

**RESPONSE TO THE UKAS AND RISK SOLUTIONS AUDIT REPORTS**  
**BY THE INSTITUTE FOR ANIMAL HEALTH**

**RESPONSE TO THE UKAS REPORT  
FROM THE  
INSTITUTE FOR ANIMAL HEALTH**

The Institute for Animal Health (IAH) welcomes the publication of the UKAS Report as part of the process of informing the public of the events that surrounded and followed the DEFRA press release of 17 October 2001. The Institute is disappointed that the final Report has not been corrected for factual errors identified by the IAH and does not reach informative conclusions or provide suggestions for any next steps to resolve unanswered questions.

**Formal Documented Systems**

The Institute will consider the Report's findings within the context of the existing high standards across a broad range of procedures in place at its Edinburgh Laboratory (IAH-E) and the standards adopted by other internationally recognised research laboratories throughout the UK. The Institute has in place comprehensive and documented formal procedures, which are continuously monitored, to comply with the demanding statutory requirements set by the Health and Safety Executive, the Home Office and the Department for the Environment, Food and Rural Affairs. The auditors chose not to visit the facilities and examine the records that would have provided evidence of these.

**The Institute would challenge, therefore, the accuracy of the Report's finding that there was "no formal documented quality system covering this work".**

**Relevance of ISO/IEC 17025 Standard**

The Report focusses heavily on a comparison of quality assurance standard ISO/IEC 17025 to IAH practices. IAH find this approach puzzling and unhelpful.

This standard was not in place at the time of the key events and IAH can find no evidence that it is used as a benchmark system for UK research establishments.

The quality assurance standard ISO/IEC 17025 is used for accreditation of testing and calibration laboratories. The IAH is familiar with this and other similar international standards and works to these for its own diagnostic and clinical trial work. Some of the principles and elements of schemes such as ISO/IEC 17025 may be helpful in guiding standards in research laboratories such as IAH.

**However, the Institute does not believe that ISO/IEC 17025 as a whole is an appropriate standard for academic research laboratories.**

### **Limitations of Audit**

The IAH notes that the Report is based on a severely time-limited visit to IAH-E which resulted in:

- No planning or briefing meeting(s) with IAH
- No interviews with the key staff in post at the time when most of the experimental work was conducted
- No inspection of key systems upon which the Report comments.

The UKAS audit focussed on samples produced for two experimental protocols, designed in 1990, to investigate the efficacy of rendering procedures. The UKAS auditors also looked at the use of these samples in a further protocol, which started in 1997, to ask questions about the possible selection of BSE-like strains in meat and bone meal produced by rendering processes. It was this latter experiment, which, upon extension in October 2000, had the amended MAFF policy objective to address the question “is there BSE in a pool of TSE infected sheep brains?”.

The samples that were audited had been derived from BSE-affected cattle brains and scrapie-affected sheep brains, collected in Veterinary Investigation Centres (VIC) between 1990 and 1992. These brains had then been processed, labelled, stored frozen at and despatched to IAH-E from Prosper de Mulder's (PdM) pilot rendering plant at Doncaster. Records of the samples and protocols used prior to receipt of the samples by IAH-E were made and held by these organisations, but, as far as the IAH is aware, few, if any, of these records have been retained. From the time of receipt of these samples at IAH-E specific records pertaining to their use at the IAH-E continue up to the time that samples were sent for analysis to the Laboratory of the Government Chemist (LGC) on 11 September 2001.

At the time that the rendering experiments were initiated, virtually all research at the IAH-E was performed on experimental material generated by the Institute and covered by the comprehensive sample management systems that were, and continue to be, in place at IAH-E. The rendering experiments produced new and unique sets of externally provided materials that had to be fitted into these systems. In focussing solely on, and generalising from, these experiments the UKAS auditors received a restricted and unrepresentative view of the procedures in use at that time and today. The auditors did not visit IAH-E's animal facilities where most of the documented records and standard experimental protocols pertaining to the samples in question are held and were available for inspection. Nor did the UKAS auditors visit the IAH's Compton Laboratory (IAH-C) where much of the experimental work on the rendering studies was carried out and, importantly, where several of the relevant samples are still stored in freezers.

**The Institute is concerned, therefore, that the authors of this UKAS report may have based their findings on an unrepresentative and limited examination of procedures in place at IAH-E.**

## **RESPONSE TO THE RISK SOLUTIONS AUDIT REPORT**

### **BY THE INSTITUTE FOR ANIMAL HEALTH**

The Institute for Animal Health (IAH) welcomes the Risk Solutions Report which comprehensively documents the extensive, complex and inter-related nature of the work on the pool of scrapie affected sheep brains over the last decade and provides a detailed record of the samples held at the IAH. The IAH appreciates having the opportunity to respond to this helpful Report, but notes that the Institute's response was required to be prepared within 24 hours of receipt of a draft report which the IAH was told was not absolutely final. The IAH's comments must, therefore, be read with this in mind.

#### **Apparent Substitution**

The Report correctly notes that a proposed apparent substitution could have occurred at any point between the collection of the sheep brains at the Veterinary Investigation Centres (VIC), the processing of the samples at Prosper de Mulder's (PdM) pilot rendering plant, the various experimental uses at the IAH and the speciation tests at the Laboratory of the Government Chemist (LGC). However, the Report overwhelmingly focusses on the procedures and samples at the IAH and, disappointingly, does not extend and complete this useful record of the experiments by examining and documenting in any detail the time-lines, sample management, handling and storage arrangements at the VICs, PdM and LGC. Some of these issues are considered in Section 3.2.2 of the Report, but the auditors appear unable to present details verified by examination of any documents, presumably because, as the Report notes, all records at the VICs and PdM have been destroyed.

#### **Terms of Reference**

As the title "An Investigation of the Substitution of Scrapie Brain Pool Samples" clearly indicates, the scope of the Risk Solutions audit was tightly constrained by

the Terms of Reference (TOR). These start from the premise that a substitution occurred and therefore the Report necessarily sets out with the assumption that a substitution did occur. The IAH considers that it is unfortunate that the TOR did not include the consideration of the real possibility of contamination or limitations to the DNA-based tests. The Report indicates that “contamination can not be completely ruled out” , but does not extend the scope of the study to consider it, nor does it look at contamination scenarios. Reflecting the starting assumption of the TOR, the Report concludes that one “can not say with certainty the point at which the substitution occurred”, but the IAH consider that it would be more correct to say that one can not say with certainty that **any** substitution occurred.

### **Scope of the Audit**

In considering the options for substitution the Report suggests that the audit examined all possible scenarios, not just those within the IAH. The Report records that personnel at PdM and the State Veterinary Service (SVS) were interviewed, but, as noted above, there is little detailed evidence presented in the Report about samples and processes in any organisation other than IAH on which to judge the likelihoods of the scenarios presented. It is, therefore, difficult to assess the strengths of the conclusions about some of the scenarios set out in the Report. Nevertheless, the IAH notes that, using their scenarios, the Risk Solution auditors have identified key samples, which could be tested to help resolve ambiguities as to the identity of their contents. These coincide with the samples identified for further testing by the IAH’s independent audit.

### **DNA Tests**

The IAH commend the Risk Solutions auditors for raising openly the dilemma posed by the apparent contradiction between the results of the limited PrP genotype test conducted by IAH in 1997 and those of the DNA speciation test conducted by LGC in 2001. The IAH agree with the Risk Solutions conclusion that “It is difficult to find any substitution scenario that is consistent both with

the test results and what we can conclude about the care taken in handling, storage and labelling of the materials at each point in the experiment.”

Unconstrained by the TOR’s assumption that a substitution happened an observer might be open to an explanation based on potential limitations of the tests themselves considering the highly degraded nature of the material being analysed. For example, one scenario that could be considered, which is consistent with all of the data gathered by this audit, is that the sample is substantially ovine (as was thought by the IAH scientists and was indicated by the 1997 genotype test) but was contaminated, perhaps significantly, by bovine material (about which the IAH scientists have always been concerned and which the LGC DNA speciation test confirms).

### **The Problem of Sample Degradation**

It is important that the LGC do not conclude that their results prove that there is no ovine DNA in the sheep brain pool samples, but, correctly, that the tests they used were unable to detect any ovine material. All parties agree that the material in the sheep brain pool samples is highly degraded, although there is some debate as to the extent, and, therefore, consequences of this degradation. The IAH consider it likely that, after denaturation to produce the single stranded DNA template required for any PCR based test, less than 10 percent of the DNA would be large enough to be detected by the methods used. It may, therefore, be premature to conclude that there is no ovine DNA in the sheep brain pool samples, especially if for some unknown reason the putative sheep DNA in these samples degraded more extensively than the putative cattle DNA.

Thus, the IAH agree with the Risk Solutions’ recognition that “both or one of the genotype tests are in error in some way”, although the IAH would add the important caveat that the tests themselves may not be “in error”, but that the “error” may lie in the failure to fully recognise the potential limitations of one or

other or both of the tests applied. The IAH would also agree that, in order to reduce the uncertainty surrounding this and other issues raised by the audit, relevant samples would require analytical testing. The IAH subscribe to Risk Solutions' reservation that, if tests are to be conducted, they must be very carefully designed such that they ensure to the satisfaction of all parties that the results of the tests would be unambiguous and informative.

**The Risk Solutions Report suggests that it is unlikely that it will be possible to define precisely the composition of the sample of scrapie affected sheep brains. The IAH agrees with this and the conclusion that the scrapie affected brain pool should not be used to determine whether BSE was present in the UK sheep flock in the early 1990s.**