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## HOUND SURVEY NOTES OF MEETING ON 6 DECEMBER 1993 IN OLD LIBRARY CVL

1. Present: Mr K Taylor  
Dr D Matthews  
Mr R Bradley CVL  
Mr G Wells CVL  
Mr A Scott CVL  
Mr R Higgins Thirsk VIC  
Mr P Gayford

2. The meeting was called to consider how two of three options to take the hound survey forward could practically be carried out, so that when the options were put to the Tyrrell committee any likely difficulties could be highlighted.

3. To attempt transmission from three hound brains into mice.

- 3.1 The NPU Edinburgh had indicated that there should be no particular problems with this. Only two strains of mice RIII and IM would be used. These strains were in fact also held at CVL and it was pointed out that CVL could do the work.

- 3.2 The NPU had been informed that the tissue might be contaminated with a protozoon possibly toxoplasma. Provided that formalin fixed tissue was used in the study this should not pose a problem.

- 3.3 Mr R J Higgins in conjunction with Mr G A Wells and Mr A C Scott would, by the end of the year, identify the three brains that were from the "positive" end of the lesion spectrum. These would need to be SAF inconclusive (fibrils observed) and histopathologically unresolved. They would also identify the best sites of the brain to sample for the survey. These would be likely to be a portion of the medulla near the obex and a portion of spinal cord. Very little (less than a gram) of tissue was required. At the same time three "negative" brains from the negative end of the lesion spectrum would also be identified. These "negative" brains would be held pending the work on the "positive" brains. The kennels from which the hound brains were derived should be geographically well separated.

- 3.4 There would be a need to warn the Tyrrell committee of some of the constraints that this exercise might impose.

- 3.4.1 There would be a species barrier. To avoid the barrier altogether it would have been preferable to have carried out the transmission work first in dogs. It was pointed out, however, that if a spongiform encephalopathy agent

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associated with BSE was present in sufficient titre one would expect that it would express itself in mice, with similar incubation periods and lesion profiles as agents causing spongiform encephalopathies in other species had done.

3.4.2 The material had not initially been taken with a transmission experiment in mind. There was an outside possibility that contamination with BSE agent could have occurred in the post mortem room at the time of removal of brain material or in the histology cabinet. Equipment would have been thoroughly disinfected before dealing with the hound brains, but not to the extent that contamination could be ruled out completely.

3.5 The fixed material from the three selected "positive" and three "negative" brains would be submitted to Pathology Department CVL for storage. It was suggested that the Tyrrell committee be asked to agree that there was no need to keep any of the other material in formalin that remained at Thirsk.

4. To create a baseline of healthy dog brains by examining a small number of young 2/3 year old dogs and middle aged 6/7 year old dogs.

4.1 For this project there was a need for the dogs to be intravenously euthanased and for the brains to be removed carefully and placed in formalin within 30 minutes of death. A portion of fresh cervical cord would also be taken for SAF examination.

4.2 Identification of suitable dogs would not be easy and the difficulties would need to be put to the Tyrrell Committee. It has been established that very long toxicological studies are not undertaken these days and almost all dogs used for "so called" long term toxicological trials are euthanased before they are two year old. Possible sources of material included:

4.2.1 A reputable laboratory had indicated that it had some formalin fixed material from the 1970s from six to eight-year-old dogs. The material had been carefully removed and placed rapidly in formalin. No frozen fresh material was available for SAF examination. The dogs had been used in drug trials that would have been unlikely to have affected the brains. If the material was to be used the two drug companies involved would need to give their agreement and, as this would be a delicate matter, it was thought that an approach to the companies would be best to be left until after the Tyrrell Committee meeting.

4.2.2 Companies involved in future toxicological studies might be approached, but as already stated the animals would be likely to be under two-years-old. SAF material may be available from these cases.

4.2.3 Two companies had been identified that bred their own dogs. Over a period of time it might be possible to obtain sufficient brains of appropriately

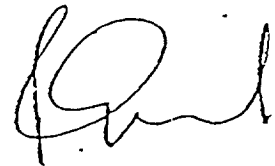
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aged animals. SAF material should be available. Such an approach carried considerable risk stimulating questions about the outcome of the original survey which would be difficult to answer at present.

4.2.4 The fourth possibility was to go back to the hound kennels that had produced "negative" brains in the survey and to organise collection of brain material which was better removed and more rapidly fixed than was possible in the survey. SAF material should also be available.

4.3 Approaches to companies or kennels in all these cases would have to be carefully handled and it was thought that, because of this, it would be best to wait until the Tyrrell Committee had made a decision on the need for the work before any approach was made. The Committee would need to be appraised of the difficulties.

4.4 The draft document that had already been prepared for the next Tyrrell Committee meeting on 26 January would be amended if necessary to take account of the views of the meeting.



10/12/93