MEMORANDUM

To: Carlene Dias
Peter Gibson
Jim Moir

cc Gary Austin, Dr B Wagstaff, Dr Mary Brennan, Dr Marcela Contreras, Richard Walker, Richard Fry

From: Sue Cunningham

Date: 7th October 1997

Re: CJD Briefing - 6th October

You will probably have seen the stories in this morning's papers about CJD. They reflect a briefing given at the Department of Health yesterday to update health and science correspondents on the current state of knowledge about the disease.

As far as the Blood Service goes, our Line to Take remains the same, ie

> "The NBS position is based on the view expressed at the WHO expert meeting on CJD held in March this year. That meeting concluded that there has been no definite or even probable instance of transmission of CJD by blood, blood components or blood products. At this stage, blood transfusion should continue to be considered safe in respect of CJD.
>
> "Alternatives for any blood product should always be considered and administration should only occur if the clinical benefit is perceived to exceed the risk, even though it may be only theoretical."

The only new element in the story is the information about the epidemiological study being carried out by the CJD Surveillance Unit in Edinburgh. This is an anonymised study and we are co-operating with the Surveillance Unit in tracing donations and the patients who received them. We will ourselves not know which of the records we are following up belong to the three patients who died of CJD and which to controls. All the information will go back to the Surveillance Unit in Edinburgh for analysis to discover whether or not there is any link between blood transfusion and the transmission of CJD

In all our dealings with the media, we will be stressing that the benefits of blood transfusion far outweigh the negligible, if any, risk of contracting CJD. We will also reassure donors that there is no risk of contracting CJD through giving blood.

If you have any queries about this, do please let me know.

CJD - BRIEFING FOR 6 OCTOBER 1997

Numbers of Cases

Sporadic Creutzfeldt-Jakob Disease (CJD)

1 CJD is the principal human TSE. It is rare, with an annual incidence of 0.5-1 case per million population worldwide. The disease was first described in the 1920s and is predominantly (85% of cases) a sporadic disease (i.e. with no identifiable cause) but about 14% of cases are familial and associated with gene mutations. Less than 1% are iatrogenic (accidentally transmitted from man to man as a result of medical procedures). In sporadic cases the average of onset is between 55 and 75, although younger patients are found in iatrogenic and familial cases.

New Variant CJD(nvCJD)

2 The National CJD Surveillance Unit identified in early 1996 a previously unrecognised form of CJD. The disease has occurred over the last two years in a group of patients under the age of 50 (ie. younger than typical CJD cases which usually occur in late middle age), with unusual clinical features (for example, a longer duration of illness and behavioural change) and a distinctive appearance in the brain tissues. **To date there have been 21 cases of nvCJD confirmed by the CJD Unit, of which one is still alive. Only one case of nvCJD has been confirmed outside the UK, in France.**

Apparent increase in numbers of sporadic CJD

3 There has been an increase in the number of cases of classic sporadic CJD recorded in England and Wales for the period 1970-April 1996, with the greatest increase in those over the age of 75 years. Substantial increases in the reported incidence of CJD have also been observed in other countries who monitor the disease, including those where BSE is rare or absent. These increases are most likely to reflect improved case ascertainment, especially in the older age groups, rather than a real increase in the disease.

Research published in Nature 2 October

Background to the work:

Research was put in hand at the Neuropathogenesis Unit, Edinburgh, at the time the identification of new variant CJD (nvCJD) was announced in March 1996, concerning the strain typing in mice of material taken from three nvCJD patients. Preliminary results of the research were published by Moira Bruce and colleagues in *Nature* on 2 October. Four strains of inbred mice were challenged with central nervous system tissue from three nvCJD patients which was injected into their brains.

Mice of the strain known from earlier experiments to be the most vulnerable to BSE have now succumbed to a neurological disease. The mice developed symptoms at the same time after challenge as mice of the same strain did when challenged with BSE and the

lesion pattern in their brains also corresponds to the pattern in mice challenged with BSE. Mice in the next most vulnerable strain are now showing signs of disease, again the symptoms appeared at the same time as they would for BSE. All these strains of mice have been challenged with BSE from a number sources (cattle, sheep, cats etc.) and it is known that the incubation times and patterns of brain damage remain remarkably consistent for BSE from whatever the source, and are quite distinct from other transmissible spongiform encephalopathies (TSEs) such as classic CJD and scrapie.

The same edition of *Nature* also reported separate experiments by an independent team at London University headed by Professor Collinge who is a member of the Spongiform Encephalopathy Advisory Committee (SEAC). These experiments also show that nvCJD behaves like BSE and that it does not behave like other CJD agents when tested in ordinary mice and in mice with the normal copy of the gene related to these diseases replaced by a human gene.

The results were considered by the Spongiform Encephalopathy Advisory Committee (SEAC) on 16 September SEAC concluded that the research provided convincing evidence that the agent which causes BSE is the same as that which causes nvCJD. The Committee also concluded that the necessary measures to protect public health and animal health are in place and saw no need for any change in the light of these new findings.

A "news and views" article by Professor Pattison, chairman of SEAC, and Professor Almond, also a SEAC member, commenting on the findings also appeared in the same edition of *Nature*. The authors point out that they are not writing in the capacity of SEAC members. This will be entitled "human BSE" and concludes that the evidence is the most compelling to date in support of a link between BSE and nvCJD. It also says that the new evidence does not allow any firmer conclusions to be drawn about the number of nvCJD cases that will occur in the UK population.

Importantly, the article also says that this evidence does not allow them to draw any firmer conclusions about the route by which the victims of nvCJD were infected. The authors say that various possibilities exist, including a common source for BSE and nvCJD and transmission from cattle to people via an intermediate species. However, the authors say that they believe that the most likely exposure was via the consumption of beef products that included infected offal before it was banned from human food late in 1989. The authors do not think that a recent report in the UK popular press of a case of nvCJD in a vegetarian of 11 years invalidates this view.

The Advisory Committee on Dangerous Pathogens (ACDP) considered the implications for worker safety on 18 September. They concluded that the BSE agent should now be classified as a human pathogen, but that given there is still no evidence of occupational transmission and the precautionary approach adopted by the ACDP the controls currently in place are sufficient.

Line to take

General

* The opinion of SEAC is that this new research provides convincing evidence that

the agent which causes BSE is the same as that which causes nvCJD. The most likely explanation of the cases of nvCJD to date remains exposure to BSE before the introduction of the specified bovine offals (SBO) ban in 1989.

* SEAC's advice to Government has always been based on the assumption that the two disease agents are the same and that BSE may cause disease in humans. The Committee again concluded that the necessary measures to protect public health are in place and saw no need for any changes in the light of these new findings.

On the likely number of cases in the future

* Mathematical modelling carried out by members of the CJD surveillance Unit has produced a range of possibilities from less than a hundred cases to tens of thousands, depending on the assumptions used. There is still a lot we do not know about the disease, including important information on the incubation period, the route of infection, the level of exposure required to cause disease and the role of genetic susceptibility. It is likely to be some years before we have enough information to make soundly based predictions.

* A specialist sub-group of SEAC has been set up to report to both SEAC and the Chief Medical Officer (CMO) to assess the information about the epidemiology of nvCJD and develop as far as possible advice on trends in the disease.

On the implications for worker safety

* The ACDP has considered the implications for worker safety and concluded that, the existing precautionary measures and guidance are sufficient for the protection of workers.

On the safety of beef

* This new evidence strengthens the belief that nvCJD and BSE are linked. It does not tell us anything about the mechanism by which BSE could pose a risk to humans and it does not provide any new evidence to suggest that the risk is bigger than had previously been thought. The UK independent advisory committee, SEAC, has discussed this and has confirmed that in its view there is no need to further strengthen the safeguards already in place to protect public or animal health.

Will this make it more difficult to lift the export ban?

* This should not affect the assessment of the export ban. We accept that the scientific rational for lifting the ban has to be carefully considered by EU scientists, but this new information merely confirms the working assumption which UK and EU scientists have adopted, that BSE and nvCJD are linked. It strengthens the evidence for that link, but that is all it does.

On the calls for a public inquiry

* [The Government is aware that relatives of the new variant patients and others want an independent judicial inquiry. This request is currently under consideration].

On a no-fault compensation scheme

* There are no current plans to introduce a no-fault compensation scheme. Any claims for compensation would be considered in the context of the Government's legal obligations.

Research Strategy on TSEs

See Annex A for current position on research into CJD and blood

See Annex B for general background on strategy

Funding of research

The UK has a long history of research into TSEs and in the five years up to 1996-97 some £50million was invested in this area.

Government expenditure on research in this field is now running at some £23m per year. Expenditure over the next three years is expected to be about:

1997-98	(£ million)
MAFF	12.64
BBSRC	3.95
MRC	3.6
DH	1.5
TOTAL	21.7

1998-99	
MAFF	13.04
BBSRC	4.02
MRC	2.5
DH	3.72
TOTAL	23.27

1999-2000	
MAFF	13.49
BBSRC	3.47
MRC	2.5
DH	3.63
TOTAL	23.09

NOTE: previous versions of this given to the funders group showed a DH expenditure of £2m in 1997-98. £0.5m has since been given up from the DH RD budget (which would otherwise have gone unspent because not all projects could get underway this year).

ANNEX A

TSE INFECTIVITY OF BLOOD AND BLOOD PRODUCTS:CURRENT RESEARCH POSITION

BACKGROUND

DH hosted two workshops of experts in TSEs and Blood Transfusion in June 1997 to determine what was known in this area, what was currently under way and what more should be done. The findings of these workshops have been considered by SEAC, the joint TSE Funders Group, The TSE Research Advisory Group and the High Level Committee overseeing progress on TSE research. Recommendations from these comittees are now being implemented.

FINDINGS

* The causative agent has still not been definitively determined but it is widely believed to be an abnormal form of a naturally occurring protein. Epidemiology studies are crucial but will take many years to yield results. Diagnostics are being developed but they are not yet sufficiently sensitive to differentiate low levels of the distorted protein eg in fluids like blood. Currently, the only reliable way of determining infectivity is bioassay using animal models but these take years and are limited in testing nvCJD infectivity because of the species barrier (this is thought to be of the order of 1000)

* Current epidemiology research worldwide has failed to find any evidence of transmission of classic sporadic CJD by blood or blood products. There have beeen a number of transmissions of CJD from the use of growth hormone derived from infected pituitaries and from other transplant procedures such as the use of dura mater. In addition, nvCJD may not necessarily have the same pathogenesis as classic sporadic CJD and may therefore pose different risks

* To date, MAFF studies on tissues in cattle clinically affected with BSE have shown no infectivity in blood. However the studies were somewhat insensitive because they used mice, which due to the species barrier effect may less readily detect low amounts of infectivity. Further experiments are being carried using calves as the test (no species barrier).

* A few laboratory studies using animal bioassays have indicated that some infectivity may be associated with blood fractions, including buffy coat, but that infectivity is rarely detected in whole blood. These results are preliminary and/or have problems with the validity of the experimental protocols. Most involve intracerebral injection rather than transfusion. Further careful studies are required to determine which fractions are involved, what level of infectivity is there, whether infectivity is present at pre-clinical stages of the disease and whether infection can be transmitted via transfusion in the absence of a species barrier.

RESEARCH PLAN

Epidemiology/surveillance

* Current surveillance and epidemiological investigation of cases will continue, with the aim of identifying any risk factors that may possibly be associated with the development of disease.

Diagnostics

* A number of programmes are underway to develop selective and sensitive diagnostics for the abnormal PrP protein. At present, sensitivity is insufficient to measure low levels in fluids such as blood. Screening panels are being developed to ensure that new diagnostics identify all positives correctly and selectively. The overall aim is to get a cheap, accurate diagnostic that can work on small fluid and tissue samples and hence remove infected batches from the food or medical chains. There is good interaction between those developing these tests and neuropathologists. However, it may be some time before a test for routine use is available in cases of illness when the diagnosis of CJD is suspected, and considerably longer before any means of detecting pre- or sub-clinical infection is developed.

Animal Models

* the strategy is to carry out research on a number of animal models to test whether blood or blood fractions can contain infectivity, at what stage in the disease blood is potentially infective and whether recipients can be infected by blood or blood product transfusion or treatment. Experimental models will include:
    * nvCJD into transgenic humanised mice
    * nvCJD into panels of mice used for strain typing BSE
    * nvCJD into squirrel monkeys(in the US)
    * studies of pathogenesis of BSE into cattle and sheep, together with regular blood sampling and transformation of blood and blood fractions int recipient animals

These experiments will take some years to produce results

RD2
25 September 1997

ANNEX B

Coordinated Research Strategy

8 Following the announcement of the discovery of new variant CJD (nvCJD) in March 1996, the Secretary of State for Health gave the Department of Health Director of Research and Development a remit to set up a directed programme of R&D into the **human health** aspects of TSEs, involving other funders (MAFF, MRC, BBSRC and the Wellcome Trust). To help in this task two advisory groups were set up :

* the DH TSE R&D Funders Coordination Group (FCG) to ensure that the programmes of R&D funded in this field address priority issues of national interest and constitute a coherent strategy.

* the joint DH/MRC TSE Research Advisory Group (RAG), to advise on a scientific strategy and priorities for basic and applied research on the human aspects of TSEs, covering biomedical, epidemiological and health service research.

9 A high-level progress-chasing group on TSE research has also been set up under the chairmanship of Sir Robin Butler, the Head of the Home Civil Service, with direct access to the Prime Minister. Following this, the remit of the FCG (which reports to the Butler Group) was expanded to cover **all** aspects of TSE research, including animal TSEs.

10 In collaboration with MAFF, BBSRC, MRC, HSE and the Wellcome Trust and consulting widely with the scientific community, DH published a Strategy for Research and Development Relating to the Human Health Aspects of Transmissible Spongiform Encephalopathies in November 1996. The main priority areas identified in the Strategy are:

* the nature of the relationship of new variant CJD and BSE, including current epidemiology and surveillance
* the transmissibility of BSE including aspects quantifying potential risk
* development of diagnostic techniques
* the nature of the agent and pathogenesis
* development and assessment of potential therapeutic agents

11 The funders are now collaborating in implementing this strategy through their existing extensive research programmes and by commissioning further work in priority areas. In addition, an animal health strategy relating to TSEs is being produced using similar mechanisms to those used to produce the human health strategy.

12 The aim is a co-ordinated approach by **all** funders, supported by independent scientific advice, mainly through SEAC. Joint working is planned on:

* scrapie research
* basic research on prions
* setting up a joint reagent bank

There will be an annual joint meeting to review areas for further research identified.