THE ROYAL FREE HOSPITAL

RESEARCH INVOLVING INVESTIGATIONS ON HUMAN SUBJECTS.

Department: Haemophilia Centre (Department of Haematology)

Head of Department: Name: Professor A V Hoffbrand

Head of Section: Name: Drs P B A Kernoff & E G D Tuddenham

TITLE: HEAT-TREATED HUMAN FACTOR VIII AND POLYELECTROLYTE-FRACTIONATED PORCINE FACTOR VIII IN THE PREVENTION OR MODIFICATION OF FACTOR VIII-TRANSMITTED HEPATITIS IN HAEMOPHIL

OBJECT: To assess whether heat-treated human factor VIII concentrate or PE-fractionated porcine factor VIII concentrate are less likely to transmit hepatitis than routinel used human factor VIII concentrates.

BACKGROUND: The incidence of acute non-A, non-B hepatitis after a first exposure to routine use human factor VIII concentrates (either NHS or commercial) approaches 100%. Therefore, all concentrates probably carry infective transmissible agents. Of particular concern is th high risk of chronic hepatitis following an acute attack.

A major effort is being made by several commercial fractionators to render concentrates non-infective by various procedures. We have been offered two human commercial heat-treated products (US origin) for clinical assessment. Both have been granted clinical trials exempt (CTX) by the DHSS. These products are:

Travenol Hemofil T : CTX 0116/0137A
Armour Factorate Heat Treated : CTX 0231/0038A

Additionally, we use an as yet unlicensed highly purified porcine factor VIII concentrate (Hyate:C, Speywood) on a named-patient basis to treat patients with 'resistance' to human factor VIII. Because of the source of this material, it is most unlikely to carry hepatiti and we should like to assess the product in patients without 'resistance'.

DETAILS OF PROCEDURE: Patients treated with one of these products will be those who have never previously received factor VIII concentrate, and need to be treated with concentrate to prevent or stop bleeding. The most likely groups of patients are (a) newly diagnosed infants with severe haemophilia; and (b) mildly affected adults who require surgery or sustain major trauma. The choice of product in an individual patient will depend on clinic circumstances and product availability.

In accord with current routine clinical practice, blood samples will be obtained before treatment, and then at 1 - 8 week intervals (decreasing frequency) for up to 52 weeks after treatment. The end point of the study will be a change in hepatic chemistry indicative of acute non-A, non-B hepatitis, or the absence of such changes during the follow-up period.

Other Departments involved: Those routinely involved in analysis of clinical blood samples: Chemistry, Dept. of Medicine, Virology and Haematology.

Date of Application: 1 December 1983

Assistants and their responsibilities: Clinical staff of Haemophilia Centre (Medical & Nursing) - administration of therapeutic products and blood sampling.

Patients - Method of Selection: See above

Controls - Method of Selection: No controls

WIll informed consent be obtained from the patients or guardians and from the control subjects?

a) ~~Oral~~
In writing.

b) in the presence of a witness in writing (appropriate form held in Medical Staffing).

Expected number of Patients to be observed: Up to 5

Number and frequency of observations on each patient: See above

Has the Procedure /Dosage been approved as harmless:
If so, by whom:
No. But the risks of both the trial products and standard treatment are well understood.

Drugs - If a drug is involved has approval been obtained from the Safety of Drugs Committee: ~~Yes~~/~~No~~
CTX certificates granted: see above.

Radioactive Substances - If these are involved, has approval been obtained from the Administration of Radioactive Substances Advisory Committee:
Yes/No
N/A

Has this project been submitted to any other Ethics Committee? If so which and was approval granted? Yes/No
No

Are any side effects anticipated: The side effects of porcine factor VIII are not negligible, but considered to be less serious than the certainty of hepatitis. The remote risk of AIDS is considered not to be greater than the risk with routine products, and may be less.
I undertake to report any mishaps or side effects which follow the research to the Ethical Practices Sub-Committee.

I undertake to report to the Committee if any paper in connection with this project is published, giving publication and date.

Signed GRO-C DR. P. KERNOFF Date 1 - DEC 1983

Approved by _____

(Signature only required for staff below Consultant grade).