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UCL MEDICAL SCHOOL

THE QUEEN'S ANNIVERSARY PRIZE 1994

20 May, 1996

**Personal & Confidential - Addressee only**

**TO ALL MEMBERS OF SEAC**

Dear All,

I have drafted the attached position paper on **Sheep and BSE** with the help of Richard Kimberlin. Danny Matthews and colleagues may be able to add further data on the incidence of scrapie and/or the use of meat and bone meal specific to different types of flock. I will be abroad from May 22nd to 26th but please do not hesitate to send written comments to me during that time if you wish. I look forward to seeing you on May 29th.

Best wishes.

Yours sincerely,

J.R. Pattison

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DRAFT

## SHEEP and BSE

### A. The experimental transmission of BSE to sheep.

Studies have shown that the "negative" line NPU flock of Cheviots can be experimentally infected with BSE by intracerebral (ic) or oral challenge (the latter being equivalent to 0.5 gram of a pool of four cow brains from animals confirmed to have BSE). Five of the six sheep inoculated intracerebrally developed disease between 440 and 2353 days after inoculation. The short incubation periods were found in animals homozygous for alanine at codon 136 and for glutamine at codon 171 of the PrP gene. One of the six sheep challenged orally developed disease with an incubation period of 734 days. It too was homozygous for alanine at codon 136 and for glutamine at codon 171.

Brain and spleen tissue from the orally infected sheep and the intracerebrally infected sheep with an incubation period of 440 days were inoculated into the panel of mouse strains used for strain typing. The incidence of spongiform encephalopathy in all strains of mice was high (excluding intercurrent deaths) and similar for both tissues from both sheep. The pattern of incubation periods and lesion profiles of the transmissions from the four sheep tissues was very similar to that seen with BSE from cattle and clearly different from natural scrapie in a Greyface sheep tested concurrently. These data indicate that

- sheep can be infected orally with BSE;
- the infectivity recovered from sheep is BSE-like on strain typing but in terms of one biological characteristic, recovery of significant infectivity from the spleen, BSE in sheep is scrapie-like, raising the possibility that the BSE agent might therefore become endemic in a flock;
- polymorphisms at codons 136 and 171 of the PrP gene have an important effect on the susceptibility of sheep to BSE and the incubation period.

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**B. The risk of exposure of sheep to BSE through feed.**

Production of sheep concentrates increased steadily between 1980 (131,000 tonnes) and 1994 (567,000 tonnes). This increase is greater than the rise in the sheep population. In 1980 1 tonne of concentrate per 230 sheep was produced, in 1984 1 per 125, in 1988 1 per 90 and in 1992 1 tonne per 80 sheep. This compares with 1 tonne of cattle concentrate per 3 cows in 1988 but takes no account of the more targeted use of concentrates in the national flock (or herd).

Government statistics do not record the inclusion rates of raw materials in sheep rations. Enquiries of member companies of UKASTA indicate that meat and bone meal was not used by some companies because of concerns about palatability for sheep, but it was used by others, some regularly and some irregularly depending on price. Overall the range of incorporation of meat and bone meal would have been 1-5% but it has been illegal to use meat and bone meal in sheep rations since July 1988. However exposure due to accidental contamination in feed mills might have occurred.

Two thirds of the sheep concentrates produced are for breeding ewes. Moreover hill flocks receive far less concentrates than lowland flocks. The other extreme is the early lambing flock which is smaller than hill flocks, requires winter housing and considerable supplementary feeding. Lambs born in early winter with a target of being sold as fat lambs for Easter require large quantities of supplementary feed. Regimens of intermediate intensity will apply to lowland and upland early/spring lambing depending on early access to grass and the breed. Some flocks act as sources of replacement breeding stock for later cross-breeding and thus do not need to rely on supplementary feeding prior to sale. If an early lambing flock was infected with BSE the risk to other flocks is low because most lambs are fed and slaughtered within the first few months of life and culled ewes are more likely to be slaughtered rather than sold for breeding. This information indicates that

- a search for the BSE agent in sheep should concentrate on early lambing flocks, where both lambs and ewes are likely to have been fed meat and bone meal in the past, taking genotype into account (see section A);

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- a search should include young animals to help distinguish endemic infection from that induced by contaminated feed.

**C. The incidence of scrapie in the natural flock.**

Historically scrapie cases were recorded as those which were confirmed at a Veterinary Investigation Centre, often from flocks which had not previously experienced the disease. The figures are an underestimate as many farmers would recognise the disease without submission to post-mortem examination. Nevertheless the figures for sheep scrapie cases (top line) and BSE in cattle (bottom line) by year of diagnosis are

| 1980 | 81 | 82 | 83 | 84 | 85 | 86 | 87 | 88 | 89 | 90 | 91 | 92 | 93 | 94 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 94 | 100 | 129 | 143 | 153 | 143 | 153 | 176 | 211 | 224 | 334 | 896 | 589 | 83 | 61 |
| - | - | - | - | - | - | ? | ? | 2184 | 7137 | 14181 | 25032 | 36681 | 34370 | 23944 |

The scrapie figures are distorted because payments were offered between October 1990 and August 1992 for cases when brain pools were being assembled for rendering experiments. A total of 2867 brains were collected and these were recorded in the data base. The figures are further distorted by the requirements to notify scrapie from 1993 onwards. The effect of this is that during a given two-year period only the first case in a flock is recorded and, therefore, since 1993 the statistics denote affected flocks rather than individual cases. The data indicate that

- it is impossible to say whether there has been any change in incidence of sheep scrapie coincident with BSE in cattle in the UK.

**D. The survey of sheep scrapie strains since 1986.**

To date nine isolates of scrapie contemporary with the outbreak of the BSE have been strain typed. None has proved to be BSE-like and all have strain typing characteristics within the range expected of classical scrapie. In project SE1919 at the Central Veterinary Laboratory, brains from sheep with scrapie born after January 1991 in flocks already known to have confirmed scrapie

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are being collected. Payment is offered to owners as an incentive to notify cases. Brains will be pooled according to sheep genotype at codons 136 and 171 to increase the opportunity of isolating a BSE-like strain. The project is still in the collection phase. A later collection phase is planned to include pools of LRS tissues as well as of brains.

A similar project (SE 1423) at NPU will attempt isolation from single sheep again selected according to genotype. The avoidance of pooling should increase the sensitivity of isolation but the extent of the project will not provide a nationwide screen. At a meeting on 1 February 1996, SEAC recommended that high priority should be given to a study to infect, by the oral route, scrapie-free sheep (preferably from New Zealand) of a PrP genotype known to be susceptible to BSE, and then investigate whether or not BSE was transmitted naturally to subsequent generations.

From the above data we conclude that

- results of a representative survey of the strain characteristics of the infectious agent of scrapie in the national flock since the start of the BSE epidemic are not yet available.

**E. Sheep slaughter practices.**

The age distribution of scrapie cases confirmed between 1980 and 1990 is as follows:

| Age (years) | < 1 | 1 - 2 | 2 - 3 | 3 - 4 | 4 - 5 | 5+ | Total |
|---|---|---|---|---|---|---|---|
| Number | 1 | 137 | 662 | 343 | 123 | 68 | 1334 |

In natural infection the scrapie agent is detectable (by mouse bio-assay) in the preclinical phase at 10-14 months at low to medium titre in the intestines, lymph nodes, spleen and tonsils. It appears in low titre in the brain at about 25 months and at high titre in the brain and spinal cord during the clinical phase at 34-57 months when it is also recovered from many other tissues.

Approximately half the national flock is slaughtered each year. Of these approximately 80% are lambs and 20% rams and ewes. Intestines are processed for human consumption but not brain

or spleens except to minority groups. Four Halal sheep slaughterhouses in Bradford, Leeds and Birmingham were visited in April 1996. At one of the premises, brains were being removed for supply to retail outlets, another was supplying whole skinned heads and a third had supplied brains until a few months previously. The fourth treated all heads as waste. A few spleens were said to be supplied to retail outlets from one of the premises. From the foregoing we conclude that

- brain and spinal cord could pose a major potential risk when obtained from sheep clinically-affected with the BSE agent but the agent will be present in lower titre in these tissues in preclinical animals
- if BSE has passed to sheep and behaves like scrapie it would also be present in the intestines, lymph nodes and spleen in medium titres in pre-clinical animals.

**F. Advice.**

There is not the same accurate picture of the incidence of scrapie in UK sheep as there is of BSE in cattle and CJD in humans. It is thus impossible to tell whether the incidence has changed in the past 10 years. It is important that accurate data is gathered in case BSE is linked to human disease and in case the BSE agent has been transmitted to sheep and is being naturally sustained in the flock. Scrapie could be quite common. If there was 10-fold under reporting in the year of highest recorded incidence (1991) up to 1 in 200 rams and ewes going to slaughter could be affected. We therefore advise that

- random screening of a proportion of brains from adult slaughtered sheep be considered in order to obtain a better estimate of the incidence of scrapie in the national flock.

For the same reasons as above it is essential to extend knowledge of the characteristics of the scrapie strains currently present in the national flock. Projects SE1919 and SE1423 are critical to this and we therefore advise that

Bov 92 p

- the resources devoted to these projects (and the other highly recommended project SEAC 24) be reviewed to decide whether it would be possible to minimise further the time taken to accumulate the data.

Sheep in the UK have been given 10-20 fold less by weight of concentrates than cattle and some of the concentrates fed to sheep would not have contained meat and bone meal. No dramatic rise in scrapie incidence has been reported. In young, infected animals, the spleen and lymph nodes would contain more infectious agent than the central nervous system although this changes during the second half of the incubation period.

There is currently only a theoretical possibililty that BSE has been transmitted to the national flock. In such circumstances we believe the correct response is to investigate the possibility further rather than raise public alarm about another conceivable risk. Reaction to the latter would be difficult to control (as we saw with BSE) and might do more harm than good to human health. We therefore advise only that

- further information about the destination of sheep spleens and the use of intestines is obtained
- the Department of Health gives further consideration to the possibility of discussing with minority groups the consumption of the brains and spleens of older sheep slaughtered in Halal slaughterhouses.

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Annex

Estimated Number of Purebred Ewes by Breed

| ESTIMATED NUMBER OF PUREBRED EWES BY BREED | | | | | |
|---|---|---|---|---|---|
| | TOTAL EWES MATED('000) | ALL EWES ('000) | % OF NATIONAL FLOCK MATED | NO. FLOCKS ('000) | AVERAGE SIZE |
| BREEDS | | | | | |
| HILL BREEDS | | | | | |
| Scottish Blackface | 2,567 | 3,092 | 14 | 9.7 | 273 |
| North Country Cheviot | 497 | 585 | 3 | - | - |
| South Country Cheviot | 13 | 13 | * | - | - |
| Cheviot unspecified | 175 | 211 | 1 | - | - |
| Shetland | 11 | 12 | * | - | - |
| Hebridean | 2 | 1 | * | - | - |
| Soay | 1 | 1 | * | 0.2 | 6 |
| Swaledale | 1,209 | 1,410 | 7 | 4.9 | 253 |
| Dalesbred | 153 | 185 | * | 0.9 | 183 |
| Derbyshire Gritstone | 77 | 86 | * | 0.4 | 215 |
| Roughfell | 123 | 147 | * | 0.8 | 153 |
| Lonk | 26 | 30 | * | 0.2 | 127 |
| Herdwick | 24 | 26 | * | 0.4 | 63 |
| Welsh Mountain | 1,627 | 1,861 | 9 | 5.5 | 306 |
| Hardy Speckled Face | 815 | 862 | 4 | 3 | 285 |
| Beulah | 508 | 529 | 3 | 3.2 | 167 |
| Radnoor | 18 | 19 | * | - | - |
| Black Welsh Mountain | 11 | 12 | * | 0.6 | 19 |
| South Welsh Mountain | 4 | 4 | * | - | - |
| Improved Welsh | 30 | 34 | * | - | - |
| Glamorgan Welsh | 2 | 2 | * | - | - |
| Brecon Welsh Cheviot | 59 | 75 | * | - | - |
| Exmoor Horn | 26 | 32 | * | 0.2 | 108 |
| LONGWOOL/CROSSING BREEDS | | | | | |
| Bluefaced Leicester | 30 | 33 | * | 2.5 | 12 |
| Border Leicester | 28 | 30 | * | 0.8 | 38 |
| Friesland | 11 | 14 | * | - | - |
| Bleu de Maine | 7 | 7 | * | 0.5 | 15 |
| Cambridge | 6 | 6 | * | 0.1 | 54 |
| Rouge de l'Ouest | 4 | 4 | * | 0.2 | 18 |
| Wenslydale | 3 | 4 | * | 0.2 | 13 |
| Colbred | 2 | 1 | * | - | - |
| ABRO Damline | 2 | 2 | * | - | - |
| Improver | 1 | 1 | * | - | - |
| Teeswater | 1 | 1 | * | 0.3 | 3 |
| Leicester | 1 | 1 | * | - | - |
| Oldenburg | 1 | 1 | * | - | - |
| Westphalian | 1 | 1 | * | - | - |
| LONGWOOL EWE BREEDS | | | | | |
| Romney Marsh | 217 | 262 | 1 | 1.4 | 161 |
| Devon and Cornwall Longwool | 28 | 30 | * | 0.5 | 55 |
| Devon Closewool | 51 | 51 | * | 0.4 | 122 |
| Whitefaced Dartmoor | 1 | 1 | * | - | - |
| Lincoln Longwool | 3 | 4 | * | 0.2 | 19 |
| Greyfaced Dartmoor | 4 | 4 | * | - | - |

* denotes less than half %

Bov 96p

Estimated Number of Purebred Ewes by Breed

| | | | | | |
|---|---|---|---|---|---|
| TERMINAL SIRE BREEDS | | | | | |
| Suffolk | 429 | 459 | 2 | 14.6 | 31 |
| Texel | 97 | 107 | * | 3.2 | 32 |
| Dorset Down | 22 | 23 | * | 0.8 | 29 |
| Hampshire Down | 15 | 17 | * | - | - |
| Charollais | 5 | 5 | * | 0.6 | 9 |
| Southdown | 4 | 5 | * | 0.2 | 19 |
| Oxford Down | 3 | 4 | * | 0.3 | 12 |
| Shropshire | 3 | 4 | * | 0.1 | 33 |
| Ile de France | 3 | 4 | * | - | - |
| Vendeen | 2 | 2 | * | 0.1 | 24 |
| Meatlinc | 1 | 1 | * | | |
| SHORTWOOL EWE BREEDS | | | | | |
| Clun Forest | 124 | 130 | * | 1.7 | 77 |
| All Dorset Horn | 124 | 139 | * | 0.8 | 31 |
| Lleyn | 68 | 74 | * | 0.9 | 77 |
| Kerryhill | 47 | 48 | * | 0.7 | 76 |
| Jacob | 41 | 45 | * | 2.5 | 17 |
| British Milksheep | 6 | 7 | * | 0.2 | 27 |
| Ryeland | 2 | 1 | * | - | - |
| Llanwenog | 3 | 3 | * | 0.2 | 20 |
| | | | | | |
| Early lambing breeds shaded | | | | | |

* denotes less than half %

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Annex

## SCRAPIE CASES RECORDED BY BREED FROM 1st JANUARY 1993 TO 31st MARCH 1996

| BREED | 1993 | 1994 | 1995 | 1996 | TOTAL |
|---|---|---|---|---|---|
| BEULAH | 1 | 1 | 0 | 0 | 2 |
| BLEU DE MAINE | 13 | 6 | 2 | 0 | 21 |
| BLUEFACED LEICESTER | 0 | 0 | 1 | 0 | 1 |
| BORDER LEICESTER | 0 | 0 | 2 | 0 | 2 |
| CAMBRIDGE | 2 | 0 | 1 | 0 | 3 |
| CHAROLLAIS | 14 | 14 | 7 | 1 | 36 |
| CHEVIOT UNSPECIFIED | 2 | 0 | 3 | 0 | 5 |
| CROSS BREED | 53 | 33 | 35 | 10 | 131 |
| DALESBRED | 0 | 0 | 1 | 0 | 1 |
| DARTMOOR GREY RACE | 1 | 1 | 0 | 0 | 2 |
| DORSET DOWN | 1 | 0 | 3 | 0 | 4 |
| EXMOOR HORN | 1 | 0 | 0 | 0 | 1 |
| FRIESLAND | 1 | 0 | 0 | 0 | 1 |
| GREYFACED DARTMOOR | 1 | 0 | 2 | 0 | 3 |
| HALF BRED | 3 | 2 | 1 | 2 | 8 |
| HERDWICK | 1 | 0 | 0 | 0 | 1 |
| HAMPSHIRE DOWN | 1 | 0 | 1 | 0 | 2 |
| MASHAM | 1 | 0 | 1 | 0 | 2 |
| MULE | 47 | 7 | 10 | 1 | 65 |
| NORTH COUNTRY CHEVIOT | 0 | 1 | 0 | 0 | 1 |
| ROMNEY MARSH | 0 | 1 | 0 | 0 | 1 |
| ROUGE DE L'OUEST | 2 | 0 | 2 | 1 | 5 |
| ROUSSIN | 1 | 0 | 2 | 0 | 3 |
| SCOTTISH HALF BRED | 0 | 2 | 0 | 0 | 2 |
| SHETLAND | 17 | 12 | 11 | 11 | 51 |
| SHROPSHIRE | 0 | 1 | 1 | 0 | 2 |
| SOAY | 1 | 0 | 0 | 0 | 1 |
| SOUTH DEVON | 0 | 2 | 0 | 0 | 2 |
| SUFFOLK | 31 | 18 | 13 | 3 | 65 |
| SWALEDALE | 23 | 6 | 3 | 1 | 33 |
| TEXEL | 18 | 10 | 3 | 11 | 42 |
| UNKNOWN | 35 | 34 | 47 | 0 | 116 |
| VENDEEN | 0 | 1 | 0 | 0 | 1 |
| WELSH HALF BREED | 11 | 3 | 7 | 0 | 21 |
| WELSH MOUNTAIN | 3 | 1 | 4 | 0 | 8 |
| WENSLYDALE | 1 | 0 | 0 | 0 | 1 |
| WHITEFACED DARTMOOR | 1 | 0 | 0 | 0 | 1 |
| TOTAL | 287 | 156 | 163 | 41 | 647 |

Early lambing breeds shaded