



EUROPEAN COMMISSION
HEALTH & CONSUMER PROTECTION DIRECTORATE-GENERAL

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

THE SAFETY OF BOVINE EMBRYOS

AMENDMENT TO THE SSC OPINION OF 18-19 MARCH 1999
ON THE POSSIBLE VERTICAL TRANSMISSION OF
BOVINE SPONGIFORM ENCEPHALOPATHY (BSE)

ADOPTED BY THE SCIENTIFIC STEERING COMMITTEE

AT ITS MEETING OF 16 MAY 2002

BACKGROUND AND MANDATE:

On 2 January 2002, Commission Services were provided with a report on the outcome of recent studies on embryo transfer from cattle clinically affected with bovine spongiform encephalopathy. These studies are here being referred to as the *Embryo Transfer Experiment*¹. The Commission subsequently submitted the following question for opinion to the Scientific Steering Committee (SSC):

In the light of the outcome of the Embryo Transfer Experiment, can the SSC confirm or review its opinion of 18-19 March 1999 on vertical transmission of BSE? In particular, is there a need to maintain measures other than those prescribed by the IETS to ensure the safety of bovine embryos?

The SSC asked the TSE/BSE *ad hoc* Group to evaluate the report on the studies and to provide the scientific bases to address the above questions. This evaluation, prepared under the rapporteurship of Dr.D.Heim, was finalised on 2 May 2002. Is attached to the opinion.

OPINION

On the basis of the evaluation report prepared by the TSE/BSE *ad hoc* Group, the SSC concludes that its opinion of 18-19 March 1999 on vertical transmission of BSE concerning semen and embryo, can be confirmed. With regard to the BSE-safety of bovine embryos, there is from the scientific point of view no need for further measures other than those prescribed by the International Embryo Transfer Society (IETS) protocols.

REPORT FROM THE TSE/BSE AD HOC GROUP

This evaluation, prepared under the rapporteurship of Dr.D.Heim, was finalised by the TSE/BSE *ad hoc* Group at its meeting of 2 May 2002.

1. Extract, with regard to cattle with BSE, from the opinion on the possible vertical transmission of BSE adopted by the SSC 18-19 March 1999.

With regard to cattle with BSE, the SSC stated in 1999:

"In situations where there has been a high incidence of infection via feed, there is a risk of transmission from dam to offspring, by a mechanism that is not understood. In the presence of maternal preference of transmission, there may be a higher risk from material derived from the female than from the male animal. On the basis of the data currently available, the Scientific Steering Committee concluded that:

- *The results of all epidemiological studies undertaken to date have been consistent with a rate of maternal risk enhancement of approximately 10% in the offspring of dams within 12 months of the onset of clinical signs of BSE. Where the time lapse between parturition and onset of clinical symptoms is longer than 12 months, the rate of maternal transmission is reduced. Whether infectivity is transferred directly before birth or after birth by a variety of mechanisms (e.g., calf infection by contaminated material, environment contaminated with blood, faeces, infected feed, etc.) is uncertain and should be further investigated.*
- *There are no scientific data to support the hypothesis that infected calves are unduly sensitive to infection on a genetic basis.*

¹ Wrathall et al, 2002. Studies on embryo transfer from cattle clinically affected with bovine spongiform encephalopathy (BSE). Draft Paper submitted for publication to the Veterinary Record.:

- *On the basis of the limited data available, it appears that there is no enhanced risk of the development of BSE in the offspring of sires who developed BSE. It is therefore unlikely that semen constitutes a risk-factor for BSE transmission.*
- *Preliminary results from the incomplete embryo transfer study suggest an extremely low risk of transmission (95% confidence limits: 0-1.5%). These results are consistent with maternal transmission being mediated later in the gestational period either during or following birth of the animal.*
- *transmission of BSE by artificial insemination is unlikely for semen derived from BSE-affected bulls early in their incubation period;*
- *transmission of BSE via embryos is unlikely provided International Embryo Transfer Society (IETS) protocols are used.*

However, the Scientific Steering Committee noted that, in the absence of any infectivity studies on semen, embryos, fetal tissue, milk and colostrum by i/c inoculation of the homologous species in bovines, ovines and caprines, and in the absence of all the necessary experimental and epidemiological data as detailed in the report, precise estimates of these risks cannot be made.”

Although the SSC considered that risk management options are beyond the scope of its mandate, it proposed in 1999 a list of measures which could be considered.

2. Background for revision:

The, in 1999 still incomplete, embryo transfer study has been completed and submitted for publication as Wrathall *et al* (2002)¹. This paper forms the basis for the request whether the SSC opinion of 1999 can be confirmed or needs revision.

In this study, semen from 13 bulls, 8 with clinical BSE, was used for artificial insemination (AI) of 167 clinically affected cows in the terminal stages of BSE. It was found that the BSE status of the bull had no significant effect on the proportion of viable embryos recovered. The resultant embryos were collected seven days after AI. The embryos were treated according to the recommendation of the International Embryo Transfer Society (IETS).

587 viable embryos were transferred into 347 recipient heifers imported from NZ and 266 live offspring were born, of which 54,1% had a BSE positive sire as well as a BSE positive dam. The recipients and the offspring were monitored for 7 years after transfer resp. birth. None showed signs for BSE. All brains were examined for BSE by histopathology, Immunohistochemistry (IHC) and SAF – all were negative.

29 of the recipients died. The brains of almost all casualty recipients were examined for BSE by histopathology, IHC and SAF. One was not examined by histology, IHC due to severe autolysis, but SAF was negative; three were negative by histology and IHC, but had no SAF-test.

Eleven offspring were aborted and six were stillborn. Histopathology was done for ten aborted and five stillborn, ICH on 7 aborted and five stillborn, one stillborn was tested with SAF – all were negative.

Twenty of the live born offspring died/euthanized because of other diseases. Brain examinations were done, but one calf, which died when 13 days old, was not examined.

1020 non viable embryos were sonicated and inoculated i.c. into 48 susceptible mice (RIII and C 57), which were 700 days p.i. all negative.

Additionally, uterine flush fluid samples from 41 cows (consisting of cellular debris, mucus and occasionally blood) were tested for BSE infectivity by ic and ip in 946 mice. One of these mice (R III), examined 447 days p.i., had some vacuolar pathology. All other mice with injections of flush fluids from the same cow were negative when finally killed and examined:

- All recipients into which the embryos sired by BSE-affected bulls were transferred, and all the offspring of those bulls remained BSE-negative. These supports the conclusion that transmission of BSE by AI is unlikely for semen derived from BSE-affected bulls even in the late incubation period.
- All embryo-recipients and all the offspring remained BSE-negative. This supports the view that transmission via embryos is unlikely provided IETS protocols are used.
- One mouse inoculated with uterine flush fluid samples from a BSE affected donor cow showed vacuolar pathology. While such pathology is the basis of interpretation of the assay, its occurrence in a single mouse (1/21 mice in the group in which the brain was examined) cannot be taken as evidence of successful transmission.

On the basis of the above, the TSE/BSE ad hoc Group concludes that the SSC Opinion of 18-19 March 1999 on vertical transmission of BSE concerning semen and embryo can be confirmed. From the scientific point of view there is no need for further measures other than those prescribed by the IETS.