



## INDEPENDENT REVIEW OF THE ORIGIN OF BARB CASES

### ISSUE

1. In November 2004, Defra appointed Professor William Hill, (Emeritus Professor, Institute of Evolutionary Biology, School of Biological Sciences, University of Edinburgh) to carry out an independent review of its work on BSE cases Born After the Reinforced Ban in 1 August 1996 in the UK (known as BARB cases).
2. As part of his review Professor Hill has requested the opportunity to seek comments from SEAC on BARB cases and the key issues he should address in his report. This paper provides background information to, and summarises SEAC's previous consideration of, BARB cases. Questions that Professor Hill would like the committee to consider are given at the end of the paper.

### BACKGROUND

#### BARB cases

3. On 31 July 1996, additional BSE control measures to restrict the recycling of animal protein in animal feed were introduced to include a total ban on the sale or supply of any mammalian meat and bone meal (MMBM) or any feedstuff known to include MMBM. Following a recall scheme for feed containing MMBM, it also became an offence from 1 August 1996 to possess feed for farmed livestock containing MMBM. Despite these control measures, as of 26 January 2005 there have been 93 cases of BSE detected in cattle born after the reinforced ban.

## Previous SEAC consideration of BARB cases

4. In 2003, SEAC considered data on BARB cases as well as the possible causes/origins of BARB cases including:
  - Residual cross contamination of feed as a source of infection,
  - A maternally associated risk factor for infection,
  - Other sources of infection, e.g. scrapie agents,
  - Non-feed routes of transmission e.g. via contaminated soil or water,
  - Infection associated with an enhanced genetic susceptibility to low levels of exposure to the infectious agent,
  - A spontaneous occurrence of BSE in cattle,
  - Horizontal transmission occurring from unidentified carriers.
5. On the evidence presented, SEAC agreed that residual feed contamination with the BSE agent seemed to be the most plausible explanation for BARB cases. It was noted that this contamination might be due to the use of imported feed materials from EU countries that had not implemented feed controls similar to those in the UK, until 2001<sup>1</sup>. However, the committee considered that other possible routes of transmission such as maternal or environmental transmission could not be excluded as being possible origins of at least some of the cases. The committee suggested a number of areas of research including genotyping, biochemical and strain typing studies of BARB cases. In addition, a SEAC *ad hoc* Epidemiology subgroup on UK BARB cases was convened to advise on the design of a case-control study to examine hypotheses for the source of infection in BARB cases to be conducted by Professor John Wilesmith (Defra) (membership and terms of reference of the group is given at Annex 1).
6. The *ad hoc* Epidemiology subgroup met in March 2004 to review proposals for the case-control study on BARB cases. The group agreed to a three-stage, sequential approach to the design of the study. The first and second stages would identify factors that could be used to define the criteria for entry into the study for cases and controls. Stage 3 would be a case-control study utilising the results collected in the first two stages.

---

<sup>1</sup> The European Union's Scientific Steering Committee (SSC) came to a similar conclusion in an opinion published in 2003: [http://europa.eu.int/comm/food/fs/sc/ssc/out353\\_en.pdf](http://europa.eu.int/comm/food/fs/sc/ssc/out353_en.pdf)

7. A second meeting of the *ad hoc* Epidemiology subgroup is scheduled for early April 2005 to discuss the results of the first and second stages and the design of stage three. SEAC will receive a report on the outcome of the *ad hoc* subgroup's consideration at its meeting in April 2005.

### The Hill Review

8. In November 2004, Defra commissioned Professor William Hill to examine the BARB studies currently taking place (see Annex 2). As part of the review Professor Hill has requested the opportunity for SEAC to comment on BARB cases and he will also attend the *ad hoc* Epidemiology subgroup as an observer.

### **ADVICE SOUGHT FROM THE COMMITTEE**

Professor Hill would welcome comments from members on any particular issues they think he should address now or in the near future, including the following:

- BARBs show similar epidemiological and neurological features to earlier BSE cases, but with no strong geographically biased distribution (e.g. to East Anglia). How does that conform with the most likely hypothesis that BARB cases are caused by ingestion of contaminated feed, either an exogenous source or perhaps long stored?
- Spontaneous cases: As a baseline to assess any incidence of spontaneous disease of endogenous origin, how reliable are levels of BSE incidence reported from testing in countries that are purportedly free of the disease or have it at very low levels?
- Ingestion of BSE contaminated feed was clearly the primary transmission route for BSE, possibly with additional low-level maternal-associated transmission. Many alternative hypotheses (e.g. medicines, non BSE feed contamination) have been propounded, together with environmental contamination with BSE material. Could any be a plausible or contributory cause of the relatively few BARBs cases?

**MEMBERSHIP AND TERMS OF REFERENCE OF  
AD HOC EPIDEMIOLOGY SUBGROUP ON UK BARB CASES**

**Members**

Professor N. Gill (Chair), *Health Protection Agency*

Professor P. Smith, *London School of Hygiene and Tropical Medicine*

Professor S. Cousens, *London School of Hygiene and Tropical Medicine*

Professor J. Wilesmith, *Defra*

Dr P. Farrington, *The Open University*

Professor V. Beral, *Cancer Research UK*

Professor N. Day, *Cambridge University*

Dr G. Medley (SEAC Member), *University of Warwick*

Mr P. Jinman (SEAC Member), *Private Veterinary Surgeon*

**Terms of Reference**

To provide scientifically based advice on the design of an epidemiological study to examine and distinguish the various hypotheses for the source of infection of BSE in BARB cattle in the UK.

To advise on the type of statistical analysis of the surveillance data, collected half-yearly by the State Veterinary Service.

To recommend and prioritise further work that should be undertaken to help resolve outstanding epidemiological issues identified by the expert group.

## ANNEX 2

### DEFRA PRESS RELEASE ANNOUNCING HILL REVIEW

#### **INDEPENDENT EXPERT TO REVIEW DEFRA'S WORK ON BSE CASES BORN SINCE 1 AUGUST 1996 IN THE UK**

Professor William Hill FRS, Emeritus Professor at the Institute of Evolutionary Biology, School of Biological Sciences of the University of Edinburgh has been appointed by Defra to carry out an independent review of their work on BSE cases born since 1 August 1996 in the UK.

The Chief Veterinary Officer, Debby Reynolds said, "I am delighted that Professor Hill has agreed to undertake this review for us. There has been enormous progress in reducing the number of cattle infected with BSE in the UK since the first case was found in 1986. Much of this can be attributed to the controls that were put in place to prevent the spread of the disease in meat and bone meal, an ingredient that was used extensively in animal feed prior to 1988. These controls have gradually been tightened over ensuing years and in the UK particularly so since 1 August 1996.

Despite this we have had 99 cases of BSE born since 1 August 1996. The current advice, which has been considered by both SEAC and a European scientific advisory committee, is that feed contamination still remains the most plausible explanation, as the feed controls in some parts of Europe were not introduced until 2001. We have work in place to test this theory. However, there are also other possible explanations for at least some of these cases. We want to eradicate this disease and it is important for us to be sure that we are not overlooking any important factors and that the work we are doing is comprehensive and scientifically sound.

We have therefore invited Professor Hill to take a look at what we are doing. We have deliberately chosen someone who is eminent in his own field but who has not been involved in TSE work before. He can be expected to probe and challenge the evidence. If we can meet this challenge it will give us reassurance that we have not overlooked anything that might prevent us from getting rid of the disease by the end of 2010. If we have overlooked something it will give us time to put in place some additional studies.

I have asked Professor Hill to report his findings to me within the next six months and I will ask SEAC to consider these."

23 November 2004

---

Notes for editors

1. Professor William Hill OBE, BSc, MSc, PhD, DSc, FRSE, FRS is Emeritus Professor of Animal Genetics at the School of Biological sciences of the University of Edinburgh. His group undertakes theoretical and experimental studies on population and quantitative genetics and on their application to animal improvement. Professor Hill was formerly Dean and Provost of the Faculty of Science and Engineering at the University of Edinburgh, he has consulted extensively in the UK animal breeding industry and chaired Defra's National Consultative Committee on Animal Genetic Resources. He is also an editor of Genetical Research and senior editor designate of Proceedings of the Royal Society, Series B.

2. The hypothesis that cases born after the reinforced feed ban (BARBs) are due to an exogenous feed source arising from the perfectly legal handling and shipment of meat and bone meal in European ports up to January 2001 comes from John Wilesmith following a detailed analysis of epidemiological data on the first 59 cases. This analysis has been considered by the EU's Scientific Steering Committee and more recently by EFSA.

3. A SEAC ad-hoc group is overseeing a case control study the primary objective of which is to test this hypothesis. In addition Defra is funding work to investigate the genetic homogeneity of the PrP gene in BARB cases. Professor Hill will consider all of this work as part of his remit.

4. Further details of the legislation in place relating to feed controls and information on BARB cases can be found on the Defra website at [www.defra.gov.uk/animalh/bse/controls-eradication/feed-ban.html](http://www.defra.gov.uk/animalh/bse/controls-eradication/feed-ban.html).

---