UNIVERSITY COLLEGE LONDON MEDICAL SCHOOL

A[illegible]nistration
Gower Street
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Telephone 0171 387 7050
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From the Dean

UCL MEDICAL SCHOOL

THE QUEEN'S ANNIVERSARY PRIZES 1994

JRP/cw

Internal Ext: 6358

7 April, 1997

[Redacted]
National Blood Service
Northern Zone
Bridle Path
Leeds LS15 7TW

Dear [Redact

I became conscious recently that nobody has replied to your letter and enclosure of 12 November 1996 concerning SEAC's view of the framework proposal from [Redacted] and [Redacted] . Please accept my apologies for the delay. We have not been completely idle. In fact the framework proposal has stimulated much interesting discussion.

SEAC and the DH/MRC TSE Research Advisory Group have both considered the research that might be carried out on the possible TSE infectivity of blood and blood products. Both groups conclude that whilst current risks of TSE infection from blood are low further research is needed. The categories of research include: the detection of any aberrent PrP protein in blood, blood components or blood concentrates; transfusion experiments carried out in suitably sensitive animal models; and research into the effects of leucodepletion.

The DH/MAFF Joint Funders Group is considering future research commissioning at its meeting today. One of the areas being considered is the safety of blood and blood products and a call for proposals is likely to be issued in late April or May at which time the Research Division of the Department of Health will contact you again.

Once again thank you for the stimulating paper from [Redacted] and [Redacted] and with apologies for the delay in this reply. With best wishes.

[Redacted]

DEPARTMENT OF HEALTH

5094 Skipton House 80 London Road London SE1 6LW Telephone 0171 972 2000
Direct line 0171 972 5048

Professor [Redacted]
C/O UCL Medical School
Administration
Gower Street
London WC1E 6BT

Date: 26 March 1997

[Redacted]

MINOR AND WILLIAMSON PAPER - CJD AND BLOOD

Further to [Redacted] letter to you of 18 March, I am writing about the handling of the SEAC response to [Redacted]

The DH/MRC Research Advisory Group considered the Minor/Williamson framework proposal as part of a wider discussion on blood and blood products. Overall, the RAG's conclusions were that on current evidence the likelihood of TSE infectivity of blood and blood products is low but this might change in the light of nvCJD.

The group concluded that further work is needed, but that appropriate animal models are required and the work is probably dependent on a specific diagnostic to detect PrP at very low levels in blood and blood fractions.

RAG were not strongly supportive of the Minor and Williamson proposal, but did note that transfusion tests were likely to be more meaningful than intracerebral injection. In addition, leucodepletion may need to be considered. Overall, these conclusions match well with those of SEAC in December.

The Funders Group will consider future research commissioning on 7 April. In the meantime, I attach for your consideration a draft reply to [Redacted] along the lines discussed above.

[Redacted]

3.4.97

DRAFT

Dear [Redacted]

A Framework Proposal To SEAC On Experimental Approaches To The Transmissibility Of TSEs By Blood And The Effects Of Leucodepletion

Thank you for sending me the above framework proposal, which has stimulated much interesting discussion.

SEAC and the DH/MRC TSE Research Advisory Group have both considered the research that might be carried out on the possible TSE infectivity of blood and blood products. Both groups conclude that whilst current risks of TSE infection from blood are low, further research is needed. Categories include: detection of any aberrant PrP protein in blood, blood components or blood concentrates; transfusion experiments carried out in suitably sensitive animal models: once these groundrules have been established, a consideration of the effects of leucodepletion.

The DH/MAFF Joint Funders Group will be considering future research commissioning at its meeting on 7 April. One of the areas considered for further research will be the safety of blood and blood products. A call for proposals is likely to be issued in late April or May, at which time the Research Division of the Department of Health will contact you.

Once again, thank you for your stimulating contribution.

Yours sincerely

[Redacted]

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Direct line 0171 972
5357
Fax No: 0171-972-5558

[Redacted]

Ref: 4L173A

c/o UCL Medical School
Administration
Gower Street
London WC1E 6BT

18 March 1997

Dear [Redacted]

RE: MINOR AND WILLIAMSON PAPER - CJD AND BLOOD

Further to your phone call this morning, just a brief line to say where we are on this. As I indicated to you, the paper has been seen both by the MSBT (chaired by [Redacted]) and by the joint DH/MRC Research Advisory Group (RAG) (chaired by Professor Borysiewicz). The MSBT, of which [Redacted] is a member, is meeting next week and will be discussing it then. The RAG only met recently and the broad issue of blood transmission will now be taken up by our Funders Group in the light of the RAG comments.

[Redacted] will be in touch with you shortly to discuss the handling of the response from SEAC to [Redacted] about the Minor and Williamson paper.

Yours sincerely

[Redacted]

c.c. [Redacted]
[Redacted]

SEAC 38/3

A FRAMEWORK PROPOSAL TO SEAC ON EXPERIMENTAL APPROACHES TO THE TRANSMISSIBILITY OF TSE BY BLOOD, AND THE EFFECT OF LEUCODEPLETION

The above paper by P D Minor and L Williamson was sent to [Redacted] by [Redacted] Of the National Blood Service, Northern Zone.
A copy of the paper and related correspondence is attached.

UNIVERSITY COLLEGE LONDON MEDICAL SCHOOL

Administration
Gower Street
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WC1E 6BT

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Direct Line, 0171 209 6303
Fax 0171 383 2462
Email [Redacted]@ucl.ac.uk

From the Dean

UCL MEDICAL SCHOOL

THE QUEEN'S ANNIVERSARY PRIZES 1994

18 November, 1996

[Redacted]
Clinical Director,
National Blood Service,
Northern Zone,
Bridle Path, Leeds LS15 7TW.

Dear [Redacted]

Thank you for your letter of the 12 November 1996 and the attached paper from [Redacted] and [Redacted] I am now passing the correspondence on to the secretariat of SEAC with a view to our discussing the issue at our next meeting on December 5th.

Best wishes.

Yours sincerely,

[Redacted]

Copy [Redacted]
[Redacted]

12 November 1996

PF/CAP

[Redacted]
The Dean
UCL Medical School
Administration
Gower Street
LONDON
WC1E 6BT

OFFICE
14/11/96

Dear [Redacted]

At the meeting of the Standing Advisory Committee on Transfusion Transmitted Infection (SACTTI), that you attended in July we discussed the desirability of identifying possible avenues of research that might be informative in identifying the likely risk of CJD, and the recently described variant, being transmissible via blood transfusion. My recollection from the meeting is that it was accepted that the desirability of undertaking research in this area would be enhanced if firmer evidence became available identifying a link between the new CJD variant and BSE. From my perspective recent events have provided further circumstantial evidence of a link and I feel it is now important that serious consideration is given to undertaking research in this area.

Following the meeting in July Philip Minor and Lorna Williamson began to prepare a proposal outlining the areas in which SACTTI believe further information would inform us of the risk posed to recipients of blood transfusion by TSE's. I enclose a copy of this with this letter. I hope that it will be possible for this paper to be considered by SEAC and will be grateful for any assistance you can give to this end. [Redacted] Medical Director of the NBA, will be sending the proposal to the Advisory Committee on the Microbiological Safety of Blood and Tissues (MSBT), chaired by [Redacted]. This group has given support in principle to preparation of proposals in this area and hopefully will consider the paper at a forthcoming meeting.

Thank you for the assistance you have given us over the last few months, the Transfusion Medicine community is keen to address the issue of CJD and blood transfusion and your informed input has been of great value.

Best wishes.

Yours sincerely
[Redacted]

Northern Zone
Bridle Path
Leeds LS15 7TW

Tel: 0113 2148600
Fax: 0113 2148741

A framework proposal to SEAC on experimental approaches to the transmissibility of tse by blood, and the effect of leucodepletion

[Redacted] National Institute for Biological Standards and Control, Blanche Lane, South Mimms, Potters Bar, Herts, EN6 3QG

[Redacted] Regional Blood Transfusion Centre, Long Road, Cambridge, CB2 2PT

Background

Observations on the possible transmission of agents of transmissible spongiform encephalopathies by blood are unclear and to some degree controversial (P Brown, Current Opinion in Haematology 1995, 2: 472-477). There is no evidence for an epidemiological link between the use of blood or blood products and CJD in humans, but the power of the studies is not clear, and probably small. While there are published examples of experimental transmissions, all have features which make it difficult to draw definitive conclusions on which to base public health policy. Consequently a conservative regulatory position has been taken both in Europe and in USA in which individuals known to have CJD or believed to be at risk of acquiring it are excluded from donation. Those considered to be at risk include individuals with a case of CJD in the family, or in some

countries those who have received dura mater transplant. The implementation of such exclusions is difficult, depending on the definition of 'family' and knowledge on the part of the patient which may not be available. The action regarding product recall to be taken should a donor subsequently be identified as in a group at risk is even more difficult. In one analysis up to fifty percent of products would have been withdrawn in one country in one year alone, creating problems of supply and public confidence on a major scale. As the need for action is not based on unequivocal data, there is unacceptable ambiguity in regulatory approaches. The possibility that BSE may transmit to humans is a further major complication in the UK blood and blood product supply.

Possible relevant questions which could be addressed on an experimental basis include:

1. Can TSE be experimentally transmitted by whole blood in a transfusion?
2. If so, can the frequency be reduced by leucodepletion?

The considerations involved are so complex, that the following experimental proposals should be regarded as tentative and a basis for discussion. The need for information, however, is unequivocal.

1. <u>Can TSE be experimentally transmitted by whole blood in a</u>

transfusion.

The experimental model is determined among other things by what is known of the pathogenesis of the particular tse. Convenient laboratory models are available for hamsters, and experimental transfusion procedures are under development. Otherwise, mice are the animal of first choice in that they are relatively cheap, there are well defined inbred strains so that individuals can be immunologically compatible with respect to transfusion, the distribution of infectivity throughout the time course of infection is well characterised and known for many systems, and the animals can be chosen to eliminate any possible species barrier. The volume of blood which can be transfused and the technical difficulties posed are not known. Larger animals such as sheep or cows have the advantage that transfusion may be technically more straight forward, and the disease may more closely approximate to natural CJD infection. Scrapie in sheep is known to involve a phase in which lymphoid tissues have higher infectivity than neural tissues, so that transmission by transfusion seems a real possibility. In contrast infectivity in BSE has been detected only in neural tissue and distal ileum following oral infection; it is not proven which more closely resembles CJD. As part of the concern stems from the possibility that BSE can be transmitted to humans, the bovine model may be preferred.

The most practical model is likely to be the mouse for which there is a great deal of available experimental information. It

will be necessary to establish a time course of infection in blood, brain and lymphoid tissue in so far as it is not yet available using the most sensitive routes of inoculation, presumably intracranial. The infectivity of the blood samples when given intravenously would be determined at the same time. The blood might be given fresh to mimic the transfusion setting most closely; it is conceivable that "live" blood would have a greater infectivity than extracts from it as the cells could persist for a longer period in the recipient animal.

The agent to be used could be a human CJD preparation, a VCJD preparation, a BSE preparation or a mouse adapted laboratory strain. Of these the mouse adapted strain is likely to give the clearest experimental result, because of its high infectivity and known characteristics, while the VCJD preparation would address a more immediate concern. There is a case for studying both in parallel experiments. The infectivity of all samples would have to be quantitated by reliable methods.

Leucodepletion and experimental studies into TSE

During infection with naturally occurring TSE, infectivity has never been detected in blood. However, in experimentally infected rodents, blood and blood constituents appear to contain the infective agent, both during the prodrome and once symptoms appear. Because the infective agent is associated with cell membranes and because of experimental evidence that buffy coat

can transmit the agent, the role of leucoreduction of blood components is again under consideration. Leucoreduction could be used initially in experiments designed to establish the risk, if any, of TSE from transfusion of various blood components. Only once the results of such experiments are available can the question of routine leucoreduction of components be considered.

The effect of leucodepletion on experimental transmission by blood assumes that transmission by blood is possible. There is limited information on the levels of infectivity achieved in experimental systems when assayed by intracranial inoculation which suggests that infectivity is present in low amounts. The effect of leucodepletion may therefore be greater than the effect which can be measured experimentally in so far as it would only be necessary to reduce infectivity slightly to make it undetectable.

<u>The potential of current leucodepleting technologies</u>

An average unit of white blood (450 mls) contains 2-5 x 10^9 leucotyes. By traditional processing techniques, most of these leucocytes end up in the buffy coat, which is transfused as part of the red cell concentrate. Platelets produced by the traditional platelet rich plasma method or by conventional apheresis methods contain 1-5 x 10^8 leucocytes/pack. The UK Guidelines for Transfusion Services (Red Book) define a leucocyte depleted unit of red cells or platelets as one containing <5 x 10^6 x leucocytes/pack, although the Council of Europe are considering lowering this definition to <1 x 10^6. Two methods

are in general use for the production of leucocyte depleted components, namely the use of polyester fibre filtration (for red cells and platelets, many manufacturers) and certain apheresis techniques (for platelets only, Cobe Spectra and LRS). Both filtration and apheresis (LRS) can now achieve $<10^5$ leucocytes/pack under optimal conditions i.e. when applied to blood <2 days old.

Flow cytometric studies have shown that leucodepleting filters remove granulocytes and lymphocytes with equal efficacy, monocyte removal is particularly efficient. Lymphocytes passing through leucodepleting filters retain viability, as demonstrated by a case of transfusion-associated graft-versus-host disease (TA-GVHD) following transfusion of filtered red cells.

Lesser degrees of leucocyte removal can also be achieved using 'bottom and top' (BAT) processing technology in which the buffy coat is taken off the red cells during processing (80-90% leucocyte removal, residual leucocytes 10^8/unit). The buffy coats can then be used as the start material for platelet production, resulting in platelets with only 10^7 leucocytes/therapeutic dose. This methodology is standard in Holland and Sweden, not used at all in the US, and has been introduced patchily but increasingly across the UK.

Clinical use of leucodepleted components

Because of cost and lack of convincing evidence of clinical benefit, the use of fully lecodepleted components is currently highly restricted. The only absolute indications arising from the Edinburgh Consensus Conference on Leucodepletion in 1993 were aplastic anaemia and recurrent transfusion reactions, with acute leukaemia and neonatal/intra-uterine transfusion unproven indications. However, because of the multiple immunological and virological hazards associated with leucocytes, provision of leucodepleted blood for neonates is increasing and will soon become standard practice. A further indication is to prevent CMV transmission if CMV seronegative components are unavailable. Less than 5% red cells and no more than 20% of platelets issued are currently lecudepleted (NBS London and South East Components Group, 1995).

Because of its increased costs and loss of red cells during processing, bottom and top technology has not yet become routine practice in the UK. Blood Centres are increasingly using this technology primarily to meet platelet demand, with buffy coat depleted red cells as a by-product. Thus most red cells are still issued with the buffy coat in place.

Experimental leucoreduction

Current leucodepleting filters are designed for human therapetuic doses of blood and components i.e. 250-450 mls. Leucoreduction

of smaller volumes of blood for experimental purposes is generally carried out using Ficoll-Hypaque or other density gradient systems. The degree of leucoreduction achieved is likely to be much less than with filtration, but has the advantage that leucocyte fractions can be separated from each other and can be harvested for injection or culture. The design of experiments using buffy coats and leucoreduced components will aid the understanding of the potential transmissibility of TSE by blood.

2. Can TSE transmission be reduced by leucodepletion?

Effective methods are available for leucodepletion of units of human blood for transfusion to susceptible individuals. The reduction in leucocyte content can be in excess of 10^5 fold. Experimental systems for leucodepletion of murine blood are also described, although they may use different mechanisms and be less effective. A correlation between efficiency of leucodepletion and reduction in infectivity, would be of great value. It is not known if similar systems could be applied to sheep and cows.

CP139

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Direct line 0171 972 5607/5623

[Redacted]
Government Building, Block B
Toby Jug Site
Hookrise South
Tolworth
Surbiton
Surrey KT6 7NF

28 April 1997

Dear [Redacted]

WORKSHOP RELATING TO THE LEVEL OF INFECTIVITY FROM TSEs IN BLOOD AND BLOOD PRODUCTS
10.00 ON 17 JUNE 1997 AT DEPARTMENT OF HEALTH, SKIPTON HOUSE, LONDON SE1 6LW

I have great pleasure in inviting you to take part in a small workshop to examine the research that is needed to determine the possible level of infectivity from TSEs in blood and blood products. Whilst there is no evidence that TSEs have been transmitted in this way, a number of committees advising on the health issues of TSEs have recommended that this area is revisited following the occurrence of a number of cases of new variant CJD.

I hope that the workshop will identify those experiments that might be carried out to determine definitively whether there is any risk of infectivity and, if so, at which stage of the disease this occurs. I also hope that the time-scale and cost of the research might be estimated and those laboratories most likely to be able to conduct such research successfully identified.

I look forward to seeing you on the 17th June.

Yours sincerely

[Redacted]

[Redacted]
Research and Development Division

2.7.4/4

CP139

Skipton House 80 London Road London SE1 6LW Telephone 0171 972 2000
Direct line 0171 972 5607/5623

[Redacted]
Chief Scientists Group
Room G17
Nobel House
17 Smith Square
London SW1P 3JR

23 April 1997

Dear [Redacted]

WORKSHOP RELATING TO THE LEVEL OF INFECTIVITY FROM TSEs IN BLOOD AND BLOOD PRODUCTS
10.00 ON 17 JUNE 1997 AT DEPARTMENT OF HEALTH, SKIPTON HOUSE, LONDON SE1 6LW

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I look forward to seeing you on the 17th June.

Yours sincerely

[Redacted]

[Redacted]

Research and Development Division

[Redacted]

I have asked for [Redacted] to be invited also

cc as before

2794/4

CP139

Skipton House 80 London Road London SE1 6LW Telephone 0171 972 2000
Direct line 0171 972 5607/5623

[Redacted]
Chief Scientists Group
Room G17
Nobel House
17 Smith Square
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23 April 1997

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I look forward to seeing you on the 17th June.

Yours sincerely

[Redacted]

Cc [Redacted]

[Redacted]
Research and Development Division

3

DEPARTMENT OF HEALTH

Press release

97\335

Thursday 6th November 1997

SEAC ADVICE ON SAFETY OF BLOOD AND BLOOD PRODUCTS ACCEPTED

Health Secretary Frank Dobson announced today that he had accepted advice from the Spongiform Encephalopathy Advisory Committee (SEAC) on possible precautionary steps to protect recipients of blood and blood products from any possible risk of contracting new variant CJD (nvCJD).

Mr Dobson, said:

"The Government will continue to take whatever scientifically necessary action is practicable to protect the public from any risk of contracting nvCJD.

"The Government accepts the advice it has received from SEAC and the MSBT and I have therefore asked the Department's Director of Research and Development, Professor Swales, to commission an assessment of the risks of human to human transmission of nvCJD through blood and blood products. Meantime, I have instructed the National Blood Authority (NBA) to start work towards the possible extension of leucodepletion of blood in order that they are prepared in the event that the risk assessment indicates that this would be a sensible precautionary measure."

The Government will publish the results of the risk assessment and their response as soon as they are available.

Mr Dobson added:

"These are purely precautionary measures. No-one who needs treatment with blood or blood products should have any hesitation about accepting it; any risk of nvCJD will be far outweighed by the risks of damaging health through not doing so.

"Blood donors are not at any risk. The gift of blood is a very precious one which is invaluable to the health service and to the health of patients."

[MORE]

Richmond House 79 Whitehall London SW1A 2NS
Telephone: 0171-210 3000

54

SEAC's advice was also considered by the Advisory Committee on the Microbiological Safety of Blood and Tissues (MSBT) and the Government has taken account of their views in its response.

A copy of the advice received from SEAC is attached.

In line with the recommendations of the review of SEAC published in September 1997, a summary of the SEAC meeting held on 24 October 1997 is also published today. This is the first SEAC Meeting Public Summary.

NOTES FOR EDITORS

1. Enquiries to Lindsey French DH Press Office 0171 210 5233.

2. The Scottish National Blood Transfusion Service (SNBTS) is responsible for blood transfusion services in Scotland. The Scottish Office has confirmed that the SNBTS will be taking the same action as the National Blood Authority in England.

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SPONGIFORM ENCEPHALOPATHY COMMITTEE - ADVICE TO MINISTERS

HUMAN BLOOD AND BLOOD PRODUCTS

The Committee have recently concluded that the transmissible agent of nvCJD is indistinguishable from that of BSE but distinctly different from any of the forms of classical CJD. Recent research (some unpublished) suggests that the pathogenesis of nvCJD differs from that of classical CJD and the former may have more involvement of lymphoreticular tissues possibly involving circulating lymphocytes. Therefore it is logical to seek to minimise any risk from blood or blood products by reducing the number of lymphocytes present.

SEAC recommends that the Government should consider a precautionary policy of extending the use of leucodepleted blood and blood products as far as is practicable. It will be for the National Blood Authority to devise a strategy to implement such a policy. It will take time to achieve full implementation and SEAC recommends that planning begins soon while the risk assessments suggested below are carried out.

It is not possible at present to estimate accurately the risk of transmitting nvCJD by blood transfusion. The magnitude of the risk will depend, *inter alia*, on the number of blood donors who are incubating nvCJD and this is not known. However, SEAC recommends that risk assessments, making assumptions of various possible incidences of nvCJD, be carried out to inform decisions on any measures which may be necessary to protect recipients.

BEEF

SEAC reviewed the safety of beef in the light of its discussion on human blood and blood products. Transmission experiments in mice have not found infectivity in the spleen, tonsil, lymph nodes or white blood cells of BSE infected cattle.

The Committee conclude, therefore, that no further measures governing beef and beef products for human consumption, are necessary.

[ENDS]

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SPONGIFORM ENCEPHALOPATHY ADVISORY COMMITTEE

97/333 **Thursday 6th November 1997**

SEAC MEETING PUBLIC SUMMARY

The Spongiform Encephalopathy Advisory Committee (SEAC) met on 24 October 1997 at the offices of the Ministry of Agriculture, Fisheries and Food, Tolworth.

The Committee conducted its regular review of the emerging experimental data and of the epidemiology of BSE and nvCJD.

The number of cases of BSE continues to be in line with predictions about the decay of the epidemic.

No new confirmed cases of nvCJD in the UK had been notified by the CJD Surveillance Unit since the last meeting. Subsequent to the meeting, however, a single case has been confirmed taking the total to twenty-two.

The Committee reviewed the safety of blood and blood products and has provided advice to Government on these matters (copy attached).

The Committee considered further papers relevant to the hypothesis that the organophosphate, Phosmet, is in some way causally linked to the BSE epidemic. It was noted that the epidemiological evidence is better accounted for by the view that the BSE epidemic is due to the widespread use of animal feed contaminated with the transmissible agent of BSE than by the OP theory. Central to the latter is the bio-accumulation of OP in treated animals however the available evidence does not support such accumulation. The Committee concluded that experimental evidence would be required to justify further consideration of a role for organophosphates in the epidemiology of BSE. Proponents of the theory were free to apply to funding agencies for resources to conduct such experiments. However, on the evidence to date the Committee did not feel that special priority should be given to this area of research.

[MORE]

57

The Committee reviewed the production and use of tallow. It noted the restrictions in the UK on the sources of raw material used in the production of tallow for food, feed, cosmetic, medical or pharmaceutical products and was impressed by UK tallow production controls. The Committee noted that imported tallow was not subject to the same restrictions nor required to reach the same standards but that the implementation of Commission Decision 97/534/EC would result in the exclusion of Specified Risk Materials from the production of tallow across all Member States from January 1998.

The Committee also reviewed the production and use of gelatin. It noted that plants in the UK manufacturing gelatin for food, feed, cosmetic, medical or pharmaceutical use have been brought under official control. The Committee also noted that all UK gelatin manufactured for these purposes from bovine raw material utilised only imported ingredients. They noted that implementation of Commission Decision 97/534/EC would exclude Specified Risk Materials from the source materials used for gelatin manufacture in all Member States.

The Committee is due to meet again in December.

[ENDS]

DEPARTMENT OF HEALTH

DRAFT Press Release

Richmond House 79 Whitehall London S
e: (Department of Health) 0171-210 3000 (Press Office) 0171-210 5221 Fax: 0

R0641-07 **Thursday 6th November 199**

SEAC ADVICE ON SAFETY OF BLOOD AND BLOOD PRODUCTS ACCEPTED

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Mr Dobson, said:

"The Government will continue to take whatever scientifically necessary action is practicable to protect the public from any risk of contracting nvCJD.

"The Government accepts the advice it has received from SEAC and the MSBT and I have therefore asked the Department's Director of Research and Development, Professor Swales, to commission an assessment of the risks of human to human transmission of nvCJD through blood and blood products. Meantime, I have instructed the National Blood Authority (NBA) to start work towards the possible extension of leucodepletion of blood in order that they are prepared in the event that the risk assessment indicates that this would be a sensible precautionary measure."

The Government will publish the results of the risk assessment and their response as soon as they are available.

Mr Dobson added:

"These are purely precautionary measures. No-one who needs treatment with blood or blood products should have any hesitation about accepting it; any risk of nvCJD will be far outweighed by the risks of damaging health through not doing so.

"Blood donors are not at any risk. The gift of blood is a very precious one which is invaluable to the health service and to the health of patients."

SEAC's advice was also considered by the Advisory Committee on the Microbiological Safety of Blood and Tissues (MSBT) and the Government has taken account of their views in its response.

A copy of the advice received from SEAC is attached.

In line with the recommendations of the review of SEAC published in September 1997, a summary of the SEAC meeting held on 24 October 1997 is also published today. This is the first SEAC Meeting Public Summary.

NOTES FOR EDITORS

Enquiries to [Redacted] DH Press Office 0171 210 5233

New file – blood products plus copy in Statements (SEAC) 18/7/11

(4)

restricted - policy

[Redacted]
[Redacted]

From: [Redacted]

Date: 6 November 1997

Cc: [Redacted]

Disappointing that despite our efforts to get them w/DH end up seeing the indemnities to ports on the day of the announcement - & more criticism for ports! expect on the way

[Redacted]

[Redacted]

6/11

NVCJD AND BLOOD

1 Further to Mr Skinner's submission of 3 November, I attach a copy of the briefing provided to FCO for briefing posts and UKREP. This includes the final versions of the summary of the SEAC meeting of 24 October, SEAC's advice to Ministers and the DH press release announcing Ministers' response, which are being published today 6 November at about 4.00 pm.

2 Publication was originally planned for tomorrow, but was brought forward in view of the media coverage yesterday.

[Redacted]
502A SKH
GTN 396 25643

2/11

[Redacted]

From: [Redacted]

Date: 6 November 1997

PUBLICATION OF SEAC ADVICE - HUMAN BLOOD AND BLOOD PRODUCTS

1 As we discussed I attach a draft telegram for posts to advise them of the forthcoming publication by the Department of a summary of the last meeting of the Spongiform Encephalopathgy Advisory Committee (SEAC), including specific recommendations on blood and blood products, and a Departmental press release to be published at the same time today 6 November at about 4.00pm.

2 You confirmed that FCO will take forward liaison with UKrep on informing the Commission.

[Redacted]
502A Skipton House
GTN 396 25643
FAX 396 25558

Draft telegram for posts

You will wish to alert host Governments and the EU Commission (UKREP) that the UK Department of Health is publishing the following attached documents on 6 November:

- summary of the 24 October meeting of the Spongiform Encephalopathy Advisory Committee (SEAC), the expert scientific committee which advises the UK Government on all aspects of Transmissible Spongiform Encephalopathies;

- SEAC's advice to the UK Government on blood and blood products, and

- A Department of Health press release announcing that Ministers accept SEAC's advice on safety of blood and blood products.

The advice on the leucodepletion of blood is likely to attract attention and you may wish to draw on the attached Q&A briefing provided by the Department of Health in response to any questions. This includes lines to take on the issue of the recall of blood and blood products from donors who subsequently contracted nvCJD, since the advice on blood in relation to nvCJD may well give rise to enquiries on this related issue, and on the question of the safety of beef in the light of SEAC's discussion on human blood and blood products.

UKREP will therefore wish to alert DGVI and XXIV on this last point as well as DGV more generally.

SEAC ADVICE ON BLOOD AND BLOOD PRODUCTS - Q&A BRIEFING

Are there any measures which could be taken to reduce the risk of nvCJD transmission in blood?

We do not know whether nvCJD is transmissible in this way, but that we cannot assume it behaves in the same way as classic CJD. We will be considering whether there are additional measures which we could take.

SEAC have recommended leucodepletion - will you introduce that now?

SEAC did not recommend leucodepletion - they recommended that Ministers consider a precautionary policy of extending the use of leucodepleted blood "as far as is practicable". They also recommended that a risk assessment be carried out to assess the risk of the transmission of nvCJD by blood or blood products and that this assessment should inform any decision on what further action should be taken to protect patients. This is exactly what we are doing.

Meantime, the National Blood Authority is working on a planning strategy to implement that policy, should the risk assessment indicate that this would be a sensible precautionary measure.

How long would it take to set it up?

That is precisely the sort of question the NBA needs to assess in their planning strategy.

What would leucodepletion cost?

As part of their preparatory work, the NBA will be assessing the costs to the NHS of introducing leucodepletion of blood.

Will you guarantee that money will be made available for this?

We have accepted SEAC's advice to carry out a risk assessment. We need to see what it shows, and make the decision in that light. The Government will continue to take whatever steps are necessary to protect the public.

What about the research by Oesch et al published in *Nature* on 6 November describing a test to detect nvCJD - can you use this to test blood?

This work is an important step in the development of an in-vivo test for BSE and nvCJD. Further research is still required to validate the efficacy of this test and to extend it to the detection of very small amounts of abnormal prion in fluids such as blood.

MAFF and the Department of Health have been in discussion with Professor Oesch and others on the development of this kind of approach into a simple on-line tsest for TSEs.

BEEF

Does SEAC's advice on human blood have any implications for the safety of beef - what about the blood in beef?

SEAC reviewed the safety of beef in the light of its discussion on human blood and blood products. TRansmission experiments in mice have not found infectivity in the spleen, tonsil, lymph nodes or white blood cells of BSE infected cattle.

SEAC therefore concluded that no further measures governing beef and beef products for human consumption are necessary.

BLOOD PRODUCT RECALL

Background

In line with the views of the European expert Committee on Proprietary Medicinal Products (CPMP) that plasma derived blood products identified from nvCJD donors should be recalled as a precautionary measure, the UK has recalled products on two occasions within the last week.

Why are these products being recalled?

The products were derived from plasma from a blood donation by a person who has subsequently been confirmed as having died of new variant CJD. The Medicines Control Agency has instructed the Bio Product Laboratory , in line with the views of the Committee on Propriety Medicinal Products (CPMP), to recall the product. This is a purely precautionary measure which we hope will reassure the public about our safety procedures.

What are the products?

Albumin and Factor VIII

What are they used for?

Albumin is used in the treatment of burns, shock and chronic liver disease. Factor VIII is used in the treatment of haemophilia.

Will patients have received other components from this donation?

Yes. The red cells and platelets are likely to have been used within 1 to 5 weeks of donation.

Which hospitals and Centres have received products?

Our ethical advice is that no benefit would be served by naming these and it would only lead to unnecessary concern on the part of patients attending those hospitals.

In CMO's statement of 6 October he said that there had been no withdrawal of blood products where one of the contributing donors had developed CJD. Why the recall in the case of nvCJD? Doesn't this mean that there are real risks to patients of nvCJD transmission through blood transfusion or use of blood products?

There is no epidemiological evidence to suggest that classic CJD can be transmitted between humans through blood transfusions or the use of blood products. We do not know whether the same will apply to nvCJD. That is why we are taking this action as a precautionary measure.

I must stress that patients who receive blood transfusions are in urgent need of blood and usually have a severe illness. Without a transfusion, they may be at immediate risk of losing their life, or of sustaining severe and possibly permanent damage to their health. All clinical procedures have some element of risk attached - it is the balance of the risk which is important. Any negligible risk of nvCJD transmission is far outweighed by the immediate benefit to the patient of the medical treatment.

You have previously said that one suspected and three confirmed cases where patients died of nvCJD were blood donors - have these all been traced?.

We understand that the second blood product recall (on 4 November) is the final stage of the exercise to trace the fate of the donations made by the four donors who were subseqently identified as having developed nvCJD. The tracing exercise, which was announced at the scientific briefing on nvCJD given to the media by theChief Medical Officer on 6 October, is now complete. We are pleased that the National Blood Authority (NBA) have been able to complete this exercise so quickly.

Clearly you are concerned that there is a risk of nvCJD transmission in the blood or blood products. What action has been taken to trace the recipients of the blood?

Recipients of blood components will be identified as a part of the research being carried out by the CJD Surveillance Unit.

What are you telling them?

Recipients of implicated blood components are not being told that they have received them - this follows from ethical advice.

You are withdrawing a product because it might cause harm and yet people who might already have been affected won't be told? Don't they have a right to know?

At present there is no benefit to recipients in informing them that they might possibly have come in contact with the nvCJD agent, as what evidence there is suggests that any risk is negligible. There is no way of telling whether any recipient has contracted nvCJD, and even if there was, there is no treatment that could be offered to them.

These are very difficult decisions which have been considered on more than one occasion by the Ethical Committee overseeing the epidemiological study. They took the view that the study to trace the recipients should be carried out anonymously, in view of the very low risk of transmission, the lack of a diagnostic test and the absence of any treatment for the condition.

This will of course be kept under review in the light of scientific advances and the advice from national and international expert committees.

If you are not telling them, what are you doing to ensure that those people who have received nvCJD implicated blood do not pass it on - ie donate blood or organs?

The Department and the NBA are actively considering what further measures, if any, might be necessary to reduce any risk of a transmission of that nature.

What are you going to do to protect the blood supply from nvCJD?

We are doing whatever the experts, the Committee on Propriety Medicinal Products (CPMP), the Spongiform Encephalopathy Advisory Committee (SEAC) and the advisory Committee on the Microbiological Safety of Blood and Tissues (MSBT), advise us is necessary. The issue is under continual review.

Current steps form a three pronged attack (in line with Council of Europe guidelines, and the advice of CPMP, SEAC, and MSBT).

1. Surveillance

* The CJD surveillance unit will continue to monitor closely the prevalence of CJD.

* Current epidemiological investigation of cases will continue with the aim of identifying any possible risk factors.

2. Research

* DH hosted two expert workshops in TSEs and blood transfusion in June 1997 to determine the current knowledge base, what research was already underway and what more needed to be done.

* Some £50 million has been spent on TSE research over the last 5 years and over the next 3 years a total of around £68 million has been allocated. This includes research now in progress to develop diagnostic tests and the testing of blood transmissibility in animal models.

3. Screening

* Blood donors are carefully questioned to screen out those who may be at risk.

Shouldn't you only take blood from vegetarians?

We would simply not be able to meet the demand for blood if we were to rely on vegetarian donors alone. This would put the lives of countless patients at risk. We transfuse over 800,000 units of blood in our hospitals every year.

Our blood stocks are already under severe pressure and we need, now more than ever, to increase - not decrease - the number of regular donors. It is therefore vital that this latest information does not put people off donating.

Are blood donors at risk?

Categorically no. The gift of blood is a very precious one which is invaluable to the work of our health service and to the health of patients.

SPONGIFORM ENCEPHALOPATHY ADVISORY COMMITTEE

SEAC PS1

SEAC MEETING PUBLIC SUMMARY

SPONGIFORM ENCEPHALOPATHY ADVISORY COMMITTEE MEETING
24 October 1997

The Spongiform Encephalopathy Advisory Committee (SEAC) met on 24 October 1997 at the offices of the Ministry of Agriculture, Fisheries and Food, Tolworth.

The Committee conducted its regular review of the emerging experimental data and of the epidemiology of BSE and nvCJD.

The number of cases of BSE continues to be in line with predictions about the decay of the epidemic.

No new confirmed cases of nvCJD in the UK had been notified by the CJD Surveillance Unit since the last meeting. Subsequent to the meeting, however, a single case has been confirmed taking the total to twenty-two.

The Committee reviewed the safety of blood and blood products and has provided advice to Government on these matters (copy attached).

The Committee considered further papers relevant to the hypothesis that the organophosphate, Phosmet, is in some way causally linked to the BSE epidemic. It was noted that the epidemiological evidence is better accounted for by the view that the BSE epidemic is due to the widespread use of animal feed contaminated with the transmissible agent of BSE than by the OP theory. Central to the latter is the bio-accumulation of OP in treated animals however the available evidence does not support such accumulation. The Committee concluded that experimental evidence would be required to justify further

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consideration of a role for organophosphates in the epidemiology of BSE. Proponents of the theory were free to apply to funding agencies for resources to conduct such experiments. However, on the evidence to date the Committee did not feel that special priority should be given to this area of research.

The Committee reviewed the production and use of tallow. It noted the restrictions in the UK on the sources of raw material used in the production of tallow for food, feed, cosmetic, medical or pharmaceutical products and was impressed by UK tallow production controls. The Committee noted that imported tallow was not subject to the same restrictions nor required to reach the same standards but that the implementation of Commission Decision 97/534/EC would result in the exclusion of Specified Risk Materials from the production of tallow across all Member States from January 1998.

The Committee also reviewed the production and use of gelatin. It noted that plants in the UK manufacturing gelatin for food, feed, cosmetic, medical or pharmaceutical use have been brought under official control. The Committee also noted that all UK gelatin manufactured for these purposes from bovine raw material utilised only imported ingredients. They noted that implementation of Commission Decision 97/534/EC would exclude Specified Risk Materials from the source materials used for gelatin manufacture in all Member States.

The Committee is due to meet again in December.

SPONGIFORM ENCEPHALOPATHY COMMITTEE - ADVICE TO MINISTERS

HUMAN BLOOD AND BLOOD PRODUCTS

The Committee have recently concluded that the transmissible agent of nvCJD is indistinguishable from that of BSE but distinctly different from any of the forms of classical CJD. Recent research (some unpublished) suggests that the pathogenesis of nvCJD differs from that of classical CJD and the former may have more involvement of lymphoreticular tissues possibly involving circulating lymphocytes. Therefore it is logical to seek to minimise any risk from blood or blood products by reducing the number of lymphocytes present.

SEAC recommends that the Government should consider a precautionary policy of extending the use of leucodepleted blood and blood products as far as is practicable. It will be for the National Blood Authority to devise a strategy to implement such a policy. It will take time to achieve full implementation and SEAC recommends that planning begins soon while the risk assessments suggested below are carried out.

It is not possible at present to estimate accurately the risk of transmitting nvCJD by blood transfusion. The magnitude of the risk will depend, *inter alia*, on the number of blood donors who are incubating nvCJD and this is not known. However, SEAC recommends that risk assessments, making assumptions of various possible incidences of nvCJD, be carried out to inform decisions on any measures which may be necessary to protect recipients.

BEEF

SEAC reviewed the safety of beef in the light of its discussion on human blood and blood products. Transmission experiments in mice have not found infectivity in the spleen, tonsil, lymph nodes or white blood cells of BSE infected cattle.

The Committee conclude, therefore, that no further measures governing beef and beef products for human consumption, are necessary.