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ANNEX F

COMMERCIAL IN CONFIDENCE

COMMITTEE ON SAFETY OF MEDICINES

NOT FOR PUBLICATION

BOVINE SPONGIFORM ENCEPHALOPATHY WORKING GROUP

Minutes of a meeting held at 2.00 pm on Wednesday 31 October 1990 in the 19th floor Conference Room at Market Towers.

Members and Invited Experts

Professor J G Collee (Chairman)
Professor A W Asscher
Professor A Campbell
Professor C Berry
Dr R H Kimberlin
Dr B J Kirby
Dr P Minor
Dr D M Taylor
Dr D A J Tyrrell
Dr W A Watson
Dr R G Will

Department of Health
(Medicines Control Agency and
Other Department of Health Staff)

Dr D Jefferys
Dr J Raine
Dr F Rotblat
Dr H Pickles
Dr K A Winship
Dr J Purves
Dr B R Matthews
Mr J Sloggem
Dr I Boyd
Dr S Eisen
Mr M Love
Mr W Burton
Mrs B Shersby (Secretary)

Ministry of Agriculture
Fisheries and Food (MAFF)

Dr A Lee

Apologies for absence were received from Professor Rawlins, Professor Lawson and the representative of the SHHD.

1. Introduction and Announcements

1.1 The chairman welcomed the members to the fourth meeting of the Working Group.

1.2 The members of the Working Group were reminded that the papers and proceedings were confidential and should not be disclosed.

1.3 Declarations of interest have been recorded in the minutes as matters arise.

2. Previous Meeting

2.1 The minutes of the meeting held on 4 July 1990 were agreed with the following amendments:-

Para 4.6 p.4 line 1
change "module" to "model".

Para 4.6 p.4 line 14
delete "potential", replace by "currently recognised".

3. Matters Arising

3.1 Para. 3: Progress to date in discussions with Smith Kline Beecham (SKB) on their range of allergen products, using animal sourced materials was reported and the advice of the Working Group sought in relation to further action with regard to this group of products, for which there appears to be a continuing clinical requirement.

Sheeps-wool - Advice was given that where sheeps wool was obtained from UK sourced animals it should be obtained from a closed flock in the female line certified free from scrapie. Rams may be introduced into the flock, since they tend to be less susceptible to scrapie than sheep.

Goat-hair - The licence holder should be advised to obtain material from a specified herd of goats, and the BSE guidelines for collection of animal material should be observed.

Cat-hair - The licence holder should be advised to ensure that cat's hair is obtained from healthy animals. Colonies which may contain sick animals under care should be avoided.

Cow-hair - The preferred source would be Australia or New Zealand or a closed herd in the UK. It is understood that SKB has a closed herd in the UK, used to obtain sera for the production of their vaccines, and the company should be encouraged to use this source, since they were concerned that decontamination procedures necessary for overseas sources and required by the anthrax regulations could denature the material and alter its antigenicity.

Beef-Veal - from Holland. The licence holder should be advised to specify that the veal is from milk-fed animals.

Mycological Media - containing ox-liver sourced from Italy as a component are acceptable as the source is not UK, provided that the usual assurances are given concerning good animal husbandry and an adequate veterinary service.

Bacteriological Media - A peptone based medium now replaces the brain heart medium used previously. Since this is highly refined and autoclaved at 132°C for 80 minutes, the Working Group considered the use of this material acceptable.

3.2 Para 4.4. The statement that ..."Sheep material has been excluded from rendering in the US" was not strictly accurate, further investigation suggests that it should be amended to read ..."Conditions have been placed upon the choice of sheep carcasses permitted to be used in rendering in the US."

3.3 In relation to the possible infection of foetal calf serum (FCS) referred to at paragraphs 4.5 and 4.6 it was suggested that the Working Group may wish to investigate further the potential for contamination of FCS during delivery of the calf. It may be necessary to extend the guidelines to cover methods of collection of FCS, should investigations reveal deficiences in cleanliness in this area.

3.4 Further to para 4.6, a report was made that a recent publication had stated that scrapie infectivity could now be detected in sheep as young as

4 months by passage into mice. The reliability of the reported studies is open to question and further evaluation.

4. European Working Party

The Working Group was informed of the intention of the CPMP to set up a Working Party to monitor the implications of BSE in relation to human medicinal products within the EC. The Working Group of CSM will be kept informed of future developments in this area.

5. Epidemiology of BSE

5.1 The comparative data for confirmed cases of BSE in the United Kingdom up to 26th October were presented by MAFF (Table 1)

Table 1

	1 Sept 89	15 Dec 89	5 Jan 90	8 June 90	29 June 90	5 Oct 90	26 Oct 90
Confirmed cases (cc)	6,398	8,627	9,093	14,374	15,288	18,795	19,667
Farms or herds with cc	4,091	5,109	5,322	7,635	8,014	9,129	9,357

These figures for confirmed cases are represented graphically at Annex 1.

Concern was expressed that the number of confirmed cases continues to rise. It was pointed out however that no cases have been confirmed to date in cattle born after the ban on ruminant feed on 18 July 1988, (two and a quarter years ago) and that no evidence has been produced to date of maternal transmission of the disease. The increase in incidence in 1989 appears to be due to an increase in exposure of cattle from recycling of infected cattle carcasses via meat and bone meal from 1984 to July 1988.

6. Feline Spongiform Encephalopathy

To date, ten cases of spongiform encephalopathy in cats have been confirmed histopathologically in Great Britain and one in Northern Ireland. Experienced cat neurophysiologists state that no cases of SE had been observed in cats prior to the present outbreak. It may be helpful to the understanding of the condition if the owners of affected animals could be questioned about feeding practices.

7. Spongiform Encephalopathy in Exotic Ungulates

No new cases have been reported.

8. Spongiform Encephalopathy in a pig

The Spongiform Encephalopathy Advisory Committee has reported the development of a spongiform encephalopathy in a pig inoculated experimentally with BSE (Annex 2). The condition resulted from massive doses given by an unnatural route. This is the first and only known case of a spongiform encephalopathy in a pig and the outcome was useful from the point of view of demonstrating the nature and symptoms likely to be observed in this species, since a video record was produced at the time of the incident. An oral transmission experiment is being undertaken by MAFF and particular note will be made by observation in the field to determine whether any symptoms approximating to those

observed in the reported case develop spontaneously in any animals. The probability that infection in pigs will develop as a result of oral ingestion is extremely remote. Nevertheless the Spongiform Encephalopathy Advisory Committee and MAFF both recommended and the Government has introduced a Statutory Instrument (SI 1990 No 1930) prohibiting the use of specified bovine offals (already prohibited from food for human consumption) in all animal feed including pet food.

9. Porcine Material in Human Medicines and Devices

9.1 As a result of the statement issued by the Spongiform Encephalopathy Advisory Committee chaired by Dr D A J Tyrrell, a member of this Working Group, and the ban on feeding of certain bovine offals to pigs referred to at para 8.0 above, the Working Group considered the extent to which porcine material is used in medicines and devices intended for human use and whether action to avoid or limit the use of any such material, originating in the United Kingdom is warranted at the present time.

9.2 A list of all medicinal products using porcine material in their manufacture which is sourced in the UK was presented by the MCA. The total number of products in each category was small and the majority related to heparin (derived from lymphoid material) and insulin derived from the pancreas (non-lymphoid material). There are only two products using porcine brain and these use corticotrophin BP, made from porcine pituitary, sourced from outside the UK and obtained in conformity with the guidelines for collection of animal materials issued by the Department of Health and MAFF.

The Medical Devices Directorate (MDD) reported that the UK Heart Valve Registry lists 13 manufacturers of porcine heart valves only one of which is currently producing valves using UK sourced material and a further one of which may return to manufacture later in the year, as well as one UK manufacturer of heparin-coated blood collection tubes.

9.3 The unanimous view of the Working Group was that since transmission of spongiform encephalopathy has only been seen under experimental conditions and in a single animal, no action with regard to human medicines or medical devices is warranted at present.

9.4 Advice to MDD - The use of evacuated blood collection tubes containing bovine-derived heparin was discussed with reference to possible infective hazards. It was generally thought that any risk was remote and minimal.

10. Dural Implants - Request for Advice

10.1 Dr David Taylor declared a non-personal specific interest in Lyodura and Lyoplant. He stayed to answer questions but did not take part in any discussions.

The CMO's neurosurgical adviser could not be present at the WG meeting, although invited, but will give advice on request subsequently and be available to CDSM.

The advice of the Working Group was sought in relation to grant of a licence for a product derived from bovine pericardium and renewal of product licences for implants derived from human dura mater (two products) and porcine dermis (one product).

Papers intended for the next meeting of the Committee on Dental and Surgical Materials (CDSM) were circulated to the Working Group.

10.2 Four products were considered:

This group comprises three products already licensed under the surgical materials order 1971(SI 1267) and one derived from bovine pericardium which is currently being assessed.

10.2.1

10.2.2

10.2.3

10.2.4

10.3 A background paper explained that the interest of CDSM has focussed over the past 3 to 4 years on human dura, because of concern about the transmission of Creutzfeld Jakob Disease (CJD) by its use. Further concern is now being expressed in relation to the potential presence of HIV in human material since the selection criteria may not be in accordance with DH guidance letters issued by CMO in 1990 (Annex 3) that is of course since these products were first licensed in 1984. The use of animal sourced material needs careful consideration because of potential infectivity from BSE arising from use of bovine or porcine materials in place of the human materials in surgery. The use of animal products might increase if the human dura products were no longer available, although there are now synthetic materials available for similar purposes.

10.4 Porcine Material:- The Working Group was content with the pharmaceutical recommendations to CDSM on page 4 (Section E) of the paper on apart from requiring an amendment in recommendation 2, that the reference to "ruminant protein" be changed to "specified offal". These recommendations are given at Annex 4.

10.5 Human dura material:- The two products, and dura were discussed separately, but discussions revealed that there are no major differences between the two human derived products. Four known cases of CJD have been reported as a result of the use of human dural implants. The consequences of such an outcome of treatment to the patient should be avoided and the Working Group considered ways of achieving this end. Whilst many neurosurgeons tend now to use synthetic materials in repair work, others believe the use of dura to be essential and preferable.

The Working Group discussed the feasibility of setting up experimental models of human material on which to conduct experiments into destructive procedures capable of eliminating the causative organisms. A model based on collagen gel with the causative agents of CJD or scrapie distributed throughout was proposed. Discussions concluded that artifical gels have been shown experimentally to have a structure not comparable to natural tissue. Validation using naturally infected material would be necessary to gain any degree of assurance on means of eliminating the causative organisations from dural material.

In the absence of established and effective methods of destroying agents responsible for CJD or HIV which would not also destroy or denature the material used for the implant, it was decided that the selection or choice of donors was very important. To this end the guidelines laid down by the CMO in the selection of transplant material should be adhered to in choosing the starting materials for the dura in relation to exclusion of HIV (Annex 3). There was some discussion on the recommendation that it is essential that blood from the donor is tested and found negative for HIV antibody, because of the difficulties in carrying out such tests on cadavers. Despite these difficulties, it was reported that antibody detection tests have been carried out successfully post-mortem in the past. The desirability of testing for hepatitis C antibody was discussed, but it was decided that a general policy decision on testing for its presence in human biological source material would be required for implementation. It is almost impossible to exclude donors likely to be incubating CJD, even if selection is limited to those aged under 50 years, but donors who have received treatment with growth hormone or been the recipients of transplants should be specifically excluded.

If the CDSM were minded to refuse to renew licences for human dura material, a ground could possibly be difficulty of complying with the CMO's requirements for selection of the material. These are new safety concerns, not existing when the products were licensed initially.

10.6 Bovine material:- When selection of bovine material was discussed, it was pointed out that there was a difference between animal sourced and human sourced material because in the case of the latter transmisson of a disease such as CJD does not have to surmount a species barrier. It was considered that provided the criteria used previously in the selection of bovine material were adhered to and that the material was sourced from outside the UK, then the bovine material would be acceptable. Validated sodium hydroxide disinfection procedures should be insisted upon. The Working Group endorsed paragraphs 2(a), (b) and 3 on pages 3 and 4 of the paper on Lyoplant (See Annex 4).

11. Response to Questionnaires from Industry

11.1 At the last meeting of the Working Group it was reported that some four replies were still outstanding from the holders of 1 CTC and 3 CTXs in response to the MCA's questionnaire to Industry on the use of animal products in human medicines. All replies have now been received with one holder confirming that bovine material was not used and the other three stating that the bovine material was sourced from outside the UK.

11.2 MAFF reported that where action was still outstanding, measures were being taken to follow up respondees. Assurances are being awaited that appropriate action has been carried through. A paper will be put to the Veterinary Products Committee (VPC) shortly.

12. Australian TGA action on Surgical implants

12.1 A copy of a letter sent by the Australian Therapeutic Goods Administration (TGA) to all pharmaceutical/medical device manufacturers in July 1990 was circulated for information. The attention of the Working Group was drawn to the embargo placed on implantable materials of cattle etc. origin sourced from UK/Eire and the request to consider withdrawal of supply of such products and to notify the TGA of stocks in excess of 2 months.

12.2 The MCA has had no feedback from this letter.

12.3 The MDD has had some discussions and correspondence with representatives of the TGA to explain UK actions relating to the use of bovine materials.

13. Guidance on Chemical Methods for Sterilization of Animal Tissues

The chapter on "Control of Harvesting Techniques" from "Guidance on Chemical Methods for the Sterilization of Animal Tissues used in Medical Devices" was circulated in draft form with a request from MDD for advice and comment on the content.

The Chairman suggested some editorial changes and amended minor aspects of the text, but did not consider any major amendment necessary and it was agreed that this should provide a useful document. It may require a preface to explain its limitations, since the paper omits any reference to the effects of these processes on the nature of the materials and their suitability and fitness for use after treatment. It was suggested that the MDD may wish to consider whether to extend the scope of the chapter to cover viruses as well as bacteria. However it was thought that detailed discussion of the content of the chapter was more appropriate and relevant to some other body such as Biologicals sub-committee and thence CDSM.

14. Vaccine Stocks

Dr David Taylor declared a non-specific, non-personal interest in [redacted] and took part in the discussion.

Dr Richard Kimberlin declared a specific personal interest and did not participate in the discussion but remained in the meeting.

The Working Group considered that the Secretariat should explore with the Company the possibility that the unadsorbed vaccines which had limited usage should be replaced with batches using bovine materials which complied with the guidelines, especially where the stock out date extended beyond 1991. There may be some commercial loss to the licence holder but it is unlikely to be very large. See Annex 5 for list of vaccines concerned.

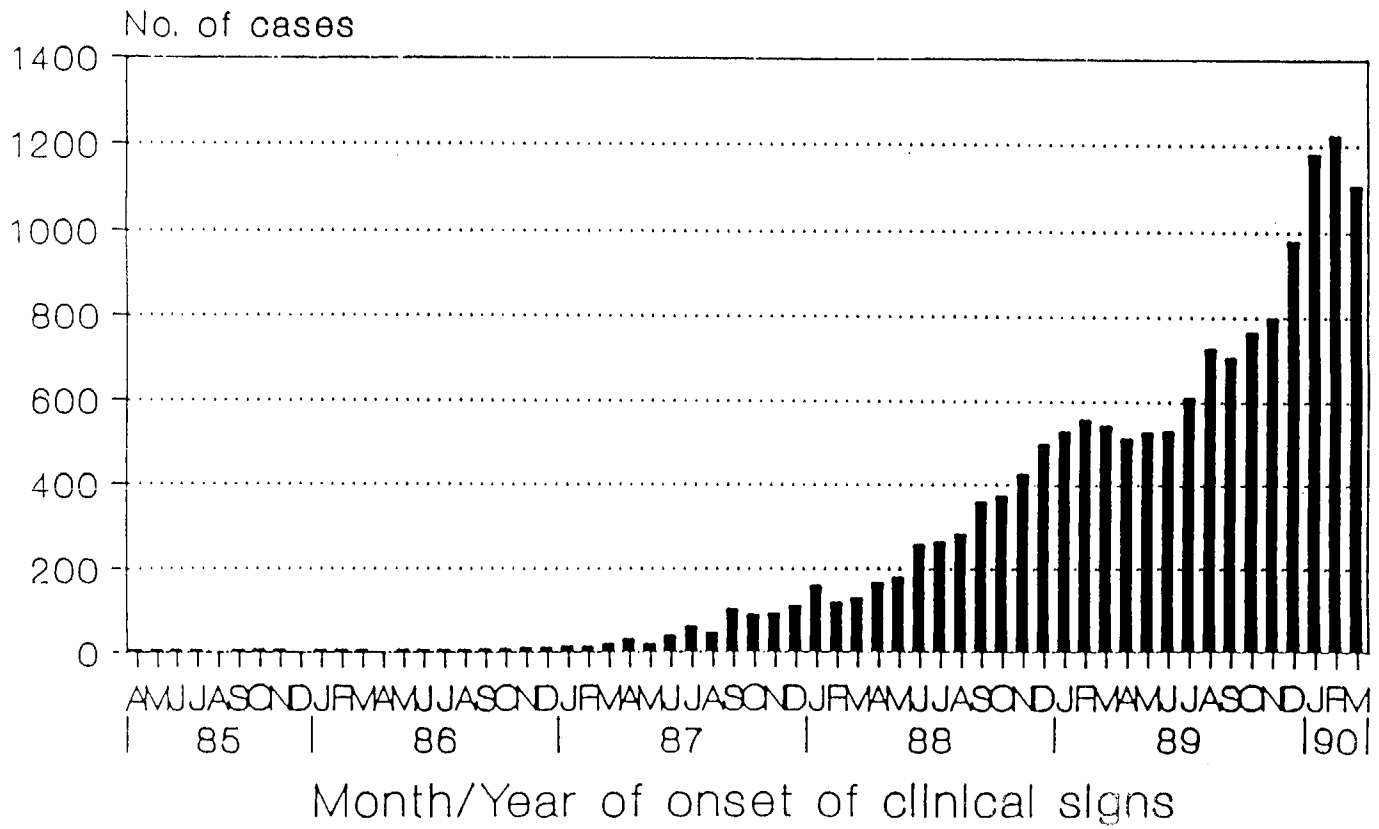
15. Any other business

There was none.

16. Date and Time of Next Meeting

A provisional time and date was set:- 2.30pm at Market Towers on Wednesday 1st May 1991.

NUMBER OF CASES BY MONTH AND YEAR OF ONSET OF CLINICAL SIGNS
April 1985 - March 1990



ANNEX I

90/10.31/3.8

ANNEX 2

SPONGIFORM ENCEPHALOPATHY ADVISORY COMMITTEE

EXPERIMENTAL TRANSMISSION OF BOVINE SPONGIFORM ENCEPHALOPATHY (BSE) TO A PIG

1. The Committee has considered the implications of recent work at the Central Veterinary Laboratory (CVL) in which pigs were inoculated experimentally with BSE. One of them became sick and was confirmed to have spongiform encephalopathy.

2. The animal was one of eight which were inoculated into the brain and other tissues with a massive quantity of material from the brains of cows suffering from BSE. On the basis of what is known about other spongiform encephalopathies, this method of giving the agent is more likely to lead to disease being transmitted than giving it by mouth. Although spongiform encephalopathy has not been found in a pig in the past, the result of this experiment cannot be ignored.

3. Since this result shows that pigs can get spongiform encephalopathy even though there is no evidence that they have done so in the field, we believe that pigs should no longer be fed with protein derived from bovine tissues which might contain the BSE agent, i.e. those bovine "specified" offals that are already excluded from human consumption. It would make sense to extend this prohibition to feed for all species, including household pets, as a number of other species have now developed spongiform encephalopathies. We are aware that many animal feed compounders and pet food manufacturers are already applying such a ban on a voluntary basis

4. As far as human health is concerned, we do not believe that this interim result requires any further action to be taken.

ANNEX 3. p.1.

DEPARTMENT OF HEALTH AND SOCIAL SECURITY
ALEXANDER FLEMING HOUSE
ELEPHANT AND CASTLE LONDON SE1 6BY
TELEPHONE 01-407 5522 EXT
GTN (2915)

Your reference
Our reference

CMO(87)5

To: All Doctors

2 March 1987

Copies to: Regional Medical Officers
District Medical Officers
Medical Officers of Environmental Health
General Managers of Special Health Authorities for the London Postgraduate Teaching Hospitals
United Kingdom Transplant Service

Dear Doctor

HIV INFECTION AND TISSUE AND ORGAN DONATION

In the light of the recent case where transmission of HIV appears to have occurred when stored skin tissue from an infected donor was used as temporary cover in the treatment of a severe burn, I write to remind you of the precautions needed in respect of any procedure where tissue from one patient is used for another, including when the tissue has been stored before use. The same rules need to apply to tissues such as bone, skin (including that used for tissue culture), bone marrow, amnion, fetal tissues, heart valves, tendons and corneas as are applied for solid organs and for blood.

The doctor who implants the tissue in a recipient has the duty to take every reasonable step to ensure it is fit for the purpose. The same guidelines that are used for selecting blood donors must be used for organ and tissue donors even if the initial removal of tissue was for the benefit of the donor. Living donors must be asked to confirm that they are not in any of the high risk groups detailed below before donations can be accepted from them or their tissue used for the benefit of another patient. Similarly, enquiries should be made in respect of cadaveric donors. Tissue and organs from those known to be in high risk groups should not be used. Within the United Kingdom those most likely to have been exposed to the AIDS virus and therefore at high risk are as follows:-

1. Men who have had sex with another man at any time since 1977.

2. Drug abusers, both men and women, who have injected drugs at any time since 1977.

3. Haemophiliacs who have received blood products at any time since 1977.

4. People who have lived in or visited Africa, South of the Sahara, at any time since 1977 and have had sex with men or women living there.

5. Sexual partners of people in these groups.

In addition it is essential that blood from the donor is tested and found negative for HIV antibodies before the organ or tissue is transplanted. Infection with HIV can occur in adults of all ages and no exception should be made for older donors. As it is possible to establish that HIV antibodies are absent within a few hours of testing, doctors are advised to establish with their pathology laboratories what facilities are available for rapid estimation of HIV antibody status within their districts when such information is likely to be required at short notice.

Special advice has already been issued with regard to the precautions that need to be taken prior to the donation of semen in the treatment of infertility by artificial insemination (donor). (CMO(86)12).

Patients who are known to be HIV antibody positive and those who are in the high risk groups for HIV infection should be asked not to carry organ donor cards and not to present themselves for blood or semen donation.

Yours sincerely

Donald Acheson

SIR DONALD ACHESON KBE
DM DSc FRCP FFCM FFOM
Chief Medical Officer

Enquiries to: Department of Health and Social Security
Alexander Fleming House
Elephant and Castle
London SE1 6BY

Telephone: 01-407-5522 Ext 6110

Further copies of this letter may be obtained from DHSS Store, Health Publications Unit, No.2 Site, Manchester Road, Heywood, Lancs OL10 2PZ quoting code and serial number appearing at top right hand corner.

Annex 3
P. 3

DEPARTMENT OF HEALTH
Richmond House, 79 Whitehall, London SW1A 2NS
Telephone 01-210 5150
From the Chief Medical Officer
Sir Donald Acheson KBE DM DSc FRCP FFCM FFOM

PL/CMO(90)2

To: All Doctors

Copy: Directors of Public Health (Region)
Directors of Public Health (District)
Medical Officers of Environmental Health
General Managers of Special Health Authorities
for the London Postgraduate Teaching Hospitals
United Kingdom Transplant Service

Dear Doctor

26 April 1990

HIV INFECTION, TISSUE BANKS AND ORGAN DONATION

Summary: This letter updates the guidance given in CMO(87)5 concerning the prevention of HIV infection by tissue transplantation. It also gives advice on the issue of consent to testing donors for evidence of HIV infection. It is important to point out that transplantation refers to the therapeutic use of any tissue in another person.

Since March 1987 when I last wrote to you on this topic a bone graft recipient in the United States developed AIDS from an implant from a donor who had initially tested negative for HIV but was subsequently found to be infected. As a result, the Centre for Disease Control (CDC) in Atlanta recommended that "all living donors of bone should be retested at least 90 days after tissue procurement and only bone from living donors negative for HIV antibody on this repeat testing should be distributed for transplantation". (Reference)

In the light of this, I asked the Expert Advisory Group on AIDS (EAGA) to review its advice on testing of tissue and organ donors for HIV antibody. EAGA confirmed the earlier advice that tissues and organs from those at high risk of HIV infection should not be used and suitable enquiries to exclude such organs should be made in respect of both living and cadaveric donors. The advice that it was essential that blood from the donor be tested and found negative for HIV before transplantation was confirmed. In addition, I am advised that it is essential that IN CASE OF TISSUES FROM LIVING DONORS WHICH MAY BE STORED PRIOR TO USE, THE TISSUE SHOULD NOT BE TRANSPLANTED UNTIL A SECOND NEGATIVE TEST AT LEAST 90 DAYS LATER IS OBTAINED. This also applies to semen for artificial insemination. A list of tissues used for transplantation is at Annex 1.

E.R.

Annex 3
P4

Where tissues or organs need to be transplanted from the donor immediately, the recipient should be informed of the extremely small, but unavoidable risk of the transplant being infected at the time when consent to operation is obtained.

The Department of Health has received several enquiries about the need for consent to testing tissue and organ donors for HIV antibodies. As always, explicit consent should be obtained before any living individual is tested for evidence of HIV infection. Further information on the ethical issues of obtaining consent including in the case of cadaveric organ donations are set out in Annex 2.

Yours

Sincerely

Donald Acheson

Reference: Transmission of HIV through Bone Transplantation: Case Report and Public Health Recommendations. MMWR 1988, 37, 597-599.

Enquiries about PL/CMO(90) 2 to: Dr S Lader, Department of Health, Friars House, 157-168 Blackfriars Road, London, SE1 8EU Telephone: 01 972 3220.

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Encs

ANNEX 1 to
Annex 3p. 5

HUMAN ORGANS, TISSUES AND BODY FLUIDS USED FOR TRANSPLANTATION WILL INCLUDE:

Kidneys, heart, lungs, liver, spleen, pancreas, Islet of Langerhans
Cornea
Skin
Dura mater
Heart valves
Trachea
Tendons
Blood vessels
Bone marrow
Bone chips
Ossicles
Fibroblast cultures
Fallopian tube
Amnion
Ova, embryos*
Semen
Fetal serum/tissues/cultures eg thymus, liver, pituitary, brain
Any other tissue used for transplantation

* In the case of embryos, both the maternal and paternal donors must be tested twice for antibodies to HIV. When fresh embryos must be used they should be treated in the same way as ova.

Current procedures for selection and screening of blood donors are not affected by this guidance.

Guidance on Human Milk donation in: PL/CMO(88)13/PL/CNO(88)7 and PL/CMO(89)4/PL/CNO(89)3.

Guidance on consent for use of fetal materials and screening for transmissible disease can be found in "Review of the Guidance on the Research Use of Fetuses and Fetal Material" (Polkinghorne Report). Chapter 6: Consent. HMSO. ISBN. 0 10 107622 3. July 1989.

ANNEX 2 to
ANNEX 3 p.6.

CONSENT FOR TESTING DONORS FOR HIV INFECTION:
ADDITIONAL INFORMATION

Donors

A donor is an individual who offers his or her tissues or organs for transplantation into another individual or individuals, or a patient from whom tissues (suitable for therapeutic use in another person) are removed as part of a therapeutic surgical procedure. In the latter case, before a surgeon places such tissues in a tissue bank or transplants them into another patient he must obtain the patient's consent, and the procedures outlined in this letter and Annex must be followed.

Consent

Specific consent should be obtained before a living donor is tested for evidence of HIV infection.

In the case of cadaveric donations, careful enquiries of relatives should be made in a sensitive manner to exclude as far as possible donors at high risk of HIV infection, around the time that consent for organ donation is requested. It should be explained to relatives that assessing the suitability of organs for transplantation will involve testing for certain infections, including HIV.

Guidelines on consent to donation of cadaveric organs have been set out in the UK Health Departments' document 'Cadaveric Organs for Transplantation, a code of practice, including the diagnosis of brain death', published in 1983.

Relatives who do not wish to be informed of test results

If a clinician is satisfied that infection of a cadaveric donor with HIV would have no implications for the health of others, relatives could be assured beforehand that, if they prefer it, the results of tests will not be reported to them.

Donors found to be infected with HIV

If a living donor is found to be infected it is necessary to proceed as for a patient tested under any other clinical circumstances and for appropriate counselling to be given.

ANNEX 2
to ANNEX 3 p7

When a cadaveric donor shows evidence of infection with HIV, the implications for the health of sexual partners and, in some cases, children of the deceased will need to be considered. Prior assurances to relatives (as in the preceding section) will not relieve clinicians from this responsibility in the exceptional case where the existence of sexual partners or offspring is established after the assurances are given. The question of what information should be given and to whom should be considered on an individual basis by the clinician(s) responsible. Careful and appropriate counselling will also be required.

Attention is drawn to the General Medical Council's statement 'HIV infection and AIDS: the ethical considerations' which was issued to all registered medical practitioners in August 1988.

ANNEX 4

The BSE Working Party's view on } was summarised by the chairman as being covered by the following paragraphs in the Working Party papers

"It is recognised that cattle affected by BSE may be symptomless in the early stages of the disease and even after the stress of being moved to the abattoir would not show any symptoms. Hence a more secure view about the absence of the potential for the presence of BSE in the source herds would be possible, if the Company unequivocally declared that the source herd management meets the requirements of the Department of Health BSE Guidelines. If these are not met in full, then a clear statement that the cattle had never been fed ruminant protein is required.

It is not clear from the Company's answer that the abattoir used is EEC approved ie that ante-mortem examination is carried out.

The production method should be validated to show that BSE is inactivated during the process. A statement that the source cattle have not been fed ruminant protein is also necessary. The acetone recovered from the process should not be re-used in production of further batches of pericardium."

The BSE Working Party were in agreement with the amendment draft pharmaceutical recommendation for CDSM.

E PHARMACEUTICAL RECOMMENDATION

The product licence for } should be renewed, on the following conditions;

1. That the pigs are slaughtered in named EEC approved abattoirs, by electro-stunning.

2. That the pigs have not been fed specified offal based feed stuffs.

3. That the pancreatin used in process is of porcine origin.

ANNEX 5

STOCK OUT DATE EX UK COMPANY, CREWE

Product	Batch No	Stock out Date	Expiry Date
Diphtheria Vaccine Adsorbed		Oct 1991	Nov 1993
Tetanus Vaccine Adsorbed		Dec 1991	Dec 1993
Diphtheria Tetanus Vaccine Adsorbed		June 1991	June 1993
Diphtheria Tetanus Pertussis Vaccine (Adsorbed)		Jun 1991	Nov 1993
Tetanus Vaccine Simple Solution		June 1993*	Nov 1992
Diphtheria Tetanus Vaccine Simple Solution		Dec 1994*	June 1993
Diphtheria Tetanus Pertussis Vaccine Simple Solution		Sept 1992*	March 1993

* The extended stock-out dates for the Simple Solution products are due to their relative low use compared with Adsorbed vaccines. These products are normally retested prior to expiry and this could extend the expiry date up to two years.

Further diphtheria toxoid component is also in-stock, which, if processed into final vaccine, could extend the above time-frames to 1995.

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