UNUSUAL CASES OF SPONGIFORM ENCEPHALOPATHY IN CATTLE

ISSUE

1. To consider the implications of emerging scientific data suggesting the existence of other strains of spongiform encephalopathy in cattle.

BACKGROUND

2. In the past few years, surveillance of cattle for Bovine Spongiform Encephalopathy (BSE) in a number of countries has identified animals with phenotypes of abnormal prion protein (PrP^{Sc}) that differ from that usually associated with BSE. Most of these animals were over the age of eight years old. Neuropathological investigations of some of these animals revealed differences in the deposition and distribution of PrP^{Sc} compared with those expected for BSE. Inoculations of mice have demonstrated the disease to be transmissible. These findings suggest that cattle may be susceptible to another strain, or strains, of naturally occurring transmissible spongiform encephalopathy (TSE).

3. At SEAC 81, SEAC considered the findings of a research paper[1] suggesting that a second spongiform encephalopathy exists in cattle with a molecular signature similar to that of a subtype of sporadic CJD (sCJD). SEAC agreed that without information on the transmissibility, it was premature at that time to conclude this was a new strain of BSE.

4. At SEAC 93, SEAC noted reports that western blot (WB) profiles of two cases of BSE in USA cattle were similar to a small number of unusual cases of BSE found in France. A study[2] of the French

[1] Casalone *et al*. Identification of a second bovine amyloidotic spongiform encephalopathy: molecular similarities with sporadic Creutzfeldt-Jakob disease. *Proc Natl Acad Sci U S A*. 2004 Mar 2;**101**(9):3065-70.

[2] Baron *et al.* Transmission of new bovine prion to mice. *Emerg Infect Dis*. 2006 Jul;**12**(7):1125-8.

cases had shown the condition to be transmissible to mice by intracerebral inoculation, with the neuropathological phenotype maintained on transmission. SEAC noted that claims had been made about the existence of further cases in cattle, that are distinct from classical BSE in other countries. It was noted that no study had examined the tissue distribution of PrP^{Sc} or infectivity in such cases.

5. At SEAC 96 the committee agreed to consider available information on unusual cases of BSE (see SEAC paper 97/1), as they will be described for the purposes of this paper, at SEAC 97.

SEAC CONSIDERATION

6. This paper summarises the published information of unusual BSE cases. At SEAC 97, the committee will also receive presentations from a number of invited experts. A list of questions based on the committee's discussion at SEAC 96 are provided at the end of the paper to focus discussions. A SEAC position statement will be published.

PUBLISHED INFORMATION

7. Published information on unusual cases of BSE is summarised below. Table 1 summarises the data on each identified case. Annex 1 details the original papers referred to in this cover paper.

Italian cases

8. Casalone *et al*[1] identified the first two cases of unusual BSE. The animals were aged 11 and 15 years by active surveillance. WB analysis showed a PrP^{Sc} banding pattern type different from that expected for BSE, with a lower frequency of glycosylation and protease resistant fragments of lower molecular weight. Genetic analysis did not detect mutations in the prion protein gene of the animals. The authors noted the WB pattern to be similar to that associated with a type of sCJD. In addition the PrP^{Sc} was more widely distributed in the brain in these animals and formed plaque-like, rather than granular deposits compared with usual cases of BSE.

9. Capobianco *et al*[3] conducted transmission experiments using wild type and bovinised mice using two inocula, one prepared from

[3] Capobianco *et al*. Conversion of the BASE Prion Strain into the BSE Strain: The Origin of BSE? *PLoS Pathog.* 2007 Mar 9;**3**(3):e31 [ahead of print]

brain material from one of the cases identified by Casalone *et al* and the other from a BSE case of the same genotype. The inocula had similar concentrations of PrP^{Sc}. Bovinised mice parenterally administered with unusual BSE case inoculum had a shorter mean incubation period (178 compared to 216 days), differing clinical signs including lethargy compared with hyper-excitability, abnormal Magnetic Resonance Imaging signals that were more widely distributed in the brain, more extensive neuropathological degeneration and more diffuse PrP^{Sc} deposition, compared with BSE inoculated mice. The sizes and extent of glycosylation of protease resistant fragments of PrP^{Sc} from bovinised mice inoculated with unusual BSE were lower than that from mice inoculated with BSE. Both inocula were also parenterally administered to a panel of four strains of wild type mice. The BSE inoculum produced a progressive neurological disease with a pattern of PrP^{Sc} deposition and lesions characteristic of BSE in all four strains. In contrast, no neurological disease or PrP^{Sc} deposition was detected in mice administered with unusual BSE case inoculum. However, on second passage, using material from these asymptomatic animals, two strains of mice developed neurological disease with a longer incubation period than mice inoculated with BSE but with a similar neurological distribution and deposition of PrP^{Sc} and with a similar PrP^{Sc} WB profile. Observations of the other two strains of mice are ongoing. The authors suggest that on serial passage the unusual BSE strain may be converted to the BSE strain.

French cases

10. Biacabe *et al*[4] reported the identification through active surveillance of three unusual BSE cases aged eight, ten and 15 years. These were distinguished from usual BSE cases on the basis of a higher molecular mass of unglycosylated PrP^{Sc}, lower levels of diglycosylation of PrP^{Sc} and differing PrP^{Sc} reactivities to anti-PrP^{Sc} antibodies on WB analysis. Genetic analysis did not detect unknown mutations in the prion protein gene of these animals.

11. Baron *et al*[2] conducted transmission experiments using wild type mice and inocula prepared from two of the unusual BSE cases reported by Biacabe *et al* and one BSE case. Mean incubation periods in the groups of mice parenterally inoculated with material from the unusual BSE cases were longer than in the group inoculated with BSE (702 and 652 days compared with 511 days). The mice displayed similar PrP^{Sc} WB patterns to those seen on

[4] Biacabe *et al*. Distinct molecular phenotypes in bovine prion diseases. *EMBO Rep*. 2004 Jan;**5**(1):110-5.

analysis of the unusual BSE cases. The distribution of neuropathological lesions and PrP^{Sc} deposits in mice administered with the unusual BSE inocula was more restricted than usually observed in mice with BSE.

12. Beringue *et al*[5] conducted transmission experiments using bovinised and ovinised mice and inocula prepared from BSE, sheep BSE, goat BSE, vCJD and unusual BSE cases similar to, and including, those reported by Biacabe *et al*. The unusual BSE inocula produced neurological disease in bovinised mice with longer mean incubation periods (401 and 414 days) compared with the other inocula (253 to 377 days). The mean incubation periods produced by the unusual BSE inocula to ovinised mice (586 to 612 days) were similar to those produced by the other inocula (560 to 704 days) with the exception of the vCJD inoculum (792 days). The incubation period of unusual BSE in bovinised and ovinised mice was reduced on second passage. Western blot analysis showed that the PrP^{Sc} phenotype produced by unusual BSE inocula was preserved on serial transmission in both strains of mice. Examination of the pathological changes and PrP^{Sc} deposition in the brain of bovinised mice showed more extensive vacuolation and diffuse, but widespread, PrP^{Sc} deposits in mice administered the unusual BSE compared with the BSE inocula. Unlike inoculations with BSE or vCJD, the unusual BSE inocula produced no detectable PrP^{Sc} in the spleen of ovinised mice. The phenotype and neuropathological distribution of PrP^{Sc} in ovinised mice from unusual BSE inocula were compared with inocula prepared from classical scrapie strains. The PrP^{Sc} phenotype and deposition produced by these inocula differed markedly. The authors conclude that these findings suggest that cases of unusual BSE represent infection with a strain distinct from other TSE agents.

German cases

13. Buschmann *et al*[6] identified two unusual BSE cases in an analysis of 27 animals aged over eight years old that tested positive for BSE during active surveillance. Western blot analysis using brain material from one animal aged 13 years showed a PrP^{Sc} phenotype similar to that reported by Biacabe *et al* witha non-glycosylated fragment of higher than expected molecular weight (designated H-

[5] Beringue *et al.* Isolation from cattle of a prion strain distinct from that causing bovine spongiform encephalopathy. *PLoS Pathog*. 2006 Oct;**2(**10):e112**.**

[6] Buschmann *et al*. Atypical BSE in Germany--proof of transmissibility and biochemical characterization. *Vet Microbiol*. 2006 Oct 31;**117**(2-4):103-16.

type). Analysis of the other animal aged 15 years showed a PrP^{Sc} phenotype similar to that reported by Casalone *et al* with a non-glycosylated fragment of lower than expected molecular weight (designated L-type). Genetic analysis of the prion protein gene of both animals did not detect unknown mutations in this gene. Bovinised mice parenterally inoculated with L-type, H-type and BSE inocula developed neurological disease with mean incubation periods of 185, > 322 (observations of mice in this group continue) and 185 days, respectively. Neuropathological changes and PrP^{Sc} deposition differed between mice administered the three inocula. More extensive vacuolation with small PrP^{Sc} plaques was observed in L-type inoculated mice compared with BSE inoculated mice whereas PrP^{Sc} granules and aggregates were observed in H-type inoculated mice.

Japanese case

14. Yamakawa *et al*[7] reported the identification of an animal aged 23 months of age identified with a weakly positive PrP^{Sc} signal during active surveillance of cattle. Western blot analysis of a brain homogenate showed PrP^{Sc} to be less resistant to protease and with a lower proportion of diglycosylated fragment and a non glycosylated fragment of lower molecular weight compared with that expected for BSE. No neurohistopathological changes or PrP^{Sc} deposits were detected in this animal. This case is very much younger than the other unusual BSE cases.

Polish case

15. Polak *et al*[8] reported the molecular characterisation of prion protein glycoforms in 12 out of 14 BSE cases detected in cattle in Poland. While eleven cases showed typical PrPSc glycoform patterns for BSE, one case showed a low content of dilglycosylated PrP^{Sc} fragments, than expected for BSE case. This unusual BSE case had relatively equal amounts of both di- and monoglycosylated PrP^{Sc}. As sheep scrapie has a low content of diglycosylated PrP^{Sc}, the authors suggest that this unusual case may be linked to sheep scrapie infection, although it needs further conformation.

[7] Yamakawa *et al*. Expert Committee for BSE Diagnosis, Ministry of Health, Labour and Welfare of Japan. Atypical proteinase K-resistant prion protein (PrPres) observed in an apparently healthy 23-month-old Holstein steer. *Jpn J Infect Dis*. 2003 Oct-Dec;**56(**5-6):221-2

[8] Polak *et al*. Prion protein glycoforms from BSE cases in Poland. *Bull Vet Pulawy* 2004; **48**: 201-05

Swiss case

16. Seuberlich *et al*[9] reported characterisation of an unusual form of spongiform encephalopathy (SE) in a 19 year old miniature zebu cattle in a zoo in Switzerland. The animal showed clinical signs for neurological impairment including anxiety, abnormal gait and posture. Neuropathological investigations showed severe spongiform changes and PrP^{Sc} deposition. WB analysis gave a higher molecular mass of diglycosylated PrP^{Sc} fragment and PrP^{Sc} fragments had a differing reactivity to anti-PrP^{Sc} antibodies than expected for a BSE case.

American case

17. Richt *et al*[10] reported the identification and characterisation of two cases of spongiform encephalopathy in cattle identified by rapid BSE testing through the BSE surveillance in the United States of America. On neuropathological examination, one animal, aged 12 years old, diagnosed as downer cow, did not show any spongiform changes in the brain. However, after applying an extended antigen retrieval method to the tissue sections, a weak PrP^{Sc} staining was observed by immunohistochemistry. Higher molecular mass of monoglycosylated and unglycosylated fragments of PrP^{Sc}, similar to the cases reported by Biacabe *et al* [4] and Buschmann *et al* [6], was detected by WB after enrichment of PrP^{Sc} in the samples. On discriminatory WB analysis, PrP^{Sc} fragments showed a differing reactivity to anti-PrP^{Sc} antibodies than expected for a BSE case. Genetic analysis did not detect unknown mutations in the prion protein gene of these animals. The other animal was characterised as a usual BSE case.

UK case

18. A case of unusual BSE in a 13 year old cow was recently reported in the United Kingdom (Annex 2).

[9] Seuberlich *et al*. Spongiform encephalopathy in a miniature Zebu. *Emerg Infect Dis*. 2006;**12**:1950-53

[10] Richt *et al.* Identification and characterisation of two bovine spongiform encephalopathy cases diagnosed in the United States. *J Vet Diagn Invest* 2007;**19**:142-54

Discussion article

19. Brown *et al*[11] discuss data on unusual BSE cases and the possibility that their origin may be sporadic and possibly may explain the occurrence of sCJD. The authors conclude that such a link is not currently supported by epidemiological evidence. Details of unusual BSE cases from Canada, Denmark, Belgium, The Netherlands, and Sweden that have not been published in the peer-review literature are included in this article.

UK BSE SURVEILLANCE

20. At SEAC 96, it was suggested that annual data on UK surveillance of cattle by age of animal be provided to allow an assessment of the extent of testing of older animals. Data on the number of animals tested by age of animal for the years 1990-2005 is provided at Annex 3 together with data on the age distribution of the UK cattle population.

DATA PROVIDED BY PRESENTERS

21. A number of the invited experts have provided synopsis of their research. In addition, Dr Yamakawa (Japan) has provided answers to the questions set by SEAC. These are provided at Annex 4.

ADVICE SOUGHT FROM THE COMMITTEE

22. The following areas for discussion and questions were developed on the basis of discussions at SEAC 96. The invited experts have been asked to consider these questions in their presentations. The committee is invited to consider and comment on the questions:

Characterisation of cases and agent

i. Are unusual cases of BSE in cattle associated with BSE or another strain(s) of TSE?

ii. With regard to unusual BSE cases what is known about:
- the pathogenesis of the disease;
- the distribution of PrP^{Sc} in different tissues;

[11] Brown et al. On the question of sporadic or atypical bovine spongiform encephalopathy and Creutzfeldt-Jakob disease. *Emerg Infect Dis*. 200 Dec;**12**(12):1816-21

- geographical and age distribution; and
- clinical characteristics?

iii. What is known about the transmissibility of unusual BSE to cattle, and other species, by parental or oral routes?

iv. Is there a relationship between bovine PrP genotype and unusual BSE cases?

Detection

v. How have unusual cases of BSE been detected?

vi. Could current BSE surveillance in the UK reliably detect unusual cases of BSE?

vii. What further information is needed to inform on the prevalence of unusual cases of BSE?

Origin of unusual BSE

viii. What is known about the likely origin of unusual cases of BSE and how are they related to BSE or other TSEs?

Animal and human health implications

ix. What, if any, are the potential animal health implications of unusual BSE?

x. What, if any, are the potential human health implications of unusual BSE in light of current BSE controls?

TABLE 1 SUMMARY OF DATA ON UNUSUAL BSE CASES

Adapted from Brown *et al.*[12]

Country	Age (years)	Breed	Clinical signs	WB profile†	Neuropathology		Transmission studies					
					Spongiform changes	IHC	1st passage in wild type mice	2nd passage in wild type mice	1st passage in bovinised mice	2nd passage in bovinised mice	1st passage in ovinised mice	2nd pasage in ovinised mice
Italy	15	Piemontese	None	L	Mild	Plaques	Asymptomatic and no PrP^{Sc} deposition in brain tissue.	Neurological disease with classical BSE PrP^{Sc}.	Neurological disease with L-type PrP^{Sc}.	Neurological disease with L-type PrP^{Sc}.	NR	NR
	11	Bruna Alpina	None	L	Mild	Plaques	NR	NR	NR	NR	NR	NR
France	15	Prim' Holstein	None	H	NR	NR	NR	NR	Neurological disease with H-type PrP^{Sc}.	NR	Neurological disease with H-type PrP^{Sc}.	NR
	10	Cross-breed	None	H	NR	NR	Neurological disease with H-type PrP^{Sc}.	NR	Neurological disease with H-type PrP^{Sc}.	NR	Neurological disease with H-type PrPSc. Distinct from ovine TSE PrP^{Sc}.	NR
	8	Charolais	None	H	NR	NR	Neurological disease with H-type PrP^{Sc}.	NR	NR	NR	NR	NR
Denmark*	14	Charolais	None	L	NR	NR	NR	NR	NR	NR	NR	NR
Poland	12	Black-white breed	None	L	Present	Positive (no plaques)	NR	NR	NR	NR	NR	NR
Japan	2	Holstein	None	L	Absent	Negative	NR	NR	NR	NR	NR	NR
	14	Japanese Black	Dystacia	L		Positive (no plaques)	NR	NR	NR	NR	NR	NR
Belgium*	5.5	East-Flemish	None	L1	Present	Negative	NR	NR	NR	NR	NR	NR

The Netherlands*	13	Black-white Holstein	NR	H	Present	No plaques	NR	NR	NR	NR	NR	NR
Sweden *	12	Mixed Charolais	Recumbent	H	NR	Positive (no plaques)	NR	NR	NR	NR	NR	NR
Switzerland	19	Zebu	Typical BSE	H	Typical BSE	Positive (no plaques)	NR	NR	NR	NR	NR	NR
Germany	13	Angus	NR	H	Absent	Positive (no plaques)	NR	NR	NR	NR	NR	NR
	15	Holstein Freisian	NR	L	Absent	Positive (no plaques)	NR	NR	NR	NR	NR	NR
USA	12	Brahma cross	Falling	H	Absent	No plaques	NR	NR	NR	NR	NR	NR
	10	Red crossbred	Recumbent	H	Absent	No plaques	NR	NR	NR	NR	NR	NR
Canada*	16/17	Charolais	Recumbent	H	NR	Positive (no plaques)	NR	NR	NR	NR	NR	NR
UK	13	Galloway	None	H	NR	NR	NR	NR	NR	NR	NR	NR

* Information from Brown et al[11]. † Lower molecular weight (L) or higher molecular weight (H) glycopatterns by western blot. NR – not reported.

PUBLISHED PAPERS ON UNUSUAL CASES OF SPONGIFORM ENCEPHALOPATHY IN CATTLE

1. Casalone *et al*. Identification of a second bovine amyloidotic spongiform encephalopathy: molecular similarities with sporadic Creutzfeldt-Jakob disease. *Proc Natl Acad Sci U S A.* 2004 Mar 2;**101**(9):3065-70.

2. Capobianco *et al*. Conversion of the BASE Prion Strain into the BSE Strain: The Origin of BSE? *PLoS Pathog.* 2007 Mar 9;**3**(3):e31 [ahead of print]

3. Biacabe *et al*. Distinct molecular phenotypes in bovine prion diseases. *EMBO Rep*. 2004 Jan;**5**(1):110-5.

4. Baron *et al*. Transmission of new bovine prion to mice. *Emerg Infect Dis*. 2006 Jul;**12**(7):1125-8.

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6. Buschmann *et al*. Atypical BSE in Germany--proof of transmissibility and biochemical characterization. *Vet Microbiol*. 2006 Oct 31;**117**(2-4):103-16.

7. Yamakawa *et al*. Expert Committee for BSE Diagnosis, Ministry of Health, Labour and Welfare of Japan. Atypical proteinase K-resistant prion protein (PrPres) observed in an apparently healthy 23-month-old Holstein steer. *Jpn J Infect Dis*. 2003 Oct-Dec;**56(**5-6):221-2

8. Polak *et al*. Prion protein glycoforms from BSE cases in Poland. *Bull Vet Pulawy* 2004; **48**: 201-05

9. Seuberlich *et al*. Spongiform encephalopathy in a miniature Zebu. *Emerg Infect Dis*. 2006;**12**:1950-53

10. Richt *et al.* Identification and characterisation of two bovine spongiform encephalopathy cases diagnosed in the United States. *J Vet Diagn Invest* 2007;**19**:142-54

11. Brown *et al.* On the question of sporadic or atypical bovine spongiform encephalopathy and Creutzfeldt-Jakob disease. *Emerg Infect Dis*. 200 Dec;**12**(12):1816-21.

DEFRA REPORT ON THE UK UNUSUAL BSE CASE

INFORMATION BULLETIN

Ref: 71/07
Date: 9 March 2007

Nobel House, 17 Smith Square, London SW1P 3JR
Out of hours telephone 020 7270 8960

2005 case of H-type BSE in a cow

During routine research carried out by the Veterinary Laboratories Agency (VLA), test results have revealed a single case of H-type Bovine Spongiform Encephalopathy (BSE) in the UK in 2005. This form of BSE has already been identified in several other European countries in addition to Japan, Canada and the United States of America.

The cow died on a farm in Dumfries and Galloway at 13 years of age. The carcass was sampled and tested for BSE in accordance with EU requirements for testing all fallen stock aged over 24 months. Test results confirmed the presence of BSE. The carcass was incinerated and the offspring from this cow were culled in line with current BSE regulations.

In August 2006 the VLA began a retrospective examination of brain samples taken from previous BSE cases as part of a research programme designed to analyse different types of BSE in the national herd. The aim of the study is to determine whether unusual cases of BSE, had in fact occurred in the UK in the past. The studies are ongoing however this case has been identified as H-type. All forms of BSE are treated identically therefore no additional action would have been required in this case.

The Spongiform Encephalopathy Advisory Committee (SEAC) will examine all the available data on this case during a discussion of different forms of BSE worldwide at their next meeting on 10 th May 2007.

Notes to editors

1) SEAC briefly discussed information on the different forms of BSE worldwide, at their February 2007 meeting. The background papers for that meeting are available at http://www.seac.gov.uk/agenda/agen200207.htm

2) Japan, the USA, Canada and several European countries (including France, the Netherlands, Sweden, Switzerland, and Germany) have reported H-type BSE. Japan and several European countries (including Italy, Denmark, Poland, Belgium and Germany) have reported L-type BSE. Both types have been reported predominantly in cattle over 10 years old. In both types, the abnormal prion protein (PrP Sc) in these animals has different biochemical characteristics to that seen in BSE. Mice experimentally infected with the brains of these animals develop a disease which differs from that seen in BSE infected mice. In two L-type cases where the intact whole brain was studied, the pattern of deposition of PrP Sc in the brain differed from that in BSE.

End

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UK CATTLE SURVEILLANCE INFORMATION AND AGE DISTRIBUTION OF UK CATTLE POPULATION.

Number of animals tested by age of animals for years 1990-2005:

Surveillance year[b]	Age[c]	Healthy slaughter tested[d]	Healthy slaughter positive[e]	Fallen stock tested[f]	Fallen stock positive[g]	Casualty slaughter tested[h]	Casualty slaughter positive[i]	Clinical suspects tested[j]	Clinical suspects positive[k]
2005	<2yo	4	0	2	0	51	0	3	0
	2	25621	0	21931	0	14155	0	12	0
	3	52552	0	10015	0	22238	1	9	0
	4	53146	0	8423	0	20524	1	13	0
	5	57997	0	9317	3	22605	0	13	1
	6	56276	1	8861	2	22784	4	15	3
	7	51586	1	8217	1	20131	2	20	3
	8	37501	1	6952	2	16584	2	10	0
	9	9048	0	5179	3	12225	12	12	2
	10	2610	2	4400	5	10245	22	22	13
	11	1988	1	3207	3	6929	34	9	5
	12	1324	1	2099	8	4444	16	14	9
	13	943	0	1365	6	2705	15	1	1
	14	515	0	932	4	1601	7	2	0
	15	296	0	703	1	1077	2	2	0
	16	150	0	352	0	562	4	1	1
Grouped data:	17+	813	0	8164	6	10077	6	0	0
	Unknown	909	0	0	0	94	0	14	1
	Total	**353279**	**7**	**100119**	**44**	**189031**	**128**	**172**	**39**

[a] A summary of the BSE surveillance testing and test results, as carried out by the country.

[b] Year in which testing for BSE carried out. Enter the most recent year of testing first.

[c] Age of animal at time of testing (and therefore at time of death).

[d] Number of animals that entered the healthy slaughter stream that were tested for BSE.

[e] Number of animals that entered the healthy slaughter stream that tested positive for BSE.

[f] Number of animals that entered the fallen stock stream that were tested for BSE.

[g] Number of animals that entered the fallen stock stream that tested positive for BSE.

[h] Number of animals that entered the casualty slaughter stream that were tested for BSE.

[i] Number of animals that entered the casualty slaughter stream that tested positive for BSE.

[j] Number of BSE clinical suspect animals that were tested for BSE.

[k] Number of clinical suspect animals that tested positive for BSE.

Surveillance year	Age	Healthy slaughter tested	Healthy slaughter positive	Fallen stock tested	Fallen stock positive	Casualty slaughter tested	Casualty slaughter positive	Clinical suspects tested	Clinical suspects positive
2004	<2yo	27	0	37	0	24	0	3	0
	2	8510	0	18426	0	13022	0	16	0
	3	43478	0	9098	0	19675	0	33	0
	4	71844	2	8948	2	19391	3	26	1
	5	72190	0	8766	1	19800	1	30	4
	6	68467	0	8808	0	18925	6	24	0
	7	56136	1	7805	1	16526	4	27	3
	8	13107	0	6521	6	13773	22	43	12
	9	2837	1	5652	9	11775	35	44	24
	10	2195	4	5299	6	9869	36	33	22
	11	1426	2	2929	10	5686	23	16	11
	12	1302	0	2856	13	4882	11	11	6
	13	565	0	1297	1	2094	18	6	0
	14	385	1	1285	1	1661	8	4	2
	15	188	0	833	7	971	5	1	1
	16	117	0	378	4	451	5	2	1
Grouped data:	17+	546	0	4513	1	5483	3	1	1
	Unknown	166	0	0	0	33	0	22	2
	Total	**343486**	**11**	**93451**	**62**	**164041**	**180**	**342**	**90**

Surveillance year	Age	Healthy slaughter tested	Healthy slaughter positive	Fallen stock tested	Fallen stock positive	Casualty slaughter tested	Casualty slaughter positive	Clinical suspects tested	Clinical suspects positive
2003	<2yo	3	0	22	0	34	0	4	0
	2	366	0	15536	0	11585	0	23	0
	3	35623	0	9024	0	19102	1	24	0
	4	64758	2	7406	0	17372	4	43	4
	5	62950	6	7208	1	16812	11	52	4
	6	51866	0	9585	2	15432	7	34	6
	7	11877	1	6006	8	14092	33	51	35
	8	2589	2	6123	18	14536	70	88	59
	9	2004	3	4736	13	10578	57	60	35
	10	1518	1	4851	12	9494	52	32	19
	11	1235	2	2377	8	5341	31	22	10
	12	801	1	2616	6	4374	17	15	6
	13	437	1	1326	4	2029	11	4	1
	14	280	1	1003	6	1409	4	9	2
	15	182	0	854	6	1000	12	4	4
	16	115	0	316	3	485	4	0	0
Grouped data:	17+	464	0	1037	3	2172	1	0	0
	Unknown	566	0	0	0	22	0	4	0
	Total	**237634**	**20**	**80026**	**90**	**145869**	**315**	**469**	**185**

Surveillance year	Age	Healthy slaughter tested	Healthy slaughter positive	Fallen stock tested	Fallen stock positive	Casualty slaughter tested	Casualty slaughter positive	Clinical suspects tested	Clinical suspects positive
2002	<2yo	3	0	22	0	28	0	16	0
	2	7984	0	16290	0	11268	1	26	0
	3	31836	0	9425	0	18216	0	55	0
	4	49562	1	7818	1	16579	5	55	1
	5	61897	3	7607	2	16123	9	57	7
	6	12241	6	7182	11	15459	62	124	76
	7	1985	1	7404	29	15276	127	213	169
	8	1691	1	6132	24	12494	82	145	108
	9	1325	0	4310	19	7647	48	68	48
	10	1107	0	5082	13	7301	50	47	29
	11	789	0	2288	11	3441	27	11	6
	12	591	2	2662	10	3174	22	20	12
	13	319	2	1125	6	1420	16	8	4
	14	211	0	873	4	1133	13	6	6
	15	136	0	775	4	771	12	8	5
	16	56	0	309	3	370	3	0	0
Grouped data:	17+	799	0	2734	4	8323	23	0	0
	Unknown	538	0	21	0	7	0	14	4
	Total	**173070**	**16**	**82059**	**141**	**139030**	**500**	**873**	**475**

Surveillance year	Age	Healthy slaughter tested	Healthy slaughter positive	Fallen stock tested	Fallen stock positive	Casualty slaughter tested	Casualty slaughter positive	Clinical suspects tested	Clinical suspects positive
2001	<2yo	0	0	0	0	0	0	9	0
	2	464	0	2040	0	3395	0	24	0
	3	1166	0	3386	0	6413	1	46	1
	4	12716	1	2872	1	4898	3	54	9
	5	6186	0	3096	2	5385	15	160	112
	6	223	0	3504	18	6069	74	345	287
	7	232	0	3080	23	5664	61	238	193
	8	207	0	2625	15	5224	54	129	100
	9	172	0	1818	9	3071	26	75	51
	10	115	0	1845	7	2677	12	35	21
	11	93	0	964	2	1513	10	17	8
	12	52	0	717	8	1041	7	19	11
	13	41	0	364	1	530	9	13	9
	14	28	0	248	4	386	2	6	6
	15	13	0	211	1	303	2	1	1
	16	8	0	92	0	148	1	1	0
Grouped data:	17+	11	0	187	0	208	1	0	0
	Unknown	140	0	0	0	3	1	44	4
	Total	**21867**	**1**	**27049**	**91**	**46928**	**279**	**1216**	**813**

Surveillance year	Age	Healthy slaughter tested	Healthy slaughter positive	Fallen stock tested	Fallen stock positive	Casualty slaughter tested	Casualty slaughter positive	Clinical suspects tested	Clinical suspects positive
2000	<2yo					0	0	12	0
	2					291	0	26	0
	3					388	0	57	1
	4					315	6	152	95
	5					287	23	502	416
	6					318	14	476	410
	7					235	8	254	222
	8					217	2	107	83
	9					179	1	46	35
	10					114	0	34	23
	11					70	0	15	10
	12					43	1	21	16
	13					28	0	11	8
	14					24	0	3	1
	15					10	0	2	1
	16					5	0	0	0
Grouped data:	17+					7	0	2	1
	Unknown					14	0	59	9
	Total	**0**	**0**	**0**	**0**	**2545**	**55**	**1779**	**1331**

Surveillance year	Age	Healthy slaughter tested	Healthy slaughter positive	Fallen stock tested	Fallen stock positive	Casualty slaughter tested	Casualty slaughter positive	Clinical suspects tested	Clinical suspects positive
1999	<2yo							9	0
	2							37	0
	3							106	42
	4							504	416
	5							840	736
	6							628	552
	7							285	250
	8							117	97
	9							56	46
	10							61	52
	11							28	23
	12							10	8
	13							6	4
	14							1	0
	15							1	0
	16							0	0
Grouped data:	17+							0	0
	Unknown							162	39
	Total	**0**	**0**	**0**	**0**	**0**	**0**	**2851**	**2265**

Surveillance year	Age	Healthy slaughter tested	Healthy slaughter positive	Fallen stock tested	Fallen stock positive	Casualty slaughter tested	Casualty slaughter positive	Clinical suspects tested	Clinical suspects positive
1998	<2yo							14	0
	2							44	1
	3							210	114
	4							856	736
	5							1118	994
	6							736	654
	7							279	244
	8							164	139
	9							132	105
	10							85	70
	11							43	30
	12							9	6
	13							4	3
	14							2	1
	15							0	0
	16							0	0
Grouped data:	17+							0	0
	Unknown							358	101
	Total	**0**	**0**	**0**	**0**	**0**	**0**	**4054**	**3198**

Surveillance year	Age	Healthy slaughter tested	Healthy slaughter positive	Fallen stock tested	Fallen stock positive	Casualty slaughter tested	Casualty slaughter positive	Clinical suspects tested	Clinical suspects positive
1997	<2yo							15	0
	2							44	0
	3							219	129
	4							907	806
	5							1390	1266
	6							859	748
	7							612	527
	8							331	290
	9							203	168
	10							86	72
	11							25	22
	12							11	8
	13							3	3
	14							2	1
	15							1	1
	16							0	0
Grouped data:	17+							1	1
	Unknown							632	294
	Total	**0**	**0**	**0**	**0**	**0**	**0**	**5341**	**4336**

Surveillance year	Age	Healthy slaughter tested	Healthy slaughter positive	Fallen stock tested	Fallen stock positive	Casualty slaughter tested	Casualty slaughter positive	Clinical suspects tested	Clinical suspects positive
1996	<2yo							11	0
	2							87	5
	3							399	251
	4							1702	1478
	5							1950	1741
	6							1817	1665
	7							1221	1084
	8							690	591
	9							276	213
	10							93	66
	11							41	30
	12							30	19
	13							9	5
	14							5	1
	15							2	1
	16							1	0
Grouped data:	17+							2	1
	Unknown							1936	940
	Total	**0**	**0**	**0**	**0**	**0**	**0**	**10272**	**8091**

Surveillance year	Age	Healthy slaughter tested	Healthy slaughter positive	Fallen stock tested	Fallen stock positive	Casualty slaughter tested	Casualty slaughter positive	Clinical suspects tested	Clinical suspects positive
1995	<2yo							12	0
	2							99	6
	3							685	426
	4							2058	1771
	5							3764	3495
	6							3318	3045
	7							2257	2029
	8							807	689
	9							297	220
	10							126	82
	11							70	32
	12							34	19
	13							7	4
	14							4	1
	15							2	0
	16							1	0
Grouped data:	17+							0	0
	Unknown							3841	2660
	Total	**0**	**0**	**0**	**0**	**0**	**0**	**17382**	**14479**

Surveillance year	Age	Healthy slaughter tested	Healthy slaughter positive	Fallen stock tested	Fallen stock positive	Casualty slaughter tested	Casualty slaughter positive	Clinical suspects tested	Clinical suspects positive
1994	<2yo							26	0
	2							152	14
	3							737	426
	4							3850	3432
	5							6334	5813
	6							6328	5801
	7							2409	2055
	8							705	533
	9							297	202
	10							156	84
	11							74	34
	12							31	6
	13							19	6
	14							5	0
	15							2	0
	16							1	1
Grouped data:	17+							0	0
	Unknown							8023	5888
	Total	**0**	**0**	**0**	**0**	**0**	**0**	**29149**	**24295**

Surveillance year	Age	Healthy slaughter tested	Healthy slaughter positive	Fallen stock tested	Fallen stock positive	Casualty slaughter tested	Casualty slaughter positive	Clinical suspects tested	Clinical suspects positive
1993	<2yo							28	0
	2							199	17
	3							1265	869
	4							6312	5613
	5							12474	11557
	6							5856	5224
	7							1550	1240
	8							588	384
	9							288	144
	10							136	64
	11							71	21
	12							30	5
	13							23	3
	14							8	1
	15							5	0
	16							2	1
Grouped data:	17+							1	0
	Unknown							12789	9687
	Total	**0**	**0**	**0**	**0**	**0**	**0**	**41625**	**34830**

Surveillance year	Age	Healthy slaughter tested	Healthy slaughter positive	Fallen stock tested	Fallen stock positive	Casualty slaughter tested	Casualty slaughter positive	Clinical suspects tested	Clinical suspects positive
1992	<2yo							19	1
	2							173	24
	3							1853	1356
	4							12687	11854
	5							9507	8730
	6							3330	2824
	7							1116	814
	8							471	318
	9							231	117
	10							71	19
	11							55	10
	12							26	7
	13							12	0
	14							7	2
	15							2	0
	16							1	0
Grouped data:	17+							0	0
	Unknown							14009	10973
	Total	**0**	**0**	**0**	**0**	**0**	**0**	**43570**	**37049**

Surveillance year	Age	Healthy slaughter tested	Healthy slaughter positive	Fallen stock tested	Fallen stock positive	Casualty slaughter tested	Casualty slaughter positive	Clinical suspects tested	Clinical suspects positive
1991	<2yo							27	0
	2							195	36
	3							3633	3146
	4							8303	7727
	5							4945	4555
	6							2079	1838
	7							830	637
	8							262	161
	9							132	62
	10							49	16
	11							27	9
	12							14	2
	13							8	1
	14							6	0
	15							3	0
	16							0	0
Grouped data:	17+							0	0
	Unknown							8717	7014
	Total	**0**	**0**	**0**	**0**	**0**	**0**	**29230**	**25204**

Surveillance year	Age	Healthy slaughter tested	Healthy slaughter positive	Fallen stock tested	Fallen stock positive	Casualty slaughter tested	Casualty slaughter positive	Clinical suspects tested	Clinical suspects positive
1990	<2yo							0	0
	2							1	0
	3							12	10
	4							46	45
	5							35	33
	6							19	15
	7							4	3
	8							2	1
	9							4	0
	10							3	0
	11							2	0
	12							2	0
	13							1	0
	14							0	0
	15							0	0
	16							0	0
Grouped data:	17+							0	0
	Unknown							4	0
	Total	**0**	**0**	**0**	**0**	**0**	**0**	**135**	**107**

Age of Cattle Population on 31st December 2006 in Years:

Report(s) used: MI0086
Report ran on: 07/04/2007
Ref: WL 746

Any Personal Data provided is protected under the Data Protection Act 1998

The data provided to you from this report must only be used for the purposes for which it was requested. It must not be distributed onto any other person(s) or organisation(s) without approval from the BCMS Management Information Team.

These figures include:

- Animals alive on all holdings (farms, markets, etc) on 31 Dec 2006
- Passport applications that have passed initial CTS validation checks
- Passport applications made for cattle born or Imported into Great Britain
- Registered cattle where the passport has been returned to BCMS for amendment
- Animals with anomalous movement histories
- Cattle registered to a locations used for admin purposes

These figures exclude:

- Passport applications that failed initial CTS validation checks and are in suspense
- Animals cancelled on CTS (e.g. reported in error or duplicate applications)
- Movements cancelled on CTS (e.g. reported in error or duplicate applications)
- Applications received but missing sex details (5 animals)
- Cattle that have been exported

Age in Years	Female	Male	Total Animals
0	1,341,215	1,186,295	**2,527,510**
1	1,192,413	895,029	**2,087,442**
2	712,785	193,961	**906,746**
3	597,611	40,648	**638,259**
4	543,765	24,728	**568,493**
5	430,267	18,856	**449,123**
6	391,655	18,989	**410,644**
7	341,807	18,933	**360,740**
8	278,452	23,066	**301,518**
9	259,772	39,292	**299,064**
10	206,242	28,927	**235,169**
11	98,305	1,577	**99,882**
12	61,803	862	**62,665**
13	35,860	499	**36,359**
14	21,899	308	**22,207**
15	11,885	143	**12,028**
16	8,408	74	**8,482**
17	3,563	30	**3,593**
18	2,087	16	**2,103**
19	910	9	**919**
20	650	4	**654**
Over 20	603	10	**613**
Age Not Known*	119,588	469	**120,057**
Total Animals	**6,661,545**	**2,492,725**	**9,154,270**

* For animals born before 1 July 1996 only, a default date of birth may be used where the keeper has not been able to confirm the actual date of birth.

SYNOPSES OF PRESENTATIONS BY THE EXPERTS INVITED TO PRESENT AT THE SEAC 97 MEETING AND ANSWERS TO THE KEY QUESTIONS BY DR YAMAKAWA, JAPAN.

Open session

1. Dr F. Tagliavini (Instituto Nazionale Neurologico, Italy) – will be presented

2. Dr T. Baron (Unite Agents Transmissibles Non Conventionnels, France) – will be presented.

ANSWERS TO THE KEY QUESTIONS BY DR YAMAKAWA, JAPAN.

Characterisation

1. Are unusual cases of BSE in cattle associated with BSE or another strain(s) of TSE?

   BSE

2. With regard to unusual BSE cases what is known about:

   - the pathogenesis of the disease;

     BSE/J8P/Ibaraki: an apparently healthy Holstein steer, (born in October 20001 and disclosed in October 2003) age 23 months and accumulation of extremely small amount of atypical PrP^{Sc} (**Annex 1**).

     BSE/JP24/Sasebo: Japanese Black (meat cow) (born in February 1992 and disclosed in March 2006) age 169 months and

accumulation of atypical PrP^{Sc} by WB. Vacuolation and plaque, coarse granular and linear deposition of PrP by HE and IHC, respectively. *Submitting for publication .*

- the distribution of PrPSc in different tissues;

  BSE/JP8/Ibaraki: Presence of PrP^{Sc} was limited only in the homogenate prepared from the obex region for the rapid BSE test (Plateria).

  BSE/JP24/Sasebo: WB/IHC results positive (atypical pattern/vacuolation and PrP^{Sc} deposition as described above) at cerebral cortex and cerebellum.

  adrenal glands, tonsil, kidney, lymphnode and muscles are negative for PrPSc by WB and IHC

- geographical and age distribution; and

  It is unlikely that the two atypical cases have either epidemiological or geographical relationship with each other.

- clinical characteristics?

  BSE/JP8/Ibaraki was reported as clinically healthy animal
  BSE/JP24/Sasebo was reported as Dysstasia.

3. What is known about the transmissibility of unusual BSE to cattle and other species, by parental or oral routes?

   BSE/JP8/Ibaraki: Transmission to Bovinised transgenic mice was unsuccessful. It is difficult to conclude whether this BSE was untransmissible, because the available brain sample for transmission was limited and PrP^{Sc} in the sample was extremely small amount *submitting for publication*

   BSE/JP24/sasebo: Inoculated to cattle and several mouse lines and also transgenic mice expressing Hu and Bovine PrP. *Studies are on going*

4. Is there a relationship between bovine PrP genotype and unusual cases?

   No. They have common DNA polymorphic variation similar to the cattle in Japan.

5. How have unusual cases of BSE been detected?

   Blanket BSE testing Program using ELISA (Plateria Bio Rad) and confirmed by WB and IHC. BSE/JP8 was negative in IHC but BSE/JP24 was positive.

6. Could current and historic BSE surveillance in the UK reliably detect unusual cases of BSE?

   WB should be used together with IHC for PrP^{sc} detection.

7. What further information is needed to inform on the prevalence of unusual cases of BSE?

Origin of unusual BSE

8. What is known about the likely origin of unusual cases of BSE and how are they related to BSE or other TSEs?

Animal and human health implication

9. What, if any, are the potential animal health implications of unusual BSE?

10. What, if any, are the potential human health implications of unusual BSE in light of current BSE controls?