ADVISORY COMMITTEE ON DANGEROUS PATHOGENS
TSE RISK ASSESSMENT SUBGROUP

The 5th meeting of the ACDP TSE Risk Assessment Subgroup was held on 12th July 2012 in Wellington House, Department of Health, London

Present:		
Chairman:	**Prof George Griffin**	
Members:	**Prof Jean Manson**	
	Prof James Ironside	
	Prof Malcolm Bennett	
	Dr Roland Salmon	
	Dr Simon Mead	
Invited experts:	**Prof Noel Gill**	**HPA**
	Dr Pat Hewitt	**NHSBT**
Observers and Officials:	**Dr Ailsa Wight**	**DH**
	Dr Peter Bennett	**DH**
	Mr Mark Noterman	**DH**
	Mrs Ruth Parry	**DH**
	Dr Katy Sinka	**HPA**
Secretariat:	**Dr Julia Granerod**	**HPA**

AGENDA ITEM 1 - Welcome, introductions and apologies

1.1 The Chairman welcomed everyone to the 5th meeting of the ACDP TSE Risk Assessment Sub Group (TSE RA SG). Apologies had been received from members Professor Richard Knight and Professor Graham Medley; invited experts Professor Angela Mclean, Professor Azra Ghani, and Professor Marc Turner; and observers Dr Heather Elliott, Department of Health (DH), Dr Irene Hill, Food Standards Agency, Dr Sara Hayes, Welsh Assembly Government, Mrs Julie Hitchcock, Defra, Dr Andrew Riley, Scottish Government, Dr

Elizabeth Mitchell, Northern Ireland, and Mr John Newbold, Health and Safety Executive.

AGENDA ITEM 2 - Minutes of the last meeting (May 25th 2012) and matters arising

2.1. The minutes of the last meeting were agreed with one revision:

- Footnote number two on page 8 to be deleted. This footnote had been added subsequent to the previous meeting and thus did not accurately reflect the discussions of the meeting. The footnote related to a revised classification of the appendix samples. The histopathologists had agreed via e-mail correspondence following the last meeting that strong immunolabelling with only one antibody would also qualify as positive in some cases. A revised list of 16 positives (as opposed to the 12 reported at the previous meeting) was subsequently produced.

2.2. This reclassification was further discussed. Members were informed that the expert histopathologists had agreed a position following the last meeting and felt that not only should all appendices that stained positive with two antibodies be classified as positive, but four additional appendices that stained positive with only one antibody should also be classified as positive. The reason these might only have stained positive with one antibody may be due to limitations in area of tissue and section used (i.e. the area of positivity may have been cut out from the other section tested). Thus, four of the six appendices previously categorised as 'suspect' were reclassified as positive. In an additional two appendices the immunohistochemistry (IHC) staining was indistinct and not clearly within the follicular dendritic cells (FDCs), and therefore of uncertain significance. It was noted that the previous Hilton study had also classified appendices with strong immunolabelling with only one antibody as positive, though there were some differences in the antibody concentrations used in this study. Thus, the revised definition of a positive is as follows: abnormal prion accumulation detected by IHC within the FDCs of an appendix section by either of the two prion specific antibodies used to screen the tissues – as two antibodies were used to screen the appendix

sections, the results should include whether or not the accumulation was apparent using more than one antibody.

Action: Secretariat to amend May 25th minutes accordingly and add post-meeting note to say that classification had been further clarified following the meeting.

2.3. The DH reported that following the last meeting of the TSE RA SG in May the results of the appendix study (i.e. 12-18 positives at that time) had been reported to ministers and the Chief Medical Officer (CMO). It was now proposed to inform ministers/CMO of the revised results (i.e. 16 positives) and also provide the latest statement from ACDP. It was suggested that the paper entitled 'Current understanding of vCJD,' circulated to Members prior to the meeting, be used as a basis for the statement, following agreement by the group. This paper would also be published on the ACDP website during the summer. Members queried the short turnaround time and were informed that it was necessary to have an agreed statement from ACDP for interpretation purposes. The draft statement was discussed fully under Agenda item 3 below.

2.4. The group was informed that the first draft of the main scientific paper for peer reviewed publication from the appendix study has been drafted and is now with the co-authors for comment. The planned submission date for this paper is mid-October.

2.5. Members were informed that a short piece on the results of the appendix survey would be published shortly in the *Health Protection Record* and a draft of this was presented to the group. A discussion about whether publication in the *HPR* could potentially jeopardize a peer reviewed publication ensued. It was agreed that the *HPR* piece should be shortened. This shortened draft should be agreed not only by the TSE RA SG, but also by the histopathologists, before publication.

AGENDA ITEM 3 - Discussion of interpretation of prevalence study results

3.1. As mentioned above, a paper entitled 'Current understanding of vCJD' was circulated to members prior to the meeting, with the aim of the paper forming the basis of an ACDP statement regarding the results and interpretation of the appendix survey. Members discussed the paper and the following general points were made:

- It was suggested to make the title more specific (e.g. referring to incidence and prevalence in the UK).
- The group discussed the target audience for this document. It was agreed that this was not a lay document but more a technical one designed to inform the public policy debate. The current intention of the paper was to support the planned *HPR* publication. Members were reminded that this document could be updated in the future as and as new evidence or interpretation became available.
- An preface should be added to the paper highlighting its importance and detailing the intended audience.
- A paragraph should also be added to the paper about risk reduction measures. It was suggested to add a link to the position statement from the Blood Services and also to the ACDP TSE infection control guidance. Also, the following potential further research goals should mentioned: 1) long-term surveillance, including strain characterisation, 2) control appendix surveys, 3) further prevalence studies including blood, and 4) applied research on risk reduction – e.g. decontamination.
- Concern was expressed over the way the dual strain hypothesis had been described and it was suggested to revise this. Any reference should be to "multiple" rather than dual strains.
- Further specific amendments were suggested and the revised publication can be found at http://www.dh.gov.uk/ab/ACDP/TSEguidance/DH_125868.

3.2. A paper was presented to the group outlining how the existing surgical transmission model might be modified to provide more realistic scenarios, using the dual strain or limited susceptibility hypotheses. Some implications

of each hypothesis for longer-term dynamics of infection, for patients considered as "at risk" of vCJD infection, and for managing the risks of onward infection from surgery were also briefly discussed. Members were asked to comment on the general direction of the paper.

3.3. The group agreed with the approach presented in the paper subject to a more sophisticated description of the 'dual (i.e. multiple) strain' hypothesis.
Action: Professor Manson and Dr Mead to agree and provide a draft paragraph on multiple strains.

3.4. The following noteworthy points were mentioned with regard to surgical transmission:

- A further possible scenario for lack of surgical transmissions seen is that the replication efficiently of this agent in the human host is not known.
- There is at present no definite way to prove a vCJD-related surgical transmission has occurred (though large numbers of infections might be expected to produce observable linkage of cases).
- Neurosurgical transmission has been shown to occur in primates, and in cases of sporadic CJD in humans.

AGENDA ITEM 4 - Any other business

4.1. The item 'Prion disease in fish' will be dealt with by correspondence.

4.2. A letter from Professor John Collinge (MRC Prion Unit) to Professor George Griffin (Chair of ACDP TSE RA SG) was shared with members. The letter asked for the group's view on a proposal to undertake a prevalence screen of 50,000 UK blood donors using the prototype vCJD blood test established at the MRC Prion Clinic. It was suggested to hold a joint meeting in the autumn between the ACDP TSE RA SG and the Prion Working Group (PWG) to discuss the development and potential use of blood prevalence tests in further detail. This would include, but not be confined to, potential use of the Prion Unit test.

Action: Secretariat to arrange meeting.

Secretariat
July 2012

Papers for the 5th ACDP TSE Risk Assessment Sub Group meeting on 12th July 2012

- **ACDP_RA_TSE05_P2.1** – Minutes of May 25th meeting
- **ACDP_RA_TSE05_P3.1** – Cover paper
- **ACDP_RA_TSE05_P3.2** – Paper on current understanding of vCJD
- **ACDP_RA_TSE05_P3.3** – Paper on "dual strain"
- **ACDP_RA_TSE05_P3.4** – Paper on 'vCJD transmission via surgery: variations in strain or susceptibility'
- **ACDP_RA_TSE05_P3.5** – Existing 2005 surgical risk assessment
- **ACDP_RA_TSE05_P3.6** – Paper on incidence of vCJD disease diagnoses and deaths in the UK