EUROPEAN COMMISSION
HEALTH & CONSUMER PROTECTION DIRECTORATE-GENERAL

Directorate C - Scientific Opinions

Scientific Steering Committee

REPORT ON:

MONITORING SOME IMPORTANT ASPECTS OF THE EVOLUTION OF THE EPIDEMIC OF BSE IN GREAT-BRITAIN

UPDATE PROVIDING AN EPIDEMIOLOGICAL COMMENTARY ON BSE PROJECTIONS FOR GREAT BRITAIN (GB) AND ON SURVEILLANCE, AS WELL AS ON THE OCCURRENCE OF "BORN AFTER THE REAL BAN - BARB" CASES

SUBMITTED BY THE TSE/BSE AD HOC GROUP TO THE SCIENTIFIC STEERING COMMITTEE

AT ITS MEETING OF 7-8 DECEMBER 2000

INTRODUCTION

Regular monitoring of the evolution of the BSE epidemic in Great Britain is part of the mandate of the Scientific Steering Committee (SSC). A first detailed opinion was adopted on 27-28 May 1999.

It concluded that the current and expected evolution of number of BSE cases in the UK (1999-2004) are in line with all models and stated that the tail of the epidemic would not necessarily present a constant decline, certainly not when small numbers are involved. The current (1999) numbers of BSE cases were considered to be in line with the scientific expectations.

This opinion was confirmed in the SSC's opinion of 28-29 October 1999 on *The Scientific Grounds of the Advice of 30 September 1999 of the French Food Safety Agency (the Agence Française de Sécurité Sanitaire des Aliments, AFSSA), to the French Government on the Draft Decree amending the Decree of 28 October 1998 establishing specific measures applicable to certain products of bovine origin exported from the United Kingdom.*

The SSC was invited to provide a further updated answer to the following questions:

Question 1: *How does the SSC assess the current and now-expected (2000 - 2002) evolution of the number of BSE cases (epidemic) in GB? Is the current number of cases in line with current scientific expectations? Is the current number of GB's BSE cases in line with previous scientific expectations?*

In addition, and also in the light of the recent discovery of a first BSE case born after the so-called "real feed ban of 1 August 1996" (BARB), the SSC addressed the following questions:

Question 2: *Have BSE cases fallen off at a similar rate in Scotland, England and Wales?*

Question 3: *How can the monitoring of projections be improved?*

Question 4*: How should BSE cases born after 1 August 1996 be investigated?*

Question 5: *What purposes does PrP(res) surveillance in sentinel groups of slaughtered bovines serve in GB and in EU?*

The present report was prepared by the TSE/BSE *ad hoc* Group and submitted to the SSC it at its meeting of 7-8 December 2000. It served as the basis for an opinion on the same subject which was adopted on 8 December 2000 and is available separately on the same Internet site.

1. PROJECTIONS OF GB'S BSE CASES IN ANIMALS BORN BEFORE 1 AUGUST 1996

Tables 1 to 3 show several published and other BSE projections for Great Britain, together with out-turn, that is: GB's BSE cases - by year of clinical onset, restriction or confirmation.

It is important to differentiate between dates of clinical onset, restriction and confirmation; and to ensure that when out-turn versus projection are compared, the two are tabulated on a common basis, namely: the basis used in calculating that set of projections. Date of confirmation is the most liable to administrative or work-pressure biases, see below.

The Oxford team projects BSE onsets by calendar year. Wilesmith's age-cohort modeling is by year of restriction. Routinely tabulated BSE data have been by year of confirmation, which matches neither of these. We are grateful to Dr. Donnelly, Oxford, for clarification of the above points in October 1999.

Recommendation 1: to ensure that monitoring tables - of out-turn versus projection - are appropriate to their purpose, with out-turn and projections tabulated on the exact basis used for calculating the projections.

Recommendation 2: regular perusal by TSE/BSE ad hoc group of the 3-monthly cross-tabulation of BSE onsets according to July to June birth cohort for birth cohorts pre-1981, 1981/82 up to the most recent. In addition to illustrating the last diagonal for which there are complete data, an additional table could be produced which a) imputes 'adjusted totals' for the first diagonal which is incomplete, and b) explains the methodology for imputation (which may have to take account of seasonal effects and variable reporting delays as well as BSE incubation period).

Calendar period changes in reporting delay distributions cannot be ruled out: in particular, Wilesmith has noted that the delay time from restriction to BSE confirmation for subsequently con-firmed BSE cases has lengthened since veterinarians have had to focus additionally on selective culls.

Recommendation 3: formal analysis of reporting delays would be highly instructive, and might serve to reduce previous confusions. The lag times of interest are: onset date -> restriction date [all suspects; subsequently confirmed BSE cases]; restriction date -> confirmation date [all restrictions; subsequently confirmed BSE cases]; onset date -> confirmation date [all onsets; subsequently confirmed BSE cases].

Given that BSE clinical onsets by calendar year are what the Oxford team of Anderson, Ferguson & Donnelly projects whereas subsequently-confirmed-BSE restrictions by calendar year of restriction are what the Wilesmith team projects, separate tables for out-turn versus projection are needed to understand the performance of the two types of projections. Appropriate tables are presented below.

Tables 1 and 2 show several published and other projections by the Oxford team, together with GB's BSE cases by year of ONSET, which is the basis for the Anderson, Ferguson & Donnelly projections. The Oxford projections have utilized BSE case data to mid or end 1996 except for the latest projections by Donnelly & Ferguson and by Donnelly et al. which used case data to mid 1998 (Donnelly & Ferguson) or mid October 1999 (Donnelly et al.). Only the unpublished Donnelly et al. projections in Table 2 take into account the effect of strategic culling. All other Oxford projections, therefore, to some extent *overstate* GB's expected future numbers of BSE cases. Table 2 includes unpublished, confidential results by Donnelly et al. (2000) which were made available to TSE/BSE ad hoc group after SEAC's discussion of them.

Notice that the Table 1 models which assumed no BSE maternal transmission gave higher projections for 1999 than those which assumed 10% maternal transmission for 12 or 6 months, that is: which assumed that 10 out of 100 calves born within 12 or 6 months of BSE onset in the dam were BSE infected at birth. Unless maternal transmission is assumed, higher feed risk in the early 1990s must be inferred to be able account for early-in-incubation-period BSE cases in the mid 1990s, with the burden of clinical onsets from such exposures to contaminated feed still to come as projected BSE onsets. Assuming no BSE maternal transmission is, however, contrary to empirical findings from a range of analyses, including - importantly - of BSE Maternal Cohort Study. Back-calculation from the BSE database to mid 1996 could not, however, distinguish - on a goodness of fit criterion - between no maternal transmission and 10% maternal transmission for 1 year although 10% maternal transmission for 6 months did fit better than either. Previously, AIDS back-calculation has shown the inadequacy of chi-square goodness of fit as a sole criterion for projection model choice.

Brief commentary on individual models precedes summarization of Tables 1 and 2:

Anderson (1996), no maternal transmission: No feed-based exposure after July 1996, and for 1996, expected BSE infection incidence was 0 (uncertainty range: 0 to 12,500). Feed-based incidence and uncertainty from mid 1993 to mid 1996 must have been largely assumption-based, rather than back calculated because there would have been few relevant BSE onsets in the data-base to mid 1996. *Strategic culling not taken into account.*

Ferguson (1997), no maternal transmission: Feed-based risk assumed to drop to zero by July 1996. With 6 months' more data, 1996 central estimate has increased but later central projections are all lower than in Anderson (1996) and uncertainty ranges have narrowed considerably: compare, for example, the 1999 projections which were 1900 (560 - 4040) and 1090 (660 - 2170) by Anderson (1996) and Ferguson (1997) respectively. *Strategic culling not taken into account.*

Donnelly & Ferguson (1997), no maternal transmission: Using BSE case data to mid 1998, Donnelly & Ferguson over-estimate 1997 onsets, which may be occasioned by the convenient, but incorrect, worst case assumption that selective cull had no effect in preventing BSE onsets. *Strategic culling thus not taken into account.* A model which assumed constant selective cull efficacy per birth cohort (but different between birth cohorts) produced a much better fit to the analysed data, BUT "more recent incidence data (as yet incomplete and thus not analysed) indicate that the model allowing for an effect of the selective cull under-estimates current incidence levels" – projections from it were not reported.

Anderson (1996), 10% maternal transmission for 12 months: 10% maternal transmission for 12 months is roughly consistent with Donnelly's analysis of BSE dam-calf pairs. Notice that when 10% maternal transmission for 12 months was assumed, use of BSE data to mid 1996 necessarily entailed that the estimated feed risk fell "to negligible levels by mid 1994", because - of course – few BSE onsets occur before 24 months of age, and there were not yet BSE case data from which to infer continued feed risk. Central BSE projections were lower by assuming that 10% maternal transmission pertained for 12 months because more of the already observed BSE cases could be attributed to this route, with consequent reduction in the feed-based exposure incidence and projected cases arising from this feed-based exposure before mid 1994. *Strategic culling not taken into account.*

Anderson (1996), 10% maternal transmission for 6 months: 10% maternal transmission for 6 months is roughly consistent with BSE Maternal Cohort Study. Notice that when 10% maternal transmission for 6 months was assumed, use of BSE data to mid 1996 necessarily entailed that the estimated feed risk fell "to negligible levels by mid 1994", because - of course - few BSE onsets occur before 24 months of age, and there were not yet BSE case data from which to infer a continued feed risk. *Strategic culling not taken into account.*

Ferguson (1997), 10% maternal transmission for 6 months: use of BSE case data through mid 1996 seriously over-estimated actual BSE onsets for 1996, but gave central BSE projections for 1998 and 1999 which were in broad agreement with the corresponding model from Anderson (1996) but qualified those central estimates by much narrower uncertainty ranges: compare, for example, the 1999 projections which were 680 (390 - 5910) and 640 (530 - 770) by Anderson (1996) and Ferguson (1997) respectively. The projection ranges given by Ferguson (1997: 10% maternal transmission for 6 months) have been falsified by the out-turn for both 1998 and 1999. Either the projection methodology or the assumption of negligible feed risk after 1994 or both must be questioned. *Strategic culling not taken into account.*

Ferguson (1997), horizontal transmission: projection ranges which were arrived at by using BSE case data through mid 1996 and assumption of horizontal transmission have been falsified by the

out-turn for both 1996 and 1997. Either the projection methodology or the assumption of horizontal transmission or both must be questioned. *Strategic culling not taken into account.*

Donnelly et al. (2000), 10% maternal transmission for 6 months: Estimated that 2600 BSE cases had been prevented by strategic culling. Uses revised survivorship model for 1986 and later cohorts, the 1995 survivorship model being assumed for cohorts thereafter. Differential impact of strategic culling on later birth cohorts cannot yet be estimated. Donnelly et al. comment that differences from the survivorship assumed in Anderson (1996) are negligible to the eye but that goodness-of-fit for BSE back calculations was sensitive to changes in survivorship model. *Donnelly et al (2000) take account of strategic culling* but have had to assume that the survivorship model for 1995 cohort applies to later-born cohorts, an assumption that may be made suspect by the introduction of strategic culling: time will tell. Central estimates for future BSE incidence have been revised radically upwards compared to Anderson (1996: 10% maternal transmission for 6 months), but - the authors note - are still within the Anderson (1996) uncertainty bounds. They are not, however, within the uncertainty bounds of Donnelly & Ferguson (1999: no maternal transmission and no allowance for strategic culling), which logically should be both higher and wider. Compare, for example, the 1999 projections which were 1020 (660 - 2170) and 2580 (2390 - 2800) by Donnelly & Ferguson (1999) and by Donnelly et al. (2000). Donnelly et al (2000) explain that: "feed risk in 1991-96 did not decline as rapidly as might have been hoped". The draft Donnelly et al. (2000) paper does not tabulate for comparison the 1991-96 feed risk and uncertainty as assumed or estimated in Anderson (1996: no maternal transmission) versus in Anderson (1996: 10% maternal transmission for 6 months) and Donnelly et al (2000; 10% maternal transmission for 6 months). All analyses in Donnelly et al. (2000) assume zero feed risk after 1 August 1996, having - of course - little or no onset data to the contrary by mid October 1999. Contrary evidence could emerge in time, however.

Table 1: Published and other Oxford projections by year of ONSET: NO maternal transmission versus 10% maternal transmission for 12 or 6 months

GB out-turn by year of ONSET	No maternal transmission			10% maternal transmission for		
	Anderson (1996)	Ferguson (1997)	Donnelly & Ferguson (2000)	12 months Anderson (1996)	6 months Anderson (1996)	6 months Ferguson (1997)
1996: 7422	7990 (7040 - 9310)	8450 (7670 - 9360)	*7425 (7170 - 7690)*	6740 (6080 - 8290)	7390 (6540 - 8860)	8075 (7350 - 8940)
1997: 4239	5570 (3770-8370)	5125 (4130 - 6380)	*4650 (4385 - 4945)*	3145 (2560 - 6900)	4110 (3010 - 7660)	4200 (3583 - 4940)
1998: 3095	3640 (1650 - 7760)	2630 (1820 - 4010)	3090 (2640 - 3755)	1250 (960 - 6370)	1864 (1153 - 7030)	1740 (1450 - 2100)
1999: >2176[2]	1900 (560 - 4040)	1090 (660 - 2170)	1020 (600 - 1640)	456 (360 - 5420)	680 (390 - 5910)	640 (530 - 770)
Used GB's BSE cases to	mid 1996	through mid 1996	*mid 1998*	mid 1996	mid 1996	through mid 1996

[1] For commentary on individual models, please see text

[2] Confirmed by 01 July 2000

[3] Distribution of reporting delay from diagnosis to entry on CVL's BSE database has mode of two months & mean of 3.1months, see Anderson (1996)

In summary, central projections have performed poorly, and only wisely wide uncertainty ranges for the original Anderson (1996) projections have meant that actual out-turn has remained within range. Assumptions underlying certain of the original projections, such as that feed risk fell to negligible levels by mid 1994, have been falsified subsequently, including - we assume - by the unpublished estimated feed risk in Donnelly et al. (2000). Some central models have even failed to fit well the essentially-past 1996 data, but strategic culling/slaughter could be an explanation for lower 1996 out-turn than projected.

Table 2: Published and other Oxford projections by year of ONSET: including 10% maternal transmission for 6 months or horizontal transmission

GB out-turn by year of onset	Horizontal transmission in last 6 months	No horizontal no maternal transmission	10% maternal transmission for 6 months: (as in Table 1)		Projections for strategic culling; 10% maternal transmission for 6 months
	Ferguson (1997)	**Ferguson (1997)**	**Anderson (1996)**	**Ferguson (1997)**	**Donnelly *et al* (2000)**
1996: 7422	8655 (8380 - 9440)	8450 (7670-9360)	7390 (6540 - 8860)	8075 (7350 - 8940)	7580 (7310 - 7860)
1997: 4239	5790 (5620 - 6410)	5125 (4130-6380)	4110 (3010 - 7660)	4200 (3583 - 4940)	4290 (4110 - 4510)
1998: 3095	3765 (3680 - 4070)	2630 (1820-4010)	1864 (1153 - 7030)	1740 (1450 - 2100)	3080 (2910 - 3290)
1999: > 2176[2]	2410 (2350 - 2570)	1090 (1660-2170)	680 (390 - 5910)	640 (530 - 770)	2580 (2390 - 2800)
2000 *	1560 (1520-1670)	380 (210 - 940)		235 (200- 280)	1750 (1520 - 2210)
2001 *	1010 (990-1100)	120 (60- 340)		90 (75- 105)	870 (730 - 1290)
used GB's BSE cases to	through mid 1996	through mid 1996	mid 1996	through mid 1996	mid October 1999

[1] For commentary on individual models, please see text

[2] confirmed by 01.07.2000

The Wilesmith team updates its projections regularly so that, in practice, projections seldom run more than two years ahead of the BSE case data on which the age-cohort projections were based, see Table 3. Comparison of out-turn between Tables 2 and 3 shows that there is no consistency on whether the number of onsets or number of restrictions is higher in a given calendar year. Differential reporting delays may be an explanatory factor. GB's out-turn for 1996 and 1997 was lower than projected by the Wilesmith team using case data to March 1996. Of course, those projections did not explicitly take account of strategic culling, although the method accommodates to it over time. The Wilesmith approach evolved from an initial remit to project the number of suspect cases, and thereby compensation costs and incineration burden. It has therefore paid some attention to the vagaries of reporting whereby, for example, there has been only one confirmed BSE case to date [30.04.2000] among 170 1996-born suspects, an unprecedented negative rate.

Table 3: Published and other BSE projections for GB

GB out-turn by year of restriction		Age-cohort projections: by year of restriction for subsequently-confirmed-as-BSE restrictions		
		Wilesmith		
1996	8013	8270 (8090 - 8450)		
1997	4309	5000 (4960 - 5140)		
1998	3178	3070 (2960 - 3175)		
1999	>2254[2]	1890 (1600 - 2190)	OR	*2070* *(1760 - 2375)*
2000		**1110** **(880 - 1340)**		
2001		**470** **(320 - 615)**		

[1] GB's cases to March 1996 were used for 1996-97 projections, more recent data for 1998-99 projections, and data to end September 1999 for the projection in italics. **Data to 10.04.00 used for 2000 & 2001 projections.**

[2] As confirmed by 30.04.2000

2. ESTIMATION OF GREAT BRITAIN BSE INFECTION INCIDENCE FOR CALVES BORN IN 1994 OR 1995.

METHOD 1 relies on BSE Maternal Cohort Study. The BSE Maternal Cohort Study tended to select calves from farms with multiple BSE cases. In control calves from single contributor herds, BSE incidence (and hence infection incidence, because all animals were followed to seven years of age) was 2.2%. Since calves were born mainly in 1988, and Anderson (1996) showed roughly 20-fold drop in infection incidence by 1992-93 [after Ruminant Feed Ban and other measures to control cross-contamination], this suggests that infection incidence was around 0.1% or less in 1993, that is: 100 or less per 100,000.

METHOD 2 uses the lifetable for an index birth cohort of calves, the number, N, of calves in the birth cohort of interest, and the BSE incubation period distribution - as estimated by Donnelly [7.2% of BSE-infected calves develop BSE ONSET within 3 years of their infection, 34% by 4 years, and 64% by 5 years but only 0.16% within 2 years after infection] - to work out how many BSE ONSETS should be observed from this birth cohort by 3 years of age, and by 4 years of age if BSE infection incidence is i per 100,000 with all BSE-infected calves infected either: a) at birth, or b) at around 1 year of age. The expected numbers, E_a (i, N) and E_b (i, N), can then be equated to the observed number of onsets, and the sums solved to give estimates i_a and i_b for BSE infection incidence, i per 100,000, in the birth cohort of interest.

METHOD 3 looks for back calculated estimates of BSE infection incidence. For example, Ferguson (1997) gave central estimates of zero (0, 533) and 14 (0, 115) infected bovines in 1996, or 1996 BSE infection incidences per 100,000 of zero (0, 11.8) and 0.3 (0, 2.6) if we assume 4.5 millions GB calves born per annum. Some Ferguson projection models have, however, been falsified by observed out-turns, see above.

METHODS 2 & 3 are applicable internationally.

3. ESTIMATION OF GB'S BSE INFECTION INCIDENCE FOR CALVES BORN AFTER 1.08.96.

METHOD 2 above can be applied also to estimate BSE infection incidence in calves Born After the Real Ban of 1 August 1996 (otherwise known as BARBs): both in GB and in other countries. In GB, offspring cull and feed surveys *should mean* a further substantial reduction in BSE infection incidence from that estimated for 1995. Table 4 attempts to show what might be expected with respect to BSE-onsets for BARBs. We assume 600,000 3 year survivors from calves born in August to October 1996.

Table 4: Expected BSE-ONSETS by end Oct. 1999 for BARBs born in Aug. to Oct. 1996

BARBs' BSE infection incidence, j	Expected BSE-ONSETS by end Oct. 1999 for BARBs born in Aug. to Oct. 1996: a) if infected around birth OR b) if infected around 1 year = a) 0.072 OR b) 0.0016 * # 3-year survivors from Aug.-Oct. 1996 calves * infection incidence
1 per 1,000,000	a) 0.043 OR b) 0.001
2 per 1,000,000	a) 0.086 OR b) 0.002
1 per 100,000	a) 0.43 OR b) 0.01
2 per 100,000	a) 0.86 OR b) 0.02
10 per 100,000	**a) 4.3** OR b) 0.10
20 per 100,000	**a) 8.6** OR b) 0.19

No BSE onsets by end October 1999 in GB calves born in August to October 1996 would argue against BSE infection incidence as high as 10 per 100,000 around the time of birth [Poisson probability of nil diagnosed cases when 4.3 expected is 0.013]. *Notice that onset dates may not be available until after restriction has occurred, or even after confirmation, so that onset -> restriction lag & onset -> confirmation lag may both be relevant here.*

Delayed infection incidences **of the same and lower order** can be ruled out within another year, **because** calves born in each quarter after October 1996 add further information.

4. ANIMAL AND PUBLIC HEALTH CONTROLS ACROSS EU.

Similar surveillance data should be collected across major EU countries to assess each country's BSE case incidence, BSE prevalence in older cattle coming to slaughter, and estimated BSE infection incidence in BARBs. The reason for across-EU surveillance is that animal and public health controls differ markedly across EU countries, and may be strictest in UK, see geographic BSE risk assessments. The country-specific surveillance data to be collated should include:

i) number of calves born per annum
ii) proportion of calves surviving to 3 and to 4 years of age
iii) proportion of calves born per quarter
iv) year&month of birth and year&month of BSE ONSET for calves born in 1994 and 1995; and for calves born after 1 August 1996
v) how accurately the age of a slaughtered bovine is known: only that it is over 30 months by dentition, or date of birth by animal passport, or other method?

Recommendation 4: Overview of BSE geographic risk assessments should include tabulation of the most stringent current GB/other country precautions, showing when this provision came into being (if it did) in each EU country.

5. GB'S HISTOLOGICAL SURVEILLANCE OF SLAUGHTERED BOVINES FOR PRE-CLINICAL BSE

GB has initiated histological surveillance of bovines aged 5+ years which were slaughtered in OTMS scheme. Systematic sampling involves all OTMS slaughterhouses in GB with a limit of 5 heads on any one day from a single abattoir, and sample size set to detect 0.5% prevalence with tight confidence interval. Data are not available by birth cohort of all tested animals (but ages have been worked out for 40% of sampled bovines), nor are all ages expected from the 2000 survey which began on 15 May, so that GB cannot readily answer the question: *How do the observed prevalences compare by birth cohort with those expected from back calculations?*

The GB survey was designed with a different objective in mind from checking on back-calculations: its purpose is as an independent check on the performance of GB's BSE surveillance, the same rate of decline being expected between clinical BSE cases and OTMS test positive bovines. **In addition to histology,** the same (modified) Delfia test being now used for both 1999 and 2000 surveys.

6. PRP(RES) SURVEILLANCE IN SENTINEL GROUPS TO ASSESS PREVALENCE OF POSITIVITY

Switzerland has initiated this type of surveillance in a) fallen [census], b) emergency slaughter [census], and c) routinely slaughtered bovines [5% sample].

However, statistical properties of the non-random sampling plan for routinely slaughtered bovines need to be addressed, nor are data yet available by birth cohort of the tested animals although the calendar year of birth of Prionics positives as well as of clinically suspect BSE cases is known. For example, there had been 16 cases found by the targeted surveillance programme with prionics from 1994-born bovines

Average age at routine slaughter may be considerably older in Switzerland than in UK, see geographic BSE risk for details, so that Switzerland's data may be more directly comparable with UK's OTMS sampling than is at first apparent. On the other hand, the Swiss testing may signal positive earlier in incubation period than does histology. When used with GB's OTMS scheme, the Prionics test appeared to signal only histologically positive cases. Histological data for all Swiss bovines that tested positive in the Prionics test show good agreement between the Prionics Wetern Blot and IHC. 7 from 32 Prionics and IHC positives, were histologically negative.

7. PRP(RES) SURVEILLANCE: APPLICATION TO DBES?

GB expects to export 100,000 bovines in the second year of operation of DBES for 6 - 30 month old slaughtered bovines. Table 5 gives upper limits for expected annual number of PrP(res) positives among assumed 50,000 DBES bovines aged 24 - 30 months at slaughter for a range of BSE infection incidences, k. Table 5 shows that PrP(res) surveillance in DBES lacks power at a priori plausible BSE infection incidences. Even if k = 1 per 100,000, then only one DBES bovine out of 100,000 would be expected to be infected; and if k = 1 per 1,000,000 then only one DBES in the next 10 years [unless trade accelerated] would be expected to be infected. Because DBES adds extra precautions, low age-specific positivity in BARBs in GB's OTMS scheme would afford greater reassurance in respect of corresponding DBES bovines.

Recommendation : PrP(res) surveillance of BARBs in GB's OTMS scheme would be more useful than its application to DBES.

Table 5: DBES bovines: prior expectations

Assumed BSE infection incidence in DBES bovines, k	Upper limit for expected # histology positives: a) if infected around birth, b) if infected around 1 year = a) 0.072 OR b) 0.0016 * # 24-30 month DBES bovines * infection incidence
1 per 1,000,000	a) 0.0036 OR b) 0.00008
2 per 1,000,000	a) 0.0072 OR b) 0.00016
1 per 100,000	a) 0.036 OR b) 0.0008
2 per 100,000	a) 0.072 OR b) 0.0016
10 per 100,000	a) 0.36 OR b) 0.008
20 per 100,000	a) 0.72 OR b) 0.016

Footnote : Infection likely to be detectable by histology or PrP(res) at 24-30 months if bovine was destined to develop BSE at 30-36 months.

8. DIFFERENTIAL FALL-OFF IN BSE CASES IN SCOTLAND VERSUS E&W?

Table 6 addresses differential fall-off in BSE cases in Scotland versus in England and Wales. Data for Northern Ireland are shown for completeness, but are not further analysed because they pertain to a different reporting system.

Comparison of the fall-off of BSE cases in England, Wales & Scotland for the five years, 1995-1999, gives rise to a chi-square on 8 degrees of freedom (df) of 89.8 indicating significant heterogeneity between countries. Much of this heterogeneity stems from country-specific differences between observed and expected BSE counts in 1995, as can be seen by comparison of the actual 1995 confirmations versus expected numbers, e, calculated under the assumption of a common rate of decline across countries.

Even so, BSE cases in Scotland have also fallen off at a faster rate since 1995 than have those for England and Wales [chi-square on 6 df was 20.7, still highly significant, when comparison was restricted to 1996 -99, for which the expected counts, e, are shown in bold-face].

Forthcoming papers on spatial and temporal variation in BSE cases by the Wilesmith *et al* implicate the pig:cattle ratio, and hence likely bovine exposure to BSE-contaminated pig rations, in this geographical heterogeneity.

In Scotland in 1998 there were 68 BSE restrictions per million cattle aged over 24 months as compared to 886 in England, 347 in Wales and 22 in Northern Ireland (see table 6). The BSE epidemic in Scotland has declined more rapidly than in the rest of GB. Possible explanations include low cross-contamination from pig feed because of Scotland's relatively low pig population and good standards at abattoirs.

Table 6: Confirmed BSE cases to end July 1999 by year of confirmation

Year of restriction / notification	England [as % 1996]	Wales [as % 1996]	Scotland [as % 1996]	Northern Ireland [as % 1996]	Total for Great-Britain
1995	12308 e= 12543.7	1322 e= 1193.6	671 e= 563.7	*173*	14301
1996	7076 e= 7027.5 **e = 7140.9**	636 e= 668.7 **e = 606.9**	300 e= 315.8 **e = 264.2**	*74*	8012
1997	3845 [54%] e= 3779.5 **e = 3840.5**	323 [51%] e= 359.6 **e = 326.4**	141 [47%] e= 169.9 **e = 142.1**	*23 [31%]*	4309
1998	2864 [40%] e= 2788.4 **e = 2833.4**	230 [36%] e= 265.3 **e = 240.8**	62 [21%] e= 125.3 **e = 104.8**	*18 [24%]**	3156
1999 (incomplete)	2065 [29%] e= 1006.9 **e = 1023.2**	152 [24%] e= 95.8 **e = 87.0**	37 [12%] e= 45.3 **e = 37.9**	*5 [7%]*	2254
Totals so far: 1995-99 1996-99	 28158 15850	 2663 1341	 1211 540		 32032 17731

* Northern Ireland ban was lifted on 1 June 1998. Should Scotland expect similar provision in near future on basis of rate of decline, and on low absolute number of BSE cases born prior to 1 August 1996? Answers may also depend on relative national herd sizes.

9. CATTLE > 24 MONTHS OF AGE IN THE VARIOUS PROVINCES/COUNTRIES OF THE UK

The Annual Agricultural Censuses separate animals over 2 years of age into those that are intended for breeding and those intended for slaughter. Table 7 reflects this differential counting.

Table 7: Bovines for breeding/slaughter in 1998 per UK province

	N° of animals recorded at 1998 Censuses		
Part of UK	**Intended for breeding**	**Intended for slaughter**	**Total**
England	3 005 192	228 240	3 233 432
Wales	599 200	64 400	663 600
Scotland	859 878	57 886	917 764
Ireland	706 500	96 000	802 500

10. ACKNOWLEDGEMENTS

The basis of the present report was prepared by Dr Sheila M. Bird and Mr John Wilesmith for the TSE/BSE *ad-hoc* Group, who discussed it in detail and amended it at its meetings of 31 August, 12 October and 23 November 2000.

12. LITERATURE REFERENCES

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