and sire (D554, ARQ/ARQ) were also part of the same importation. DNA analysis of material from the natural parents and G320 has been carried out by Cellmark and confirms that relationship.

4. Unfortunately, because C105 was culled at another location during the course of the 2001 FMD epidemic, it was not been possible to collect and store brain tissue for examination. Also, D301 was transferred to another study where no brain tissue was retained after slaughter. Consequently the scrapie status of both natural and surrogate dams remains undetermined. The sire was re-examined and was negative.

5. None of the offspring of the natural and surrogate dams remain available to the VLA for re-examination.

UKAS audit

6. Detection of atypical scrapie in G320 prompted a request that procedures leading to that diagnosis be audited to ensure that the result was genuine. UKAS was invited to audit procedures, and did so at the end of November 2006.

7. The final UKAS report was passed to Defra's Science Directorate in April 2007. The VLA is currently considering its response.

8. As reported to SEAC on December 7th, 2006 the audit supported the VLA diagnosis for sheep G320. At the time of the audit the VLA made the auditors aware that it had preliminary data that might subsequently result in a diagnosis of atypical scrapie in another sheep (J19), which, if confirmed, would have influenced interpretation of risk factors in the flock. By the end of the audit week, internal investigations at the VLA clearly indicated that J19 was not infected with atypical scrapie, and, as a result, has not been taken into account in subsequent investigations.

Consequential investigations

9. Investigations into the circumstances surrounding this diagnosis have centred on:-

- Auditing the livestock, imported and homebred, with a view to determining the location of any samples that represented a potential opportunity to test for scrapie, and determine the prevalence of atypical scrapie in the flock of origin.
- To consider potential sources of infection in the flock, both temporal and geographical (NZ or UK origin), as well as reviewing local biosecurity procedures for evidence of potential routes of entry.

10. The starting point was to review the flock database, to identify all animals imported into the flock, and subsequently either still alive in the flock or departed for any reason. Priority was given to the tracing of imported animals that had entered the VLA diagnostic system, as well as any other animal that had been culled or entered VLA projects, again prior to post-mortem diagnosis, and potential storage of frozen tissues in the TSE Archive. It became necessary to transfer the database to the VLA, and to populate it with new identities/sample references that animals had acquired on entry into projects or the diagnostic system. This enabled the collation of data on samples available, both fixed and frozen, with the intention that testing be prioritised where possible.

11. In parallel with consideration of samples held by the VLA, all institutes that received live animals from the source flock were contacted, and provided with a master list of identities of all animals dispatched. They were asked to review their list and to notify the VLA of any potential tissues that could be made available for further examination, particularly from animals that were imported from New Zealand, and had not subsequently been exposed to scrapie or BSE.

12. Because of the time taken to fully populate the database, and to audit the collated data, the immediate availability of fixed tissue meant that the diagnostic status of culled sheep could be reviewed relatively quickly. This proceeded by either reviewing stained slides where IHC staining was carried out by current protocols (used for the detection of atypical

scrapie), or by re-cutting and staining slides where past diagnostic protocols predated the introduction of current methods.

13. In the meantime, the database was populated with data from the TSE archive to confirm the identities of animals where frozen brain stem and/or cerebellum were likely to be available for testing with the BioRad TeSeE® ELISA.

Results

14**. Table 1** summarises the collated data for the source animals, imported from New Zealand, sorted by date of importation, date of birth, breed and sex. A total of 2003 sheep were involved.

15. Of these, 888 were listed as having left the nucleus flock for the VLA. **Table 2** summarises this information by year of departure. The expectation was that animals in shaded cells represented the optimal populations to target for testing, on the assumption that any evidence of infection would most probably have arisen from infection before importation. They left the flock within two years of arrival, but unfortunately were considered to be less than four years of age at the time. This is younger than normal for atypical cases found in the UK surveillance programme. At this time it had not been determined that these animals had actually been culled and were available to retest.

16. **Table 3** summarises the fate of all animals recorded as having entered the flock, either by importation or birth. Of the total of 5676 listed, 808 remained alive in the flock. The primary recipients of sheep from the flock were the VLA and Institute 3, although in the case of the VLA this would have included routine culls, and intercurrent deaths, while those sent to the Institute 3 were intended for projects.

17. Of the 2298 destined for the VLA, only 1082 were recorded as having a PG reference number on the Neuropathology Daybook (Table 4). This is issued on receipt into the diagnostic system. Some animals (372) were not issued with PG reference numbers despite being culled from the source flock. The majority would have been under 6 months of age and considered too young to warrant monitoring for the presence of scrapie. Another 489 were culled within specific projects, some exposed to scrapie by virtue of their locations, and others not, but where the project design did not require post-mortem examination. At the time of culling, their potential exposure to TSEs after leaving the scrapie-free flock had been considered to compromise their use for monitoring the status of the source flock. These were therefore unavailable for testing as part of this exercise. A total of 355 animals were recorded as still alive in VLA projects.

18. Of the 1082 sheep for which fixed tissue samples are available for testing, 913 had been reviewed or retested as at 6th February (Table 5a). Only one, G320, was positive. These include 49 that were exposed to natural scrapie within the VLA scrapie-infected flock, and have tested negative previously using an older IHC protocol. A negative result on retesting using current protocols will still be of value. The balance of 168 samples are considered inappropriate for re-examination for a variety of reasons (Table 5b).

19. Care is needed in the interpretation of the results of IHC examinations. As indicated in tables 6 (Imports) and 7 (Homebred), the distribution of samples by age and genotype of the source sheep highlight the fact that the majority were under five years of age at death, and the AHQ and ARR alleles were relatively poorly represented, as indeed they are in the flock as a whole. Indeed 193 out of the total 1082 were less than one year old at death. Tables 6a and 7a include small numbers of results for animals sent to two other institutes, increasing the number of imported animals tested by 123, and homebred animals by 3.

Epidemiology

20. In parallel with the UKAS audit, and testing of samples, the Standard Operating Procedures relating to the flock, and the age and genotype range of sheep tested are being analysed with a view to:-

a) considering whether or not potential routes of entry can be identified, and

b) estimating the power of the testing done to detect atypical scrapie if still in the flock at low prevalence.

21. In order to put potential risk factors into context, details of the local sheep population have been accessed from national databases. The farm is located in a county with one of the lowest sheep stocking densities in the country at under 30 sheep/km^2. In 2004, only 318 holdings were recorded as having sheep in the county, with a total of 20,947 sheep, and an average flock size of 66.

22. Only 33 of the holdings were recorded as being within a 10km radius of the sheep unit, and comprised a total of 2,506 sheep, an average flock size of 76, and a density of 8/km^2. This information is however based upon business address, and cannot identify the exact location of grazed sheep.

23. An examination of data arising from the fallen stock survey since 2002 reveals 67 suitable submissions from 45 holdings in the county, all of which tested negative for scrapie. Of the 33 in the 10km radius of the unit, six submitted a total of 7 suitable samples.

24. In the scrapie abattoir survey, only four tested sheep have been traced back to the county, two of which were from a single farm within 10km of the unit. Again results were negative.

25. The next step, apart from completion of outstanding IHC examinations, has been to carry out testing by BioRad TeSeE ELISA on those brain samples where brain stem and/or cerebellum is represented, targeting cerebellum wherever available. A total of 579 results are available, with some 20 outstanding. So far only one additional negative sheep has been added to the sample pool as a result. The other 578 were also IHC negative. (see Table 8)

26. Additionally there will be a re-analysis of brain samples made available to us by receiving institutes. None have been offered so far, other than those already included in the preliminary analyses. Most of the sheep received by institues are unsuitable by virtue of parenteral challenge or young age at death or are unavailable where still alive.

Table 1. Distribution of sheep imported from New Zealand by breed, sex and year of birth

		Imported in 1998				Imported in 2001			
Breed	**Sex**	**1994**	**1995**	**1996**	**1997**	**1998**	**1999**	**2000**	**Grand Total**
Cheviot	F				161	14	134	262	571
Cheviot	M				58			163	221
Dorset	F			157	189	4		1	351
Dorset	M		37	10	90			3	140
Suffolk	F	2	12	162	109			380	665
Suffolk	M		9	40				6	55
Total		**2**	**58**	**369**	**607**	**18**	**134**	**815**	**2003**

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Table 2. Distribution of sheep imported from New Zealand, destined for VLA by year of departure and age at departure

ImportYear	Age	1998	1999	2000	2001	2002	2003	2004	2005	2006	Total
1998	0	61									61
1998	1	27	60								87
1998	2	36	90	42							168
1998	3	3	7	18	53						81
1998	4				76	63					139
1998	5				34	44	22				100
1998	6					1	1				2
1998	7					2		5	6		13
1998	8								2		2
Sub-Total		**127**	**157**	**60**	**163**	**110**	**23**	**5**	**8**	**0**	**653**
2001	0				1						1
2001	1				54	10					64
2001	2				5	4	40				49
2001	3				2	1	11	17			31
2001	4						3	17	22		42
2001	5							3	11	24	38
2001	6								2	7	9
2001	7								1		1
Sub-Total		**0**	**0**	**0**	**62**	**15**	**54**	**37**	**36**	**31**	**235**
Total		**127**	**157**	**60**	**225**	**125**	**77**	**42**	**44**	**31**	**888**

MK 16/1/2007

as at 25 April 2007

Table 3. Summary of Sheep by Destination

Destination	Total	Imported	HomeBred
Alive- at sheep unit	808	164	644
Institute 1	41	0	41
Institute 2	22	0	22
Institute 3	1756	750	1006
Institute 4	273	40	233
Institute 5	280	37	243
Institute 6	124	124	0
Slaughter *	74	0	74
VLA	2298	888	1410
TOTAL	**5676**	**2003**	**3673**

** - in one season, permission given by Defra for surplus lambs to be sent for human consumption, under 6 months of age

MK 17/1/2007

Table 4. Summary of PG numbers for sheep destined for VLA

Destination	Alive	With PG Number	No PG Number	Grand Total
VLA Cull	0	265	372	637
VLA Project	355	817	489	1661
Total	**355**	**1082**	**861**	**2298**

A PG reference simply denotes entry into the diagnostic system for TSEs at VLA.

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Table 5.a Summary of Testing Fixed Tissue by IHC Results

New Result	Count Of PG number	Comment
N/A	168	tissue not to be re-tested or re-examined
Negative	913	
Positive	**1**	
Total	**1082**	

The positive IHC result (PG0832/06 - for AR eartag G320) is for the index case for the investigation and so not a new positive that has cropped up during the investigation

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Table 5.b Summary of Fixed Tissue which will not be tested

Testing Status	Count Of PG number	***Comment***
Exp Positive	91	Tissue has been previously tested and result is scrapie positive - these sheep had exposure to scrapie experimentally
No tissue - A	1	Sheep used in a training PM and no tissues were kept for examination
No tissue - B	20	Tissues taken for Archive request 490 - no obex available for testing
No tissue - C	56	Dam in project at HM - no CNS taken at PM due to FMD restrictions, 2001
Total	**168**	

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Table 6 **Summary of sheep <u>imported from New Zealand</u>, Tested by IHC on Fixed Tissue by Genotype and Age at examination**

Destination	VLA Project

Count of SheepID	Age(yr)									
Genotype	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**Grand Total**
??/??/QQ		1	2		3					6
AA/HH/QQ			1	1	2	8				12
AA/RH/QQ		1	1				1			3
AA/RR/QQ	2	19	15	9	19	8	2	1	8	83
AA/RR/RQ	31	35	2		3	1				72
AA/RR/RR	22	19	8	1		1	1	2		54
AV/RH/QQ		11		1				1		13
AV/RR/QQ	2	2	25	3	4	2	1			39
AV/RR/RQ		6	1	2				1		10
VV/RR/QQ		2			2	1	3			8
Grand Total	**57**	**96**	**55**	**17**	**33**	**21**	**8**	**5**	**8**	**300**

Destination	VLA Cull

Count of SheepID	Age(yr)							
Genotype	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**Grand Total**
??/??/QQ		1							1
AA/HH/QQ	1		1		1				3
AA/RH/QQ		1							1
AA/RH/RQ	1								1
AA/RR/QQ	1	4	4	4	16	19		1	49
AA/RR/RH			1						1
AA/RR/RQ	8	7	12	3	7	8		2	47
AA/RR/RR	4	2	12	6	11	8	1	1	45
AV/RH/QQ			1						1
AV/RR/QQ	3	1	2			1		1	8
AV/RR/RQ	1			1					2
VV/RR/QQ			1		2	3		2	8
Grand Total	**19**	**16**	**34**	**14**	**37**	**39**	**1**	**7**	**167**

As at 14 Feb 2007

Table 6a **Summary of all sheep imported from New Zealand, Tested by IHC on Fixed Tissue by Genotype and Age at examination – including available samples at institutes 5 & 6**

Destination	**(All)**

Count of SheepID	**AgeAtPM (yr)**												
Genotype	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**Grand Total**
??/??/QQ		1	1	2		3							7
AA/HH/QQ	1		1	1	2	2	8						15
AA/RH/QQ		1	1	1				1					4
AA/RH/RQ	1												1
AA/RR/QQ	1	6	24	19	29	40	14	13	27	19	1		193
AA/RR/RH			1										1
AA/RR/RQ	8	38	47	5	8	12	6	6	8	42	3	1	184
AA/RR/RR	4	24	31	14	13	10	2	2	2				102
AV/RH/QQ			12		1				1				14
AV/RR/QQ	3	3	4	25	3	5	2	2					47
AV/RR/RQ	1		6	2	2				1				12
VV/RR/QQ			3		2	5	2	5					17
Grand Total	**19**	**73**	**131**	**69**	**60**	**77**	**34**	**29**	**39**	**61**	**4**	**1**	**597**

For Institute 5, 7/37 imported sheep available to test.
All 124 from institute 6 available.

As at 14 Feb 2007

Table 7 **Summary of Home Bred sheep, Tested by IHC on Fixed Tissue by Genotype and Age at examination**

Destination	VLA Project

Count of SheepID	AgeAtPM(yr)								
Genotype	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**Grand Total**
AA/HH/QQ	12	2			1		3		18
AA/RH/QQ	1								1
AA/RR/QQ	24	10	11	13	1	7	8	1	75
AA/RR/RQ	4	6	5	3	3	1			22
AA/RR/RR	18	11	13	16	7	2	10	2	79
AV/RR/QQ	69	4	2	3	2				80
AV/RR/RQ	25		2	2	3			1	33
VV/RR/QQ	15	2	7	2	5	7	4		42
Grand Total	**168**	**35**	**40**	**39**	**22**	**17**	**25**	**4**	**350**

Destination	VLA Cull

Count of SheepID	AgeAtPM(yr)								
Genotype	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**Grand Total**
AA/RR/QQ	3	2	3	7	12	4	3		34
AA/RR/RQ							1		1
AA/RR/RR	2	5	9	6	7	6	2	1	38
AV/RR/QQ			2	1					3
AV/RR/RQ			2						2
VV/RR/QQ	1	3	2	4	5	4			19
Grand Total	**6**	**10**	**18**	**18**	**24**	**14**	**6**	**1**	**97**

As at 14 Feb 2007

Table 7a Summary of all AR Home Bred sheep, Tested by IHC on Fixed Tissue by Genotype and Age at Post Mortem - including available samples at institutes 5 & 6

Destination	**(All)**

Count of SheepID	**AgeAtPM(yr)**								
Genotype	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**Grand Total**
AA/HH/QQ	12	2			1		3		18
AA/RH/QQ	1								1
AA/RR/QQ	27	12	14	21	13	11	11	1	110
AA/RR/RQ	4	6	5	3	3	1	1		23
AA/RR/RR	20	16	22	22	15	8	12	3	118
AV/RR/QQ	69	4	4	4	2				83
AV/RR/RQ	25		4	2	3			1	35
VV/RR/QQ	16	5	9	6	10	12	4		62
Grand Total	**174**	**45**	**58**	**58**	**47**	**32**	**31**	**5**	**450**

Includes additional 3/243 sheep sent to Institute 5.

As at 14 Feb 2007

Table 8
AR database - Number of Sheep Tested negative by Biorad ELIZA only, or negative by IHC only,
or negative by both IHC and Biorad ELIZA,
sorted by Genotype - VLA Destined sheep (Import & Home bred)

Destination	(All)
Imported	(All)
Age At PM(yr)	(All)

Count of PGnumber	**Test**			
Genotype	**ELIZA**	**IHC**	**IHC-ELIZA**	**Grand Total**
??/??/QQ		4	3	7
AA/HH/QQ		8	25	33
AA/RH/QQ		2	3	5
AA/RH/RQ		1		1
AA/RR/QQ		49	191	240
AA/RR/RH		1		1
AA/RR/RQ		106	36	142
AA/RR/RR	1	86	130	217
AV/RH/QQ		13	1	14
AV/RR/QQ		34	97	131
AV/RR/RQ		23	24	47
VV/RR/QQ		10	68	78
Grand Total	**1**	**337**	**578**	**916**

Note: there is one negative Biorad ELIZA (PG1100/00, SheepID C084, Import) for which IHC was not done (result = N/A, i.e. tissue not to be re-tested or re-examined)

MK 19/04/2007

D Matthews
Veterinary Laboratories Agency.

CONFIDENTIAL

SEAC 97/2
Annex 2

UNITED KINGDOM ACCREDITATION SERVICE (UKAS)
ASSESSMENT REPORT

Report
With Appendices:

I **Specification of Requirements**
II **References**
III **Procedure Refererences**
IV **Review of Disease Incident Reports for the VLA/ADAS Sheep Unit 1998-2006**

Please treat as confidential

Published research and Previous SEAC and European Commission DG Health and Consumer Protection Scientific Steering Committee (SSC) advice

Sewage sludge

In a June 1996 statement[1], along with recommendations for handling waste material from cattle, SEAC considered the practice of spreading of sewage sludge on land in the context of the risk of Specified Risk Material (SRM) particles from abattoir waste potentially entering the sewerage system. Provided the particulate matter was retained and disposed of as SRM, the committee was content for abattoirs to discharge their liquid waste to sewers and for sewage sludge to be disposed of by spreading on land. Any small particulate matter passing through the trap would be diluted to such an extent as to pose negligible risk.

Gale and Stanfield[2] estimated the risks from sewage sludge based on the assumption that 1% of brain and spinal cord is lost to the sewer from abattoirs. The model predicts a risk of BSE transmission of 71 x 10^{-5} cow^{-1} $year^{-1}$ for cattle grazing on land to which sewage sludge has been applied. The authors conclude that the dose consumed by grazing cattle is insufficient to sustain the BSE epidemic in the UK cattle herd. The risk from sewage sludge derived from human, cattle and other species remains theoretical.

Birds

The possibility that birds may act as possible transmitters of BSE was considered by the SSC opinion 7-8 November 2002[3] (provided) "Necrophagous birds as possible transmitters of TSE/BSE". The SSC concluded that birds could have theoretically ingested infectious material through fallen stock. It had been proposed that the spread of the ingested infectious material could occur through faecal contamination, as it is unlikely the pathological prion protein would be destroyed in the digestive tract. The SSC concluded that the possibility of active replication of PrP^{Sc} in birds is remote but agreed that such pathways of transmission cannot be excluded given these birds cover great distances during migration.

Rodents

Concepcion and Padlan[4] have postulated that inadvertent ingestion of infected rodent parts, possibly droppings, may be a potential mode of transmission of TSEs. This postulate is based on sequence homology comparisons, which showed a close similarity between sequences of human and rodent prion proteins in a peptic fragment

[1] http://www.seac.gov.uk/statements/state07jun96.htm
[2] Gale P. and Stanfield G. (2001) Towards a quantitative risk assessment for BSE in sewage sludge *J. Appl. Microbiol*. 91, 563-569
[3] http://ec.europa.eu/food/fs/sc/ssc/out295_en.pdf

[4] Concepcion G.P. and Padlan E.A. (2003) Are humans getting 'mad cow disease' from eating beef or something else? *Med. Hypotheses* 60, 699-701

(that could result from gastric digestion) that corresponds to a PrP fragment that is protease resistant and infective. This remains a postulate.

Other organisms

Transmission of TSEs through ectoparasites has been postulated by Lupi[5]. Post *et al*[6] fed larvae of meat eating and myiasis causing flies with brain material from scrapie-infected hamsters. Two days after eating infected material, the larvae showed high amounts of PrP^{Sc} by Western blot. In further studies, the inner organs of larvae, which had been fed with scrapie brain, were extracted and fed to hamsters. Six out of eight hamsters developed scrapie. Two out of four hamsters fed on scrapie infected pupae subsequently developed scrapie.

At SEAC36 (September 1996) members considered a paper by Wisniewski et al[7], (data also published subsequently in a paper by Rubenstein et al[8]) who inoculated suspensions of mites from five Icelandic scrapie affected farms into mice, intracerebrally and intraperitoneally. Of 71 mice inoculated, 10 developed clinical TSE, with detection of PrP^{Sc} in their brains by Western blot. PrP^{Sc} was demonstrated in mite concentrates from one of the farms. The committee also received a presentation on a survey of the prevalence of mites in various cereal products. Some mites were of the same species in the Wisniewski study. SEAC concluded that it was essential that the work on mites be repeated to validate the conclusions. SEAC did not consider that the conclusions raised any public health concerns on mites and TSEs.

Post *et al*[6] found that mites exposed to hamster scrapie and subsequently fed to hamsters did not cause clinical scrapie in the hamsters.

Defra has funded two projects to study transmission of TSEs from hay mites, which are now completed.

Project SE1829

Mites of 3 different species that are present on farms in the UK were fed on material contaminated with BSE infected cow brain. The mites were found not to carry sufficient amounts of infection to cause TSE in mouse bioassays. Similarly when the exposed mites were cultured for 2-3 generations no TSE transmission was detectable by mouse bioassay. Attempts to detect conserved DNA sequences from mammalian PrP genes in mite DNA extracts were unsuccessful indicating that mites do not have PrP-like proteins. The results suggest that mites are unlikely to be significant vectors or reservoirs of TSE diseases.

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[5] Lupi O. (2005) Risk analysis of ectoparasites acting as vectors for chronic wasting disease. *Med. Hypotheses* 65, 47-54

[6] Post K. (1999) Fly larvae and pupae as vectors for scrapie. Lancet 354, 1969-1970

[7] Wisniewski H.M., Sigurdarson S., Rubenstein R., Kascsak R.J, Carp R.I. (1996) Mites as vectors for scrapie. Lancet 347, 1114

[8] Rubenstein R., Kascsak R.J., Carp, R.I., Papini M., LaFauci G., Sigurarson S., and Wisniewski HM (1998) Potential role of mites as a vector and/or reservoir for scrapie transmission. *Alzheimer's Disease Review* 3, 52-56

Project SE1828
Fifteen sheep farms with high incidence scrapie and fifteen farms with low (no reported) incidence scrapie were examined for mite infestation. Overall the results (mite fauna) were closely similar and no clear differences between high and low incidence farms were identified. Samples of mites were cultured to test their ability to carry TSEs. Mice challenged with the mite samples failed to reveal any evidence of infectivity.

Search terms with atypical scrapie on Pubmed:
The following search criteria were used with no result-
Environmental transmission of atypical scrapie
Atypical scrapie and environment
Atypical scrapie and mites
Atypical scrapie and foxes
Atypical scrapie and birds
Transmission of atypical scrapie by rodents: this revealed use of rodent models rather than transmission by mice in the field.

Code	Project title	Project Leader	Start	End date	Brief summary
Studies on the prevalence of atypical scrapie					
SE0243 (Defra)	Analysis and design of scrapie surveillance strategies in Great Britain	Victor del Rio Vilas (VLA) in a collaborative study with IAH, RVC, Oxford	01/10/05	31/03/08	Estimation of the frequency of classical and atypical scrapie in British sheep, based on data available and design of most cost-effective sampling strategies for year on year frequency estimations.
SE0248 (Defra)	A VLA audit of ovine and caprine formalin-fixed, paraffin-embedded tissues to assess suitability for a retrospective search for atypical scrapie	Paul Webb (VLA)	01/12/06	20/03/07	Survey of historical sheep material available that could be tested for the presence of atypical scrapie.(Testing regime currently being negogiated in further work.)
SE0251 (Defra)	A search for UK atypical scrapie in archival samples and in classical scrapie resistant sheep	Nora Hunter (IAH)	01/05/07	31/10/08	Survey and testing of sheep samples collected from 1960 onwards for the presence of atypical scrapie.
Studies on the transmissibility of atypical scrapie					
SE1850 (Defra)	Transmission of unclassified scrapie survey samples to conventional and transgenic mice	Peter Griffiths (VLA)	01/11/04	31/03/07	A study to establish if atypical scrapie isolates and relevant controls can be transmitted to conventional and transgenic mouse lines.
SE1847 (Defra)	Anomalous scrapie transmission to sheep	Marion Simmons (VLA)	01/11/04	31/03/11	Intracerebral and oral challenges of atypical scrapie isolates in sheep and investigation of whether lymphoreticular tissue from clinical cases of atypical scrapie carry infectivity by mouse bioassay.
SE1441 (Defra) M03054 (FSA)	The relative transmissibility of atypical forms of scrapie to humans	Rona Barron (Roslin/IAH)	01/07/06	30/06/10	Challenges of transgenic mice carrying human, sheep or bovine PRNP transgenes with atypical scrapie, classical scrapie, sheep BSE, CWD and BASE.
M03043 (FSA)	Exploring permability of human species barrier to circulating TSE agent	Olivier Andreoletti (INRA)	01/03/07	28/02/12	Challenges of transgenic mice expressing the human or animal PrP protein with a panel of animal TSEs and control human CJD. Investigating inter- and intra-species transmission.
M03055 (FSA)	Assessing the risk to humans of transmission of novel TSE isolates by cell free conversion assays	Andrew Gill (Roslin/IAH)	01/04/07	31/03/10	Cell free conversion assays to parallel work being done in transgenic mice.

Studies on the tissue distribution of atypical scrapie					
M03057 (FSA)	Investigation of infectivity of atypical scrapie in slaughter age sheep following oral dosing of young lambs	Marion Simmons (VLA)	15/01/07	31/03/12	Oral challenge of homologous genotype lambs with atypical scrapie. Animals culled at 12 months and end-point and tissues subjected to biochemical analysis. Selected tissues bio-assayed.
Other studies on atypical scrapie					
SE0240 (Defra)	Ovine PrP polymorphism: investigation of unclassified scrapie cases	Ginny Saunders (VLA)	01/01/05	31/03/06	A study which provided significant data on the correlation between Prnp genetics and the genotype of sheep carrying atypical scrapie infection.
SE1789 (Defra)	Unclassified (anomalous) scrapie survey samples: biochemical and immunological characterisation	Linda Terry (VLA)	01/04/04	31/03/07	A study on the effects of proteinase K concentrations and other assay conditions on isolates atypical scrapie.