



RESEARCH ON ABNORMAL PRIONS IN BOVINE MILK

ISSUE

1. The FSA has asked SEAC to consider the findings of research to develop diagnostic tests to detect BSE infection-associated abnormal prion protein (PrP^{BSE}) in bovine milk and to screen milk from cattle experimentally infected with BSE for the presence of PrP^{BSE}.

BACKGROUND

2. SEAC has previously considered (in 1996 and 1997) the possibility that BSE can be transmitted from dam to calf via bovine milk. In 1996, SEAC considered (statement at Annex 1) the interim results of a cohort study conducted by the Central Veterinary Laboratory (CVL) of two groups of cattle offspring (n= 315 per group) born either from dams with BSE or from dams that had reached at least six years of age without developing clinical signs of BSE. The cattle offspring were matched for herd and calving season. At seven years of age, BSE was confirmed in a number of offspring from dams with clinical BSE (n= 42/273) but also in offspring from the control group (n= 13/273). An analysis of the data, including the interval between birth of the offspring and onset of clinical BSE in dams, suggested a risk of maternal transmission in the last 6 months of the BSE incubation period but, if it occurs, it is likely to be low (approximately 10% risk from dams with clinical BSE). However, routes of transmission other than milk could not be ruled out as the cattle may have been exposed to infected feed. In addition, the study could not provide information on the route of maternal transmission (*in utero*, at birth or soon after birth).
3. SEAC concluded that there was no evidence that infectivity could be transmitted through milk. In commercial dairy herds, where the bulk of BSE cases arise, calves do not receive their mothers' milk except for the first few days of life when colostrum is produced (colostrum is especially rich in maternal lymphocytes

and immunoglobulins). Colostrum is different in nature from ordinary milk and is not sold for human consumption. In beef suckler herds, on the other hand, it is common practice for calves to be suckled by their mothers for up to six months. Existing data do not provide evidence to suggest that the rate of maternal transmission in beef suckler calves, with prolonged exposure to their mother's milk, is any different to dairy herds, where the only exposure would be to colostrum in the first few days of life.

4. In 1997, SEAC considered and accepted a report from an epidemiology Subgroup convened to consider the final results of the CVL study (statement, including the Subgroup report, at Annex 2). The Subgroup noted that BSE was confirmed in offspring from the dams with clinical BSE (n= 42/301) and from dams in the BSE-free group (n= 13/301) indicating a 9.6% (confidence limits ranging from 5.1-14.2%) risk of maternal transmission in dams with clinical BSE.
5. Statistical analysis suggested that both inherited susceptibility to BSE in contaminated feed and direct maternal transmission may have contributed to the incidence of BSE in the cohorts. The main evidence for direct maternal transmission was that the risk of BSE in the calf of an affected dam was greatest for calves born close to the onset of BSE in the dam. However, the power of the study to detect differences related to the time between BSE onset and the date of birth of a calf was limited as the majority of the calves were born within the six months prior to onset of clinical disease in the dam. The Subgroup concluded that an enhanced BSE-risk in the offspring of BSE dams involves a low level of direct maternal transmission in the late stages of the incubation period. There was therefore, some evidence for direct maternal transmission of BSE at a low level but genetic susceptibility to BSE following feed-borne exposure may also have been a factor.
6. In 1998, SEAC reviewed the processing and use of bovine milk. The committee considered data implicating lymphocytes in the pathogenesis of TSEs. The committee noted that there was no evidence of infectivity in spleen or lymph nodes of cattle infected with BSE. Low numbers of lymphocytes are left in milk after processing. The committee agreed that no changes need be made to the previous advice of the risk of BSE in milk (see paragraph 3). Later in 1998, SEAC convened a workshop to review the approaches, methodologies and current level of knowledge of key variables, central to the risk assessment of humans and animals to BSE. Again SEAC reviewed aspects of the possible risk of infectivity in milk, including milk-processing

procedures. SEAC concluded that there was no reason to change their previous advice on the safety of milk.

7. No other direct experimental data have been generated to demonstrate the presence of the BSE agent in mammalian milk.
8. Milk from animals over 30 months of age is permissible for consumption by both humans and animals. However, under EU legislation, milk from any animal suspected of having BSE may not be used for human consumption.

SUMMARY OF FSA RESEARCH

9. In November 2002, SEAC was informed about a study the FSA was commissioning due to the continuing uncertainty about potential low levels of BSE infectivity in milk. The purpose of this study was to develop methods to detect the BSE infection associated form of the prion protein (PrP^{BSE}) in bovine milk and to determine whether PrP^{BSE} could be detected in milk samples from cattle that had been experimentally infected with the BSE agent. The committee agreed that research relating to milk should be a key priority, as it was a product that could be derived from animals over thirty months of age, whose meat would not be allowed into the food chain under the Over Thirty Month rule. The committee recommended that a joint FSA/SEAC Working Group should be convened to monitor the progress of the research, advise on research approaches, evaluate the diagnostic methods developed and assess the robustness of the analytical results. The membership and terms of reference of the Group are given in Annex 3.
10. The research has recently been completed and the raw data evaluated by the joint FSA/SEAC Working Group. A prepublication paper reporting the methods used and the findings in full is at Annex 4. Please note Annex 4 has not been circulated outside of the committee. This is at the authors' request as the report contains new scientific data that have not yet been published in a scientific journal. As premature release of unpublished data may prejudice publication, the report has not been released more widely in hard copy prior to publication (this is in accordance with SEAC's code of practice). However, the authors are content for the committee to discuss the report in the public meeting.
11. A summary of the research is provided below.

Production of milk samples

12. Milk samples were collected from two groups of cattle orally challenged with bovine brain (1 or 100g BSE infected brain) at 4 - 6 months of age and an unchallenged control group (n=10 in each group). The animals first calved at around two years of age. Milk was collected during weeks 1 (containing colostrum), 10, 20, 30, and where possible 40 post-parturition for up to four lactation periods. The milk was centrifuged to produce cellular and non-cellular fractions and stored frozen.

Development of analytical tests

13. A screening test was developed using the commercially available BioRad Platelia ELISA test approved by the EU for analysis of bovine brain tissue. It is a sandwich ELISA incorporating two compatible anti-PrP antibodies. A confirmatory test based on different analytical principles to the screening test, was also developed. The confirmatory test incorporates selective binding of TSE infection-associated PrP to a resin (SEPRION a commercially available polymeric ligand that selectively binds abnormal PrP) followed by gel electrophoresis and Western blot analysis of the fraction once eluted from the resin.
14. The sensitivity of the adapted BioRad Platelia ELISA test is estimated to be 0.14 Cattle Oral (CO) LD₅₀/litre and that for the SEPRION-PAGE/Western blot test, 0.05 CO LD₅₀/litre.

Analytical procedure and results

15. The cellular fractions were analysed initially using the adapted BioRad Platelia ELISA screening test. Those samples found to be greater than 3 standard deviations (SD) from the mean of the negative control samples were defined as “reactive” and were reanalysed using by the same method, but surrounded by different control samples. As the data were markedly skewed a SD was estimated by a Median Absolute Deviation (MAD) analysis to identify the final “test-reactive” samples, all of which were then subjected to confirmatory analysis using the SEPRION – PAGE/Western blot test.
16. Twenty-eight milk samples (out of a total of 541 individual samples tested) were determined as “final test reactive” using the adapted BioRad Platelia ELISA test. Confirmatory analysis of these samples using the SEPRION-PAGE/ Western blot test resulted in 12 samples, all of which were colostrum samples

collected within one week of calving and represented in all of the challenge groups, which contained positive staining bands in the Western blot. Importantly, however, these bands were also present when the analyses were repeated omitting the prion-specific monoclonal antibody (6H4), indicating that they represented non-PrP specific staining material.

17. The data generated in this study do not provide any evidence for the presence of the abnormal BSE-infection associated prion in the milk from cattle incubating BSE at levels defined by the limits of sensitivity of the two analytical methods used.

ADVICE SOUGHT FROM THE COMMITTEE

The committee is requested:

- To note the research undertaken
- To note that the study has been unable to detect the presence of the BSE prion in the milk of infected cattle.
- To provide comment on the significance of the results in relation to this and previous studies conducted on the possibility that the BSE prion might be present in the milk of dairy cows infected with BSE.
- To note that, as a consequence of the results obtained from this study, the FSA has decided to terminate further work. It has done so taking into account that the indicative picture is one of not having demonstrated the presence of abnormal prion in milk, and because the further expenditure required would be disproportionate to the perceived risk to public health.

Annex 1

Statement- 29th July 1996 Maternal transmission of BSE

The Spongiform Encephalopathy Advisory Committee (SEAC) considered at its meeting on the 19 July 1996 an interim report on a study conducted by the Epidemiology Department, Central Veterinary Laboratory, Weybridge to investigate the possibility of cow to calf transmission of BSE. The study involved assembling two groups of animals with over 300 cattle in each. One group consisted of offspring of confirmed cases of BSE whilst the other group comprised animals born in the same herd and in the same calving season whose dam had reached at least 6 years of age without developing clinical signs of BSE. The animals in the two groups were kept until the age of 7 or until BSE or another disease intervened. BSE occurred in both groups as the cattle were born around the time of the ruminant feed ban in 1988 and the cattle, or at least some of them, in both groups would have been exposed to infected feed.

As at the 14 July 1996, 273 animals in each group had reached the age of 7 and had been slaughtered or had developed disease. 55 animals are still alive and histological results are pending for 8 animals. Of the 273 animals born to dams with BSE, 42 have developed histologically confirmed BSE. In the 273 animals born to mothers who had not developed BSE 13 were histologically confirmed as having BSE. This provides evidence that the risk of maternal transmission is approximately 10% for the BSE infected cows whose calves were studied. The statistical confidence limits for that figure are 5-15%, this range being a reflection of the numbers of animals in the study and of the numbers developing BSE. It is highly unlikely that the results from the histological examination of the brains of the 63 remaining animals will materially alter these findings.

An analysis has been made of the interval between the birth of the animals in the study and the onset of clinical BSE in their mothers. All of the calves in the study were born within 13 months of the clinical onset of BSE in their dams, and the great majority were born within 5 months of clinical onset. Thus the study does not provide a good estimate of the risk to animals born more than 6 months before the onset of BSE in the dam. However, the findings provide some, albeit limited, evidence that there is an enhanced risk of maternal transmission in the last 6 months of the BSE incubation period. It is plausible that the risk of maternal transmission reduces markedly as the interval between the birth of the calf and the onset of BSE in the dam increases. Therefore, the risk of maternal transmission observed under the study conditions is likely to be greater than would be expected for the entire population of cows.

Under field conditions, only a fraction of the BSE-infected cows giving birth would be within 6 months of demonstrating clinical signs of BSE because of the long incubation period of the disease. The average incubation period is 60 months and, if the rate of cow to calf transmission over the last 6 months of the incubation is 10% and it is insignificant before that time, then the average transmission from cow to calf over the 60 months duration of infection in an animal prior to developing clinical disease will be 1%. This would be the rate of maternal transmission that would be observed under field conditions.

Maternal transmission at the rates observed in husbandry conditions of the UK dairy herd will not lead to the permanent establishment of BSE even at a low incidence in the UK herd. It will die out, as it already clearly is doing, as a consequence of the restrictions on the primary mode of transmission through infected feed. The study itself provides no new evidence in relation to horizontal transmission. Since the meeting of SEAC on 19 July the Epidemiology Department at CVL has examined the data from this study and that pertaining to the herds from which study animals were taken and has found no evidence of horizontal transmission.

The study tells us nothing about the route of maternal transmission, which could be in utero, at birth or soon after birth. In sheep scrapie where there is also evidence of maternal transmission, infectivity can be detected in the placenta. Furthermore in sheep scrapie there is evidence of in utero transmission from an experiment where the embryo from a scrapie infected sheep was transplanted into a healthy ewe and when that ewe gave birth the lamb eventually went on to develop scrapie. Similar embryo transfer experiments are underway in cattle but results are not yet available. Infectivity has however not been detected in the bovine placenta or in milk, or in blood (see Note 1).

The Committee considered whether evidence of maternal transmission calls into question the existing recommendations to protect public health. These were drawn up on the assumption that BSE could be a risk to man, which is still not proven, and on the assumption that maternal transmission could occur. The Committee have concluded that there is no case for changing its recommendations (see Note 2) in relation to milk, meat, blood or any other product which is currently permitted.

There is no evidence from any of the transmissible spongiform encephalopathies that infectivity can be transmitted through milk. In commercial dairy herds where the bulk of BSE cases arise calves do not receive their mothers milk except for the first few days of life when they receive the special milk produced at that time called colostrum.

Colostrum is different in nature from ordinary milk and is not sold for human consumption. In the beef suckler herds it is common practice for calves to be suckled by their mothers for up to six months. Existing data do not provide evidence to suggest that the rate of maternal transmission in beef suckler calves who have prolonged exposure to their mother's milk is any different to that in dairy herds where the only exposure would be to colostrum in the first few days of life. The Committee was pleased to note that the Epidemiology Department at CVL is undertaking further detailed studies on this point, and that the results of these studies will be available very soon.

The Committee recognise the role of the ACDP and the HSE in relation to the occupational risks. The Committee draws the attention of those bodies to these new findings but does not make any recommendations for further action other than that the two bodies should consider the evidence and any implications for occupational health.

The Committee considered the position in relation to the measures to eradicate BSE, particularly in relation to any selective cull implemented by Government. It is clear from the new information that maternal transmission will not perpetuate the disease and that BSE will therefore die out even in the absence of any form of selective cull. The Committee were made aware that preliminary analyses of the effect of these new results on a culling policy had been undertaken but that these were as yet incomplete. Nevertheless the Committee recommends that the results of the completed analyses be taken into account before final decisions are made about the policy for a selective cull.

Finally, the Committee considered what further research might be of high priority in the light of the results of this study and the matter will be the subject of a separate report.

Note 1. Data from standard transmission experiments following parenteral inoculation into mice. Details are given in Table 7 of the latest *MAFF Progress Report on BSE*, published in June 1996.

Note 2. In its statement of 20 March about the new variant of CJD the SEAC said:

"The Committee does not consider that these findings lead it to revise its advice on the safety of milk."
"If the recommendations set out above [i.e., for the proper enforcement of SBO controls on the deboning of cattle over 30 months] are carried out the Committee concluded that the risk from eating beef is now likely to be extremely small."

Annex 2

Statement – 16th April 1997

On 29 July 1996, the Spongiform Encephalopathy Advisory Committee (SEAC) issued a statement on maternal transmission of BSE following its consideration of an interim report on a study conducted by the Epidemiology Department, Central Veterinary Laboratory, Weybridge to investigate the occurrence and incidence of dam to calf transmission of BSE (the cohort study).

SEAC established an Epidemiology Subcommittee to consider the final results from the cohort study. The Subcommittee was chaired by Professor Peter Smith (London School of Hygiene and Tropical Medicine), a member of SEAC. It included two further members of SEAC, Dr Richard H Kimberlin (SARDAS) and Professor Will Hueston (University of Maryland). The Subcommittee also included Professor Roy Anderson (Oxford University), Professor Robert Curnow (Reading University), Dr Peter Goodfellow (SmithKline Beecham Pharmaceuticals), Professor Dr. Ir. Aalt Dijkhuizen (Wageningen Agricultural University, the Netherlands) Professor Nicholas Day (Medical Research Council Biostatistics Unit), Dr John Williams (Roslin Institute), Dr Rosalind Ridley (Cambridge University) and Mr John Wilesmith (Central Veterinary Laboratory). The Subcommittee was assisted by Dr Sheila Gore (Medical Research Council Biostatistics Unit), Dr Neil Ferguson (Oxford University), Dr Christl Donnelly (Oxford University), Dr John Woolliams (Roslin Institute), and Ms Judith Ryan (Central Veterinary Laboratory). The Subcommittee met on four occasions, and submitted its final report on maternal transmission of BSE to SEAC on 11 April 1997.

At its meeting on 15 April 1997, SEAC considered and accepted in full the report from the Epidemiology Subcommittee.

SEAC noted that the results of the cohort study were not inconsistent with those of the case control study published in 1995 by Hoinville and others of the Epidemiology Department, CVL. That study, which involved cases of BSE born after the ruminant feed ban, did not identify significant evidence of maternal transmission, but the statistical confidence interval included a risk of up to 13 per cent (Veterinary Record (1995) 136, 312-318).

The cohort study provides no information on the mechanism of direct maternal transmission of BSE. We recommend that further research should be undertaken to shed light on the mechanism. Some research has already been carried out into potential routes of transmission from dam to calf, by testing the infectivity of tissues from BSE-affected animals, including placenta, embryos, blood and milk: no evidence of

infectivity has been found. However, given that the rate of transmission is probably low, some of these negative results may be due to the practical difficulties of detecting low levels, or a low prevalence, of infectivity. SEAC recognises that a low level of transmission would make research on mechanisms difficult, and that it would be complemented by a better understanding of the mechanisms of scrapie transmission in sheep.

Any cull based upon the slaughter of calves born to cows in which BSE has been confirmed will have only a small effect on the incidence of BSE and the duration of the epidemic. Nevertheless, Government should consider the possibilities for such a cull, and its effects.

SEAC noted that, in its statement of 29 July 1996, it had concluded that the evidence on maternal transmission did not call into question existing measures to protect public health. In the light of the Subcommittee's report, SEAC reconsidered the existing measures.

With respect to consumption of bovine products the measures currently in place to protect the consumer are considered appropriate. In particular, the Committee considered the possibility of milk being a vehicle of transmission. SEAC concludes that no evidence has been found to suggest that milk from any species affected by transmissible spongiform encephalopathies is infectious. This concurs with the opinion of the Scientific Veterinary Committee, which advises the European Commission.

With respect to occupational exposure, responsibility for assessing whether any amendments are needed to the existing Health and Safety Executive guidance rests with the Advisory Committee on Dangerous Pathogens.

Epidemiology Subcommittee statement to SEAC on maternal transmission of 11 April 1997

In July 1996 SEAC issued a statement on maternal transmission of BSE following an interim analysis of data from an ongoing study (called the "cohort study") being conducted by the Epidemiology Department, Central Veterinary Laboratory (CVL). The study was intended to determine whether maternal transmission occurred, and if so, to inform policy makers with respect to animal health implications.

The study involved over 300 "matched-pairs" of calves. One calf in each pair was the offspring of a confirmed case of BSE and the other an animal born in the same herd in the same calving season whose dam had reached the age of 6 years without developing clinical signs of BSE. The two groups of animals were born between August 1987 and

November 1989, and were taken from their natal herds between July 1989 and February 1990, aged between 2 and 24 months. They were kept on one of three experimental farms until they reached the age of 7 years or were culled at an earlier age with BSE or another disease. All animals surviving to the age of 7 years were then slaughtered and their brains were examined pathologically for evidence of BSE.

The preliminary results of the study, when most but not all of the animals had been followed to the age of 7 years, suggested that the offspring of BSE cases had an incidence of BSE that was about 10% greater than that of control animals, with statistical confidence limits (95%) ranging from 5-15%, the range reflecting the limited numbers of animals that developed BSE in the study.

By November 1996 the last of the animals in the study had reached the age of 7 years, and by January 1997 the last of their brains had been examined. As had been anticipated, the final results were not markedly different from those on which the interim analysis had been based in 1996. Of the 301 offspring of BSE cases, 42 (14.0%) developed BSE. Among the 301 offspring of the "control" dams without BSE, 13 (4.3%) developed BSE. The difference between the two risks was thus 9.6%, and was highly statistically significant with a confidence interval ranging from 5.1% to 14.2%. A paper giving the results of the study will be published shortly in the *Veterinary Record* by the Epidemiology Department of CVL.

The cohort study was set up to investigate the occurrence of maternal transmission, but interpretation of the results was confounded by the likely exposure of some of the experimental animals to contaminated feed. The results could be explained by two hypotheses, acting alone or in combination, namely direct maternal transmission of infection or inherited genetic variation in susceptibility to BSE via contaminated feed. Although most of the animals involved in the study had been born after the ruminant feed ban in July 1988, feed-borne transmission is thought to have continued beyond that date. This is consistent with the observation that the BSE risk in both of the groups was greater among animals born before the introduction of the feed ban than among animals born later. However, the difference in risk between the two groups was also greater in those born earlier, and this would not be expected if direct maternal transmission was the sole route of infection of the calves in the study. Such an effect might be apparent if cattle vary in their susceptibility to contracting BSE from infected feed. It is possible that the offspring of BSE cases may inherit, from their dams, genes associated with increased susceptibility to disease and that at least some of the difference in BSE risk between the offspring of BSE affected and non-affected dams in the study may be due to inherited

factors, rather than because of direct transmission of BSE from dam to calf.

The Subcommittee has reviewed the evidence for variation in genetic susceptibility to BSE in cattle. There is variation in the risk of TSEs according to genotype in some species. For example, polymorphisms of the PrP gene are associated with substantial variation in susceptibility to infection with the scrapie (and in incubation period) in sheep and mice and with differences in risk of CJD in humans. The Subcommittee notes, however, that the limited research so far completed has failed to identify genetic factors as a major component in the epidemiology of BSE.

To assist the CVL Epidemiology Department in the interpretation of the results of the cohort study, independent analyses of the data were conducted by three additional groups with expertise in statistical analysis (based in the Wellcome Trust Centre for the Epidemiology of Infectious Disease, University of Oxford; the MRC Biostatistics Unit, Cambridge; and the Department of Applied Statistics, University of Reading). In so far as was possible, they tried to evaluate the contributions to the risk difference between the animals in the two groups from inherited differences in susceptibility to disease caused by infected feed and from direct transmission of BSE from dam to calf. In the absence of detailed information on the genetic make up of the animals in the study, the possible genetic contribution could only be assessed by statistical modelling.

The analyses by the three groups have been submitted for publication later this year. These analyses reached broadly the same conclusions. That there was a highly significant difference in risk between the two groups of animals was clear. The findings did not definitively establish direct maternal transmission as the sole explanation for the difference in risk. The statistical model which fitted the data best involved contributions from both direct maternal transmission and inherited susceptibility. The main evidence for direct maternal transmission is that the risk of BSE in the calf of an affected dam was greatest for calves born close to the onset of BSE in the dam. However, the power of the study to detect differences related to the time between BSE onset and the date of birth of a calf was limited by the design of the study which resulted in 83.4% of the calves being born within the six months prior to onset of clinical disease in the dam.

Further investigation was necessary of the possible variation in the risk of BSE associated with the time between the birth of an animal and the onset of BSE in the dam. This was undertaken mainly by the group from the Wellcome Centre for the Epidemiology of Infectious Diseases,

University of Oxford through analyses of data on all cases of BSE born after the ruminant feed ban, which are recorded on the BSE database held by the Epidemiology Department at the CVL. The findings will be submitted for publication shortly. Evidence was found that the subsequent BSE-risk was greatest in calves born after the date of BSE onset in the dam. For calves born before onset, the risk was lower, and diminished as the interval between birth and onset increased, and no risk was apparent more than two years before onset (see next paragraph). Thus, although possibly subject to some biases, these analyses also suggested that enhanced BSE-risk in the offspring of BSE dams involves a low level of direct maternal transmission in the late stages of the incubation period.

In view of the findings of the analyses that are summarised above, the Subcommittee concludes that there is some evidence for direct maternal transmission of BSE at a low level, but some variation in genetic susceptibility to BSE following feed-borne exposure may occur. The risk of transmission of BSE from dam to calf is likely to be less than 10%, and appears to be confined to animals born after the onset of BSE in the dam or up to two years beforehand. This level of transmission is not sufficient, by itself, to perpetuate BSE in the cattle population and is likely to have only a minor effect on the rate at which the incidence of BSE declines. It is inevitable that cases infected via animal feed will continue to appear in diminishing numbers for several years. Therefore, although the number of cases infected maternally will be small, they may represent an increasing proportion of the remaining cases detected.

Given the evidence that variation in genetic susceptibility may have contributed to the results of the cohort study, and of the importance of genetic factors in TSEs in other species, the Subcommittee considers that further research is necessary to clarify whether or not variations in the PrP gene or other genes may be influencing the transmission of, or susceptibility to, BSE in cattle. Research should seek to identify polymorphisms of the PrP gene which may be associated with BSE susceptibility, including stored samples from the cohort study. There should also be a search [AVMC1] for other genetic markers, outside the PrP gene, which may be associated with an increased BSE risk in cattle.

Annex 3

Membership and Terms of Reference of the FSA/SEAC Milk Working Group

Milk Working Group Members

Prof Chris Bostock (Chairman)
Prof Simon Cousens
Dr Julian Duncan

VLA

Dr Roy Jackman
Sally Everest
Dr Jim Hope
John Kilpatrick

FSA

Alan Harvey
Dr Steve Dixon
Dr Irene Hill
Dr Trudy Netherwood
Dr Angela Clark

SEAC Secretariat

Dr Tom Barlow

Terms of reference

The purpose of the Working Group is to provide advice to SEAC and the FSA on the validity and quality of the results generated by the project (MO3016: Determination of abnormal prion protein in milk of cattle infected with the BSE agent). Although the project was subjected to independent peer review prior to commissioning, the Working Group is invited to provide comment on experimental approaches.

The Working group is asked:

- a) To evaluate the independent report of the audit of the sample collection, processing, transport/storage and analysis trail.
- b) To evaluate the validity of the analytical methods developed for the analysis of milk samples for the presence of the BSE prion.
- c) To evaluate the independent report on the validation data for the methods of analysis.
- d) To recommend whether milk sampling audit trial and methods of analysis validation data are sufficiently robust to allow the analysis of the experimental milk samples to proceed.

e) To evaluate the analytical data obtained on the experimental milk samples and comment on the significance of the results.

f) To provide comment on the experimental approaches and advise on any additional work that may be required.