Mr Brunning

CENTRAL BLOOD LABORATORIES AUTHORITY: CLINICAL TRIALS OF FACTOR VIIIY

I am replying to the points raised by Treasury in Miss Everest-Phillips letter of the 12 January.

She suggests that there is no parallel between Factor VIII treatment and whooping cough vaccine because any Factor VIII side effects would only involve discomfort. Whilst our advice remains that any adverse effect is most unlikely there is a theoretical possibility that transmission of non-A non-B hepatitis could occur.

Additionally you will be aware that Factor VIII blood products from commercial manufacturers have been known to transmit AIDS in the past before a satisfactory heat-treatment was developed.

Neither of these eventualities is likely to occur but this is the sort of risk which the patient could expect to be protected against by the ABPI guidelines.

The patients would be volunteers in as much as there are alternative licensed products which they could be given. They do not need to 'risk' the new Factor VIII in order to receive treatment.

The clinical trials now proposed are essential to prove the safety of Factor VIII in a manner comparable to that required of commercial manufacturers by Medicines Division. The clinicians involved are reluctant to participate unless patients can be offered compensation in line with the proposals of the Association of British Pharmaceutical Industries (ABPI) in the unlikely event of injury.

I attach a statement from Dr Smithies which provides a clinical statement of the extent of the trial and the unlikelihood of any compensation being required.

GRO-C

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NOTE ON CLINICAL TRIALS OF FACTOR VIIIY AND IXA

Factor VIII and Factor IX are coagulation factors derived from human blood. They are deficient in sufferers of haemophilia A and B. They are manufactured from the plasma of blood collected from volunteer donors.

In the past, methods of extracting these factors from blood plasma have not been effective in inactivating viral contaminants. As a result, haemophiliacs treated with these products have developed a type of hepatitis (non-A non-B: NANB) and more recently AIDS.

New methods are being developed by all producers of Factor VIII and Factor IX (mostly commercial manufacturers) to inactive viral contaminants, in particular HIV the AIDS virus. The Blood Products Laboratory at Elstree has developed a particularly rigorous method of heat treatment for their coagulation factors known as Factor VIIIY and IXA. Preliminary trials show not only that this method is effective in inactivating HIV, a relatively easily inactivated virus, but also it appears to be effective against the NANB agent. There is some evidence that the less rigorously heat treated commercial products do not inactivate NANB. (The virus/agent responsible for this blood borne infection has not been identified and there is no test for it.)

Currently BPL's coagulation factors are being widely used throughout the country for treatment of haemophiliacs who have previously been treated either with commercial or with BPL's non heat-treated products. At the same time, a clinical trial of the product is being carried out on approximately 20 patients who have never received coagulation factors previously (young children and mild haemophiliacs) and who have no evidence of hepatitis. There is a need to extend the trial to about 60 'virgin' patients overall, in order to product statistically valid evidence of the inactivation of NANB agents. A trial of this sort will establish the superiority of the product and assist in the

granting of product licences when these are applied for. For these extra patients to be recruited to the trial an arrangement for compensation in the event of injury needs to be made. From all the evidence so far accumulated there seems every reason to believe that these products are the most safe of any products available in the world. It is therefore most unlikely that any damage will arise from their use.

The patients currently in the trial have been given the product since April 1985 and monitored closely for any evidence of infection or other untoward effect. None has been found. Likewise patients who have previously been given other coagulation factors but are now being treated with BPL's product are being monitored for evidence of transmission of any infection. Again none has been discovered. It seems extremely unlikely that there will be any need for any compensation for patients on this treatment.

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