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HEALTH & CONSUMER PROTECTION DIRECTORATE-GENERAL

Directorate C - Scientific Opinions
C1 - Follow-up and dissemination of scientific opinions

OPINION ON

THE SIX BARB BSE CASES IN THE UK SINCE 1 AUGUST 1996

(THE SIX BARB BSE CASES BORN AND CONFIRMED IN THE UK AFTER 1 AUGUST 1996: IS THERE A NEED TO REVIEW THE OPINIONS OF THE SCIENTIFIC STEERING COMMITTEE WITH REGARD TO THE UK DATE-BASED EXPORT SCHEME AND OTHER TSE-RELATED RISKS?)

ADOPTED BY THE SCIENTIFIC STEERING COMMITTEE

AT ITS MEETING OF 29-30 NOVEMBER 2001.

OPINION

The Scientific Steering Committee (SSC) is invited to express its appreciation on the 6 BSE cases confirmed in the UK in animals born after 1 August 1996 ("BARBs"). More precisely, the SSC is invited to address the following questions:

- Does the occurrence of 6 cases of BSE in cattle born after 1 August 1996, date when the ban on feeding mammalian protein to ruminants was considered fully effective, indicate that other routes of infection of cattle with BSE than feed-borne (by feeding mammalian protein) or maternal need to be considered?
- Is there a need to immediately revise the DBES?
- Do these cases have an impact on the validity of any other SSC opinion related to TSEs?

As it can be assumed that there will be more BARB cases coming up, the SSC is invited to permanently follow these cases and to regularly assess whether there is a need to review the DBES. At such occasions, the SSC should assess any possible impact of these cases on other SSC opinions.

The Scientific Steering Committee invited the TSE/BSE *ad hoc* Group to prepare a report on the above questions. Following discussion of this report, the SSC concludes as follows:

- There are currently not enough data available that would permit firm final conclusions to be drawn as to the source of infection and each of the three following routes of transmission remain theoretically possible - be it with a varying level of likelihood - for any of the 6 BARB cases[1]:

  a) exposure to BSE through feed carried over from before 1 August 1996 or to contaminated feedstuffs;

  b) exposure to BSE through maternal transmission;

  c) other not yet identified route(s) of transmission.

  However, from the case histories, and from the circumstantial conditions that likely prevailed during the period following the implementation of the "real ban of 1 August

[1] See also the SSC opinion on Hypotheses on the origin and transmission of BSE, adopted on 29-30 November 2001.

1996" (i.e., varying standards of stock control for feed; cleanliness; occasional residual amounts of infected food or food remnants remaining in the system to be consumed later) it would look that the route of infection has a higher probability to be feed-borne (e.g., residual contamination of feed at very low levels). But the only way to eventually know the origin of these cases is to follow precisely the number and type of BARB cases along the time, to explore the possible sources of infection of each case, and to design epidemiological studies on "new" and possibly still existing sources if the number of BARB cases increases (see further).

- The predicted numbers referred to in the various SSC opinions[2], are assuming a 10% maternal transmission risk within 6 months of clinical onset and assume "zero feed risk". Since it looks that the route of infection has a higher probability to be feed-borne, the current numbers of BARB cases cannot be compared to these predicted figures. However, taking into account that:

  (1) in *absolute* terms, the number of 6 BARB cases remain largely within the range of the figures used by the SSC when carrying out its risk assessment of the DBES,

  (2) meat products are produced according to the SSC's recommendations regarding animal source, age (30 months) and removal of SRMs and

  (3) there are so far no reasons to assume widespread and systematic inappropriate implementation of the current feed ban of 1996,

  there is currently no reason for the SSC to assume an increased risk as compared to its assessments presented in previous opinions. The SSC therefore does not consider at this moment a revision of its DBES or other BSE related opinions.

[2] See: Opinion of 28-29 October on the Scientific grounds of the advice of 30 september 1999 of the French Food Safety Agency (AFSSA).

Opinion of 7-8 December 2000 on Monitoring some important aspects of the evolution of the epidemic of BSE in Great-Britain.

Opinion of 14-15 September 2000on Export from the UK of bone-in veal.

Opinion of 13-14 April 2000 on the UK decision to lift the ban on consumption of meat on the bone.

- However, once more[3] the need is emphasised for stringent controls of the current feed ban enforcement, including cross-contamination, and an appropriate programme for monitoring BSE in bovine animals. Because a feed-borne origin of the 6 BARB cases cannot be excluded and because of the high number of BSE cases in the Over-Thirty Months Scheme (OTMS) animals, it is recommended that a large and significant sample[4] of animals above 30 months[5], are submitted to an epidemiological testing program and this at least until there is sufficient evidence for reassurance[6].

  Should such program reveal a large number of (pre-clinical) BSE cases that cannot be attributed to maternal transmission or a number of cases that can directly be related to other sources of infection, or provide indications that the number of infected animals around 30 months of age is higher than has been extrapolated from the model estimates, then the validity of the DBES may / will have to be put into question. A possible practical guidance for deciding when the risk exceeds, independently from the source of infection, the level indicated in the SSC opinions of 1999 and 2000 on the DBES, could be that if the number of BARB cases would exceed the upper limit of approximately 55 cases[7] (all ages confounded) during a 12 months period of the above mentioned epidemiological testing programme in animals born after mid 1996 a new assessment would be required to identify possible new risks that were not taken into account in the SSC's opinions on the DBES. Also, if a new way of transmission other than feed or maternal would be strongly hypothesised or proven, it would indicate that the DBES is not sufficient anymore to guarantee the control of the disease in cattle and human security.

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3 See the SSC opinion of 29-30 March 2001 on "Bovine Spongiform Encephalopathy in a second UK Animal born after 1 August 1996 (Case confirmed in Northern Ireland)"

4 The SSC is currently preparing an opinion on *Minimal requirements for intensive BSE surveillance*. The sample design and size of animals above 30 months to be tested may have to be revised so as to take into account the sizes recommended in that opinion.

5 This testing scheme should not be limited to OTMS animals but include all animals above 30 months, for example from the Beef Assurance Scheme (BAS) where in September 2001 a BSE has been diagnosed in a 6 years old animal.

6 It is noted that the UK recently started implementing a compulsory programme of rapid testing of all approximately 100.000 animals of the 1 August 1996 - 31 July 1997 birth-cohort submitted for being slaughtered under the OTM scheme. In addition a random sample of 50.000 other OTMS animals as well as all casualty and fallen stock above 24 months will be tested for BSE.
The SSC recommends that cohorts of BSE positives are also tested for BSE and that in the additional survey of 50.000 animals, priority is given to the 1997/98 birth cohort. The present opinion may possibly need revision or updating in the light of the results of these test programs.

7 This is the upper limit of number of model-predicted cases in 2001, [assuming an effective feed-ban and maternal transmission only. It corresponds with a human exposure risk in 2001 of less than 1 animal below 30 months of age and possibly being in the last 12 months of incubation.

- For timely detection of new trends in the appearance of BARB cases, each case should be thoroughly analyzed with respect to maternal transmission and in order to identify critical factors related to feed (MBM and feed contaminated by other pathways) introduction of genetic material into the herd, vaccines and veterinary medicaments and environmental issues. Basic information needed includes disease and feeding history, records, surveillance and management. In this respect, the SSC reiterates the answer given to the question "How should BSE cases born after 1 August 1996 be investigated" in the SSC opinion of 7-8 December 2000 on "Monitoring some important aspects of the evolution of the epidemic of BSE in Great-Britain".

Keywords: bovine spongiform encephalopathy, BSE, born-after-the-real-ban, BARB, United Kingdom, maternal transmission, feed.

REPORT OF THE TSE/BSE *AD HOC* GROUP ON

THE SIX BARB BSE CASES IN THE UK CONFIRMED SINCE 1 AUGUST 1996: IS THERE A NEED TO REVIEW THE OPINIONS OF THE SCIENTIFIC STEERING COMMITTEE WITH REGARD TO THE UK DATE-BASED EXPORT SCHEME AND OTHER TSE-RELATED RISKS?

I. BACKGROUND, LEGAL CONTEXT AND MANDATE

The UK is currently allowed to export beef and beef products produced under the Export certified herds scheme (ECHS) (from Northern Ireland) or the Date-based export scheme (DBES). Currently no establishments are approved under the ECHS. Two abattoirs and associated cutting plants are approved under the DBES.

The DBES was based on the advice of the former Scientific Veterinary Committee and the Scientific Steering Committee (SSC). The beef and products must exclusively be derived from animals found to have fulfilled certain eligibility criteria. These include:

- The animal must be born after the date when the feed ban was considered effective (1.8.1996) and be between 6 and 30 months old
- The dam of the animal must have survived 6 months after the birth of the animal and must not be a suspect or confirmed BSE case at the time of slaughter of the eligible animal.

The other conditions of the DBES include deboning of the meat, removal of all visible lymphatic and neural tissue, a system to ensure the correct identification and traceability of the animals, traceability of the meat and products, and an effectively enforced offspring cull (slaughter and destruction of all offspring to BSE cases born after 1.8.1996 in the UK).

Six BSE in animals born after 1 August 1996 have been recorded so far. They are referred to as a "BARBs" or animals "Born-after-the-real-feed-ban")

The case histories and epidemiological inquiries into possible sources of infection were provided to the EC services but no firm conclusions could be drawn (DEFRA, 2001; SEAC, 2001). However, from the farming and feeding practices and histories of the cases, with the exception of the first case, it would look that the route of infection was more likely feed-borne either because the dam is still alive until now (cases 3 and 6) or survived without BSE symptoms for more than 6 months (cases 2, 4 and 5). DEFRA (2001), analyzing the 6 confirmed BARB cases, found no indications for neither maternal, horizontal nor environmental contamination, but only for the feed by cross contamination, for which they found possible indications that there was potential for cross contamination with meat and bone meal of feed ingredients traded between the UK and other Member States into UK from third countries.

The Scientific Steering Committee (SSC) was therefore asked to express its appreciation on the 6 BARB BSE cases confirmed in the UK since 1 August 1996 and invited the TSE/BSE *ad hoc* Group to address the following questions:

- Does the occurrence of 6 cases of BSE in cattle born after 1 August 1996, date when the ban on feeding mammalian protein to ruminants was considered fully effective, indicate that other routes of infection of cattle with BSE than feed-borne (by feeding mammalian protein) or maternal need to be considered?
- Is there a need to immediately revise the DBES?
- Do these BARB cases have an impact on the validity of any other SSC opinions related to TSEs?

II. REPORT FROM THE TSE/BSE AD HOC GROUP

II.1. 1 August 1996 as date of effective and total enforcement of the feed ban in the UK.

In the various opinions by the SSC on the Date Based Export Scheme (DBES) for UK and the Certified Herds Scheme (CHS) for Northern Ireland, only feed and maternal transmission are considered as the possible routes of infection of cattle with BSE. The grounds for selecting 1 August 1996 as the starting day for allowing the export of meat and meat products derived from cattle born after that day were based on the following assumptions (SSC Opinion of 8-9 December 1997 on The UK Date Based Export Scheme and the UK proposal on Compulsory Slaughter of the Offspring of BSE cases):

- the MBM ban is effectively enforced from 1 August 1996
- the risk of maternal transmission significantly decreases by the compulsory cull of the offspring of cows with BSE;
- at this moment there is no scientific evidence that horizontal transmission occurs;
- that there is a significantly decreased probability of animals being infected with BSE when born earlier than 6 months before the onset of BSE in the dam.

II.2 Case history

The first BARB case was confirmed on 27 June 2000 in a Holstein /Friesian dairy cow born on 25 August 1996. The animal had not been born on the farm where disease was confirmed. The animal's dam was born in 1991 and died on the farm of her birth on 14 November 1996, less than three months after giving birth to the BSE case. The animal appears to have died suddenly without any observed clinical sign.

The second BARB case occurred on 13 November 2000 in Northern Ireland in a 4 year old Limousin cow born on 10 September 1996. The animal's dam was born on 1 October 1989 and she was culled for management reasons on 30 October 1998, 23 months after giving birth to the BSE case. This case was detected, and confirmed, as a result of active surveillance and was not reported as a clinical case.

The third BARB case was diagnosed on 15 June 2001 in a Friesian cow born on 20 May 1997 in the farm where the animal remained until its death. This farm had had five previous cases of BSE and five other cases bearing the same herd mark have been confirmed on other premises. The dam of the BSE case was born at the end of 1989 and is still alive on the farm.

The fourth BARB case was diagnosed on 13 July 2001 in a Friesian cow born on 4 December 1996. It had been purchased at three years of age from another farm and there have been no previous cases of BSE on the farm of its birth. The dam was born in 1994 and slaughtered nine months after the birth of the BSE case.

The fifth case was confirmed on 23 August 2001 and was born in January 1997. It was confirmed through passive surveillance. The dam was slaughtered under the OTMS on 16 December 1998, 23 months after the birth of the case.

The sixth case was confirmed on 28 August 2001 and was born in April 1997. It was confirmed in the active monitoring of casualty slaughters (photosensitization). The dam is still alive.

II.3 Model-estimates of number of annual BARB cases possibly to be expected

1. In the SSC opinion of 7-8 December 2000 "Monitoring some important aspects of the evolution of the epidemic of BSE in Great-Britain" an update was included, providing an epidemiological commentary on BSE projections for GB and on surveillance, as well as on the occurrence of "Born After the Real Ban (BARB)" cases. For the estimation of GB's BSE infection incidence for calves born after 1 August 1996, a method was referred to, using the life-table for an index birth cohort of calves, the number of calves in the birth cohort of interest, and the BSE incubation period distribution as estimated in the paper of Donnelly *et al* (2000) All analyses in this paper assume zero feed risk after 1 August 1996, but contrary evidence could emerge in time. An explanation for differences in projections done in 1999 and 2000 by Donnelly were explained by the fact that feed risk in 1991-1996 did not decline as rapidly as might have been hoped. This could also have plaid a role in the BARB cases.

   In 2000 Donnelly *et al* (2000) revised their predictions of future case incidence of BSE upwards. For cases in animals born after mid 1996, taking into account 10% maternal transmission the following numbers were predicted[8] (95% prediction interval): 0.2 (0, 1) in 1998; 4 (1, 11) in 1999; 15 (8, 40) in 2000 and 23 (13, 56) in 2001.

2. The Spongiform Encephalopathy Advisory Committee of the UK (SEAC) in September 2000 noted that a correction was needed as the above figures did not take account of the estimated effects of the offspring and selective culls. It subsequently revised the estimated numbers of BSE cases born after August 1996 as follows:

   1999 2 (0, 5)

   2000 6 (3, 16)

   2001 9 (5, 23)

3. Assuming 10% maternal transmission and an offspring cull policy in place, Donnelly *et al* (2000) estimate that the number of animals entering the food chain

[8] Already in 1999, an assessment on behalf of the UK's Spongiform Encephalopathy Advisory Committee (SEAC) predicted that by the end of 2001, up to 42 cases born after 1 August 1996 might be identified: 4 in 1999, 15 in 2000 and 23 in 2001.

in Great Britain that are below 30 months of age and within 12 months of developing clinical disease as follows: 0.8 (0, 3) animals in 2001, 1.2 (0, 4) animals in 2000, 3.1 (0, 7) in 1999 and 6.2 (2, 17) in 1998

R. Anderson and colleagues (H.Needham, personal communication, 27.07.01), allowing for a 60% reduction in maternal transmission cases due to the Offspring Cull, estimate that the number of animals entering the food chain in Great Britain that are below 30 months of age and within 12 months of developing clinical disease to be 0.5 in 2001 and 0.8 cases in 2000.

4. It should be kept in mind that no model can predict the future number of BARB cases in the absence of knowledge of the past profile of exposure and a complete reliance on model outputs for decision making may therefore be unjustified.

   The United Kingdom conducted two "OTMS-surveys", with as main objective to obtain an independent assessment of the decline in the incidence, as adjudged by the passive surveillance system, by active surveillance of culled adult cattle. A first survey was conducted in the period January-March 1999, a second one between May and December 2000. The results of the second survey (Wilesmith, pers.comm, 7 October 2001) reveal a 0.41% of positive cases (42 out of a total sample size of 10.032) in animals above 5 years slaughtered in Great Britain under the Over Thirty Months Scheme (OTMS) (DEFRA, 2001). [9] confirmed previous estimates that the risk of exposure did not continue to decline for cohorts born between 1991 and 1995. The 1992 and 1993 born cohorts, at least, did not exhibit the sharply reduced risk of exposure for animals born in the first two years after the 1988 ban. This phenomenon is currently being investigated.

   The OTMS 2000 survey thus shows an incidence of BSE in animals over 5 years old which - had all OTMS bovines aged 5 years or older (approx. 675,000 animals) been subject to rapid BSE testing in 2000 – would have discovered 2,700 BSE positives. UJ reported only around 1,450 clinical BSE cases. Incorporation of these OTMS results may lead to further revision ofd UK's BSE projections. It is therefore prudent, in 2001. To require the BSE testing of all UK bovines over 30 months. But when analysing the results of such testing campaign, it should be kept in mind that an assumption in the models referred to in section II.3 is that the majority of animals that have experienced clinical disease have been infected as a result of calfhood exposure and that there is an age-dependent susceptibility to infection. However, adulthood exposure can and does occur and may have been (part of) the reason for the occurrence of the UK epidemic. It is thus not excluded that the basic model used to predict the number of BARB cases underestimates the number of late stage incubation period animals[10] in the population and/or the role

[9] The incidence (%) calculated for the animals at that time above between 5 and 6 years was 0.56 and 0.07 for the animals between 6 and 7 years, making a cumulative incidence of 0.63 for animals above 5 years in 1992. The peak incidence in animals >= 5 years of age occurred in 1993, when the incidence in this group was 0.89%. It should nevertheless be kept in mind that both figures result from different methodologies.

[10] These animals do not enter the human consumption chain but their offspring may. It therefore needs to be verified whether the cases detected in the OTMS population as a result of the current testing campaigns, are taken into account in the mathematical models developed used to predict estimate the future numbers of BSE cases. The basic model assumes that the majority of animals that have experienced clinical disease have been infected as a result of calfhood exposure that and there is an age-dependent susceptibility to infection.

of adulthood exposure at the start of exposure of the British cattle population. As a result the OTMS survey results may not conform to the basic model referred to in section II.3.

II.4 Source of infection

1. However, although the assumption of a risk of 10% maternal transmission during the last 6 months of incubation and after clinical onset is the most likely and most widely used assumption because it better fits the epidemic of the disease in UK, and statistically accounts for the vast majority of all possible maternal transmission cases, other maternal transmission rates and length of the period of risk for maternal transmission cannot be fully excluded. As shown in the annex (Bird, 2001), there is uncertainty about the birth interval prior to BSE onset.

   In none of the present 6 BARB cases, maternal transmission can thus be ruled out completely, even not in the cases 3 and 6 where the dam is still alive or in the cases were the dam survived the birth of the BARB case for more than 6 months without presenting BSE: case 2 (23 months), case 4 (9 months) and case 5 (11 months). But neither for is there any evidence that maternal transmission would the cause for any of the 6 BARBs.

2. Although the official date for the initiation of the "real ban" is 1 August 1996, it was in reality preceded in the previous months by the implementation of several measures which were designed to eliminate the failings of the original food ban. Hence presumably the large reduction in the number of cases from the beginning of 1996. However in a large multi-component system such as the farming industry it would not be surprising if there were varying standards of stock control for feed, cleanliness etc. It is not inconceivable that occasional residual amounts of infected feed or feed remnants remained in the system after 1 August 1996 to be consumed later.

   Residual contamination of feed (at very low levels) can thus not be excluded as a probable source of infection for the six BARBs and the few cases that preceded them earlier in 1996.

   It may be too early to tell if there will be a large number of BARBs or not, based on the numbers so far. If one wants to see how well the feed ban is working, he has to look at a cohort about a year later and wait a sufficiently long time for a significant number of animals to have reached an age where they could have come down with BSE and then to be recorded by the system. It may be sufficiently efficient to concentrate on the 1996/97 birth cohort ~~from 2000~~, include the 1997/98 cohort as from 2001 and subsequent cohorts in the following years. Given an average age of death of 5 years and a reporting delay of about 3 months, it may be premature to assess whether there are significant numbers of cases occurring up to August 1997.

However, adulthood exposure can and does occur and may have been (part of) the reason for the occurrence of the national epidemic.

Also, from the farming and feeding practices and case histories, especially the third and sixth case, it would look that the route of infection has a higher probability to be feed-borne because of the long survival of the dam.

3. An analysis of the 6 BARB cases carried out by SEAC (2001) and summarised by DEFRA (2001) did not reveal neither good evidence for horizontal transmission nor strong indications of environmental contamination as possible routes of infection.

   In fact, in the December 1996 and January 1997 cases, no previous cases of BSE occurred on the farms and there have been no calvings of cows afflicted with BSE close to the time of birth of the cases.

   In the December 1996 case, there was no livestock species present in the farm or grazing on contiguous fields. For the May 1997, January 1997 and September 1996 cases there was a possible exposure to, respectively, pig slurry, brewery and abattoir waste and blood. However, the evidence of an environmental source was not persuasive in any of these cases.

4. No firm final conclusions can be thus drawn as to the source of infection and following routes of transmission remain theoretically possible:

   a) exposure to BSE through feed carried over from before 1 August 1996; or through contaminated feed;

   b) exposure to BSE through maternal transmission.

   c) other not yet identified route(s) of transmission (e.g., horizontal transmission and/or environmental contamination) which might become evident as the BSE epidemic declines to very low levels.

      Note: Feed-borne transmission through feed allowed after the feed ban (bloodmeal, tallow) would, for the time being and pending the outcome of the SSC forthcoming opinion on alternative routes of transmission, be included in the third option.

   However, from the case histories and from the circumstantial conditions that likely prevailed during the period following the implementation of the "real ban of 1 August 1996" it would look that the route of infection has a higher probability to be feed-borne.

II.4. Feed ban implementation and BSE surveillance

1. In all analyses the assumption was made that there was no residual bovine feed risk after 1 August 1996, and hence that all infections after this date were due to direct maternal transmission of infection. If feed risk did continue after this time, the number of infected animals would be inevitably greater. On the other hand one must nevertheless accept that it is unrealistic to assume that under field conditions no single feed-borne case would occur. It is difficult to try to pre-determine a “safe-date” after which it is expected that the feed borne exposure would have ceased. It is known from experiences with BSE controls and with other feed borne exposures, such as aflatoxicosis, that it can take some time after a formal, legal

ban to exhaust the source of exposure in the feed "system". This is important for BSE as it is known that animals are susceptible to very small amounts of infective material. In terms of control and statutory interventions in Great Britain, there are still loopholes that are currently being addressed in terms of improved surveillance. The main one is the contamination of feed ingredients from MBM derived from other BSE-affected countries. One scenario is, according to DEFRA (2001) the contamination of ship's holds or other transport containers of say, soya meal, from previous consignments of MBM.

These possible and apparently minor breaches of the feed ban, even if all 6 cases would be attributable to contaminated feed, would raise less concern provided the detection rate is appropriate. All 6 BARB cases so far were born between August 1996 and May 1997 and one can / should not expect that a such drastic change in feeding practices would be 100% effective at once for a whole country and a large population of several millions of cattle.

2. The effectiveness of both the offspring cull[11], and the control of the measures implemented in mid-1996 to ensure no feed-borne transmission of BSE, are key factors to exclude the emergence of BARB cases.

   If one assumes some failure during the initial months following the complete feed ban[12] resulting in the few BARB cases observed so far, the feed borne risk should have gradually disappeared almost completely as the risk posed by animals born after 1 August 1996 should decrease as the period between 1 August 1996 and their date of birth becomes longer. Today, the total number of cases should thus not exceed the numbers estimated using scientific models integrating the current knowledge on transmission routes, the effects of eradication policies, etc.

   These estimates vary according to the source. The highest upper limit estimated so far is 56 cases in 2001 in Great Britain animals born after mid 1996, all ages confounded (Donnelly *et al*, February 2000). This value was used in the risk assessments presented in the various DBES-related opinions of the SSC and translated in approximately 1 or less animals below 30 months being in the last 12 months of incubation. It can be used as a threshold above which the risk would be considered to be unacceptably high. [The value of 56 is only indicative: on one hand the cattle population has decreased as a result of BSE and FMD eradication policies in 2001, but on the other hand the FMD epidemic has resulted in an increased adult breeding cow population. The latter is because the rendering capacity, normally used for animals taken into the OTMS, has been used for the rendering of notably sheep and cattle as a result of the FMD epidemic.)

   While there is currently no reason to assume that the BSE surveillance in animals born after 1 August 1996 is unsatisfactory and that the number of BARBs so far would be much higher than the ones reported, only an appropriate program for

[11] From the OTMS 2000 survey results that a BSE positivity of 4 in 1000 for >5 years old animals would translate into 2700 BSE-test positives going through the OTMS for only 42 of which any offspring cull was done.

[12] The TSE/BSE ad hoc Group understands that 1 August 1996 already includes a asafety margin of several months.

monitoring BSE in bovine animals could confirm that the number of BARB cases in UK is indeed as low as currently reported[13].

To confirm that the feed-ban is indeed satisfactorily implemented it becomes thus necessary to submit a large and statistically significant sample of ~~all~~ animals above 30 months, when they are slaughtered or submitted for disposal via the OTM Scheme, to a testing program similar to the ones currently developed in the other EU Member States. This would gradually provide a sufficiently large sample because the expected numbers of cases to be found as a result of maternal transmission (excluding feed-borne infectivity) is small. Should this program reveal an unexpectedly large number of (pre-clinical) BSE cases that cannot be attributed to maternal transmission or a number of cases that can directly be related to other sources of infection (feed, horizontal), or provide indications that the number of infected animals around 30 months of age is higher than what can be extrapolated from the model estimates, then the validity of the DBES may / will have to be put into question.

II.5. Human exposure risk assessment

The Date Based Export Scheme (DBES) opinion of the SSC, adopted on 9 December 1997, was based on the concept that animals born after a specific date, 1 August 1996, were guaranteed not to have been exposed to BSE agent in feed. It has to be noted that at that time a number of animals had not yet reached an age of 30 months.

In absolute terms of risk, the number of BARB cases detected so far (end September 2001) still falls within the earlier quoted intervals, at that time resulting from models assuming a 10% maternal transmission rate during the last 6 months of incubation and after clinical onset.

At this moment UK-consumers are mainly protected by the removal of the Specified Risk Materials and the "Over Thirty Months Scheme" which is based upon the incubation period, the youngest BSE case ever seen being 20 months and no cases under 31 months detected since 1997. Consumers in other Member States are in addition to this protected by the additional safeguards in the DBES (see opinion ….).

Therefore, there is currently no increased risk of human exposure to the BSE agent through consumption of meat exported under the DBES scheme, as compared to the SSC assessments presented in 1999, 2000 and 2001 (EC, 1999, 2000, 2001). Even if some or all of the 6 BARB cases reported so far would have originated from infection routes other than maternal transmission, this would be correct, provided the conditions listed in these opinions are met. These conditions included a close to perfect implementation of the total feed-ban, a careful sourcing of individual animals and their age (max. 30 months), exclusion of Specified Risk Materials and a surveillance / detection that can be considered to be reliable.

[13] The present low numbers compared to the predicted numbers could reflect a certain degree of underreporting as not all animals above 30 months culled under the different schemes (OTMS, Offspring, casualty, emergency) are tested.

II.6. Conclusions and recommendations

The expected numbers of BARBs referred to in the various SSC opinions[14] were based on assuming a 10% maternal transmission risk within 6 months of clinical onset and "zero feed risk". However, taking into account the above arguments i.e. (1) that, in absolute terms, the number of 6 BARB cases remain largely within the range of the figures used by the SSC when carrying out its risk assessment of the DBES, that (2) meat products produced according to the SSC' recommendations regarding animal source and age (30 months) and removal of SRMs, and that (3) there are so far no reasons to assume widespread and systematic inappropriate current implementation of the current feed ban of 1996, the TSE/BSE *ad hoc* group considers that at the moment neither the opinions on the DBES or other BSE issues need to be revised, nor that there exists an increased risk of humans being exposed to infectivity through meat as compared to the assessments presented in earlier opinions of the SSC.

The TSE/BSE *ad hoc* group wishes also to confirm the answer given in the SSC opinion of 29-30 March 2001 on "Bovine Spongiform Encephalopathy in a second UK Animal born after 1 August 1996 (Case confirmed in Northern Ireland)" and emphasises once more the need for stringent controls of the current feed ban enforcement, including cross-contamination, and an appropriate programme for monitoring BSE in bovine animals in order to confirm that the number of BARB cases in UK is indeed as low as currently reported.

Because a feed-borne origin of the now 6 BARB cases cannot be excluded and because of the high number of BSE cases in the OTMS[15] animals, it is recommended that all animals above 30 months, when they are slaughtered or submitted for disposal via the OTM-Scheme, are submitted to a testing program similar to the ones currently developed in the other EU Member States.

Should such program reveal an unexpectedly large number of (pre-clinical) BSE cases that cannot be attributed to maternal transmission or a number of cases that can directly be related to other sources of infection (feed, horizontal), or provide indications that the number of infected animals around 30 months of age is higher then what can be extrapolated from the model estimates, then the possible risk associated with the DBES could be considered to be higher than the level presented in earlier DBES-related opinions of the SSC.

A possible practical guidance for deciding when the risk exceeds, independently from the source of infection, the level indicated in the SSC opinions of 1999 and 2000 on the DBES, could be that if the number of BARB cases would exceed the upper limit of approximately 55 cases[16] (all ages confounded) during a 12 months period in

[14] See: Opinion of 28-29 October on the Scientific grounds of the advice of 30 september 1999 of the French Food Safety Agency (AFSSA).

Opinion of 7-8 December 2000 on Monitoring some important aspects of the evolution of the epidemic of BSE in Great-Britain.

Opinion of 14-15 September 2000on Export from the UK of bone-in veal.

Opinion of 13-14 April 2000 on the UK decision to lift the ban on consumption of meat on the bone.

[15] "Over Thirty Months Scheme"

[16] This is the upper limit of number of model-predicted cases in 2001, assuming an effective feed-ban and maternal transmission only. It corresponds with a human exposure risk in 2001 of less than 1 animal below 30 months of age and possibly being in the last 12 months of incubation.

animals born after mid 1996 a new assessment would be required to identify possible new risks that were not taken into account in the SSC's opinions on the DBES.

In order to timely detect new trends in the appearance of BARB cases, i.e. new transmission ways, each BARB case should be thoroughly analyzed in order to identify critical factors. Basic information needed includes disease history, records, surveillance and management. In this respect, the TSE/BSE *ad hoc* group acknowledges the collection of detailed epidemiological data and information set up ~~in~~ since 1999 as a support of the analysis of BARB cases should they occur (Wilesmith, pers.comm, 7 October 2001) and reiterates the answer given to question 4 "How should BSE cases born after 1 August 1996 be investigated" in the SSC opinion of 7-8 December 2000 on "Monitoring some important aspects of the evolution of the epidemic of BSE in Great-Britain"

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ANNEX: CONSIDERATIONS ON THE VERTICAL TRANSMISSION ROUTE OF BSE*[17]

Whether BSE is transmitted vertically (during pregnancy, at birth or just after birth), and whether this could signal the presence of infectivity in a wider range of tissues/body fluids than evidenced hitherto was a major concern in the late 1980s. Modest transmission experiments in mice using placenta from only four BSE affected bovines did not produce neuropathological evidence of transmission [ref = a], but this absence of evidence fails to reassure on a number of counts, see Wilesmith et al. (1994), Gore (1998), and Hill et al. (2000).

In 1993, Hoinville, Wilesmith and Richards (1995) set up a case-controls study to investigate risk factors, including maternal, for BSE cases born after the July 1988 'feed ban'. The adjusted BSE odds ratio for the offspring of affected dams was 1.5 (95% confidence interval: 0.9 to 2.4, p = 0.11) in the extended dataset; but the association between BSE incubation stage in the dam and BSE in the offspring was not persuasive that risk to the offspring of developing BSE was higher for dams which calved nearer to onset of clinical signs. Hoinville, Wilesmith and Richards also showed that animals born within a week of the calving date for a dam that subsequenty developed BSE might have been at increased risk of developing BSE (adjusted BSE odds ratio = 1.2 with 95% CI from 1.0 to 1.4, p = 0.015).

Meanwhile the BSE Maternal Cohort Study, see Wilesmith et al. (1997a) and Donnelly, Gore, Curnow and Wilesmith (1997), had been initiated in 1989 as the largest designed investigation of TSE transmission from mother-to-offspring in any species. With few exceptions, selected maternally exposed calves had been born within 6 months of BSE onset in the dam. For each maternally exposed calf, a control calf - born in the same herd and calving season - was selected whose dam had reached at least six years of age without developing clinical signs of BSE. 315 matched pairs, with birth dates from August 1987 to November 1989, were recruited from July 1989 to March 1990; and 301 pairs remained eligible for analysis, see Wilesmith et al. (1997a). Its recruitment pattern meant that the BSE Maternal Cohort Study was partly confounded by calves' potential exposure to contaminated feed on natal farms before they were purchased for study; and later, by inadvertent exposure on at least one of the three experimental farms. Calves were reared to age seven years (unless culled because suspected of having BSE, or for other necessary reasons) when they were slaughtered; all brains were examined for histological signs of BSE. Among the 301 matched pairs, 55 animals (42 maternally exposed, 13 controls) had BSE pathology, which signified a substantially higher BSE risk for the offspring of BSE affected dams. Compared to controls, the risk difference was 10% (95% CI: 5% to 14%) and the relative risk was 3.2 (95% CI: 1.8 to 5.9).

Because all calves were potentially exposed to contaminated feed before recruitment into the study, the observed risk difference could have been a consequence of i) direct maternal transmission, ii) enhanced susceptibility to feed-based infection among the offspring of BSE-affected dams, or iii) some combination of the two. Evidence of higher BSE risk to maternally exposed calves born closest to BSE onset in the dam would implicate direct maternal transmission. Such evidence was found in further analyses of the BSE Maternal Cohort Study, see Gore et al. (1997), Donnelly et al. (1997b), and Curnow et al. (1997); but strictly needed external validation.

[17] Annex prepared by Sheila M. Bird, MRC Biostatistics Unit,CAMBRIDGE

Corroboration was sought in the wider BSE database, see Donnelly et al. (1997c) and Donnelly and Ferguson (2000), which - in principle - could also address BSE risk to the penultimate calf of BSE affected dams. Gore et al. (1997) were reluctant to apply a methodology which required assumptions about the survival of calves or traceability of dams being independent of the interval from the birth of a calf to BSE onset in the dam. Only by attributing lower survival probabilities for calves born to BSE-affected dams did Donnelly and Ferguson (2000) achieve relatively coherent results about BSE risk to calf and interval from birth of calf to BSE onset in dam. Some enhanced risk apparently persisted up to 24 months but by far the greatest risk was to calves born after BSE onset in the dam. Donnelly and Ferguson (2000) did not address how consistent the fall-off in risk for the period 0 to 12 months before BSE onset in the dam was between BSE Maternal Cohort Study and analyses of the wider BSE database. They did, however, interpret the lack of any evidence for a significantly enhanced risk to animals born more than two years before BSE onset in the dam as a strong argument against ii) genetically enhanced susceptibility to BSE infection.

Interestingly also, Donnelly's re-analysis (1998) of data on the fate of the offspring of BSE-affected pedigree suckler cows in Great Britain, see also Wilesmith and Ryan (1997b), showed them to be consistent with a maternal transmission rate of up to 8% for up to 23 months before clinical onset in the dam.

Great Britain's BSE projections, however, have tended to follow the BSE Maternal Cohort Study in assuming 10% (direct) maternal transmission to calves born within 6 months of BSE onset in dam, see Anderson et al. (1996), Ferguson et al (1997) and Donnelly and Ferguson (2000). The under-forecasting of Great Britain's BSE cases in 1998 and 1999, see [EC Opinion as ref], is mainly attributed to under-estimation of the feed-based risk in the mid 1990s: it does not constitute evidence per se for mis-specification of the maternally enhanced BSE risk.

On the precautionary principle, and in accordance with Commission Decision 98/692/EC, all offspring born after 1 August 1996 to confirmed BSE cases are slaughtered without delay. The Ad Hoc TSE/BSE Subgroup has noted that there may be scientific reasons for rearing such offspring to seven years of age to determine their BSE pathology or positivity for PrP(res) in relation to interval from birth of calf to BSE onset in dam.

In summary, policy as well as projections now take maternal BSE transmission into account but there is uncertainty about the birth interval prior to BSE onset which confers enhanced risk: six months, 2 years, or any calf. In both the BSE Maternal Cohort Study and wider BSE database, calves born after BSE onset in the dam were strikingly at highest risk.

Compared even to the recent past, see Gore (1996) and Gore (1998), there is a heightened general concern in UK about the possibility of vCJD transmission from mother to child based on account of a reportedly ailing brain-damaged 11 month old infant, delivered by Caesarian section in October 1999, in whom tests for the abnormal prion protein have been inconclusive but whose mother's illness was diagnosed as vCJD in January 2000, a few months only prior to her death in May 2000. This infant is one of only very few so far who have been born within a year of maternal death from vCJD. In autumn 1997, clinical and statistical audiences placed 57% of bets on the mother-to-child vCJD transmission rate being under 1% for children born in the year before the mother's death from vCJD, see Gore (1998).

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