



REVIEW OF THE USE OF BONE DERIVED FROM CATTLE IN FOOD PRODUCTION

Issue

1. The Beef Bones Regulations 1997 prohibited not only the sale of bone-in beef to the consumer but also the use of beef bones for manufacturing food products. In 1999, these regulations were amended to lift the ban on the sale of bone-in beef and beef bones direct to the consumer, but the ban on the use of beef bones and bone-in beef in manufactured and processed products remained in place (The Beef Bones (Amendment) (England) Regulations 1999).
2. Retention of the manufacturing ban was considered prudent as there was then thought to be a possibility that bone marrow might be infective and that consumers wishing to avoid any risk associated with beef bone should be protected in circumstances where they might be unable to make a fully-informed choice. However, this ban is now out of step with legislation subsequently introduced at EU level to protect consumers from BSE. It is therefore appropriate to consider whether the residual ban on beef bones remains justified on grounds of risk.
3. The Food Standards Agency has requested advice from SEAC on the current state of knowledge regarding the infectivity of bovine bone marrow. The Agency intends to use an existing model (constructed for the over thirty months rule (OTMR) review) to assess the additional risk, if any, that would arise if the manufacturing ban on beef bones were lifted. This model already takes into account the risks from exposure to dorsal root ganglia associated with vertebral column. Thus the only additional information needed relates to beef bone/bone marrow.

Background

Previous SEAC advice on this issue

4. The data on infectivity in bone marrow was last reviewed by SEAC in November 1998 when they considered results from a mouse bioassay examining the infectivity of sternal bone marrow from cattle exposed orally to BSE. (Subsequent to SEAC's assessment, Wells *et al.* published this research in 1999 (Annex 1)).

1998

Report of infectivity detected in bone marrow from a clinical case of BSE

The following data were presented to SEAC:

5. As part of the pathogenesis study being conducted at the VLA on cattle orally infected with BSE samples of sternal bone marrow were taken from animals killed at 32, 36, 38 and 40 months post exposure. Pooled samples from each age group were subjected to mouse (i.c. and i.p.) bioassay. Evidence of infectivity was detected in the bone marrow from the cattle (n=3) killed at 38 months, but not those killed at 32, 36 or 40 months. Of the 16 mice inoculated with the 38 month sample 2 showed clinical signs of disease at 695 and 842 days, these were also positive by histopathology and PrP immunohistochemistry. In addition 4 other mice were positive by PrP immunohistochemistry alone (with survival periods of 653-923 days).
6. When SEAC reviewed this work, they suggested three possible alternative interpretations for the results for bone marrow which were positive for samples taken at 38 months after exposure, but negative for samples taken at 32, 36 and 40 months:
 - The isolated positive result might indicate the occasional occurrence of infectivity in the bone marrow of some, but not all clinically affected animals.
 - The BSE infectivity in bone marrow might be at the borderline of the sensitivity of the mouse bioassay. It was possible that the 38 month sample was the only time that infectivity levels rose above the threshold of detection. SEAC suggested that this might indicate that bone marrow could maintain a low level of infectivity over a longer time period than indicated by the experiment.
 - The isolated positive may have been due to contamination during post mortem procedures.

SEAC's conclusions

7. SEAC concluded that the risk, if any, from bone marrow is likely to be very small, and that the amount of infectivity present in cattle over thirty months of age would be very low when compared with past exposure. SEAC agreed that if the ban on beef on the bone were removed, the OTMR would provide satisfactory protection to the consumer.

1999

Publication of the mouse bioassay results (Wells *et al*)

8. The paper published by Wells *et al.* in March 1999 reports the same data that SEAC considered in 1998.
9. The authors also acknowledge that cross-contamination could not be excluded as a possible explanation for the positive result.
10. The authors also propose two additional explanations for the positive result. These include:
 - During the clinical phase of disease infectivity may spread from the central nervous system, via the peripheral nervous system, to peripheral tissues including bone marrow. However, in this case, positive results would be expected from the 40 month samples.
 - Infectivity may spread to bone marrow via the circulation. However in this case infectivity would also be expected in spleen and lymph nodes in equivalent or greater levels. No detectable infectivity was reported in spleen or lymph nodes of cattle in the study.

2002

Estimate of infectivity

11. The SSC 'Update of the opinion on TSE infectivity in ruminant tissues' (2002) gives a provisional estimate for infectivity in bone marrow as a result of the mouse bioassay of $< 10^1$ mouse i.c. + i.p. ID₅₀/g.

2003

Current results from the cattle bioassay

12. In 1996 SEAC requested that some of the samples collected in the BSE pathogenesis study should be also be tested by cattle bioassay. Comparative titration studies in mice and cattle have shown that this is approximately 500-fold more sensitive than the mouse bioassay. The bone marrow samples taken at 32 and 36 months (plus those taken at 22 and 26 months) post exposure were each inoculated i.c. into five 4 month old cattle. These cattle are still alive at 55-56 months post inoculation with no clinical signs of disease.
13. For comparison positive results from the cattle bioassay have been obtained for:
 - brainstem sampled at 32 months which produced clinical signs in the recipient animals at 22-23 months giving an estimated titre of 10^2 - 10^3 bovine i.c. ID₅₀/g (SSC 'Update of the opinion on TSE infectivity in ruminant tissues' (2002)).

- tonsil sampled at 10 months which produced clinical signs in one recipient animal at 47 months giving an estimated titre of 10^0 - 10^1 bovine i.c. ID₅₀/g (previous SEAC discussion).

Advice sought from the Committee

Members are asked to advise on the following:

Whether the scientific data indicates that there is a risk from the consumption of beef bone/bone marrow?

If so could the committee indicate what level(s) of infectivity should be used in a risk assessment of their use in food.

References

Wells GA, Hawkins SA, Green RB, Spencer YI, Dexter I, Dawson M. 1999. Limited detection of sternal bone marrow infectivity in the clinical phase of experimental Bovine Spongiform Encephalopathy (BSE). *Vet Rec.* Mar 13: **144** (11): 292-4