OUTLINE PROTOCOL

FACTORATE IIB PLASMA HALF-LIFE/RECOVERY

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1. Aim

This study forms Stage I of a proposed investigation into the potential benefits of High Purity Factorate. The results obtained will form the basis of the decision to proceed to Stage II - a trial of Factorate in the prophylactic management of Haemophilia.

2. Objective

The objective of Stage I is to compare the in-vivo half-life and recovery of High Purity Factorate with that of another commercially available Factor VIII concentrate of Intermediate Purity (Hemofil No. 2)

3. Patient Selection

a) All patients will be classified as "Severe Haemophiliacs" i.e. Factor VIII levels less than 1 per cent of normal.

b) All patients must be in non-bleeding state. The last bleed and/or treatment must have been at least 3 days (72 hours) before carrying out the test.

c) All patients will give informed consent, or in the case of those under 16 years of age consent will be obtained from the parents.

4. Patient Exclusions

Patients with antibodies to Factor VIII will be excluded.

5. Patient Numbers

The minimum number of patients required is 12. Two centres will participate, with a minimum number at each centre of 6.

6. Trial Design

Randomized, cross over study.

a) Each patient will receive each product on separate occasions with a minimum washout interval of 3 days (72 hours) between treatments.

b) The order of administration will be randomized.

7. Treatment

a) The products to be used are Factorate High Purity (Armour) and Haemofil (Travenol)

b) The dose given will be calculated in units/kg so that the patient's Factor VIII level will be raised to 50%

c) The dose will be given by i.v. injection, following the normal procedures for the use of Factor VIII.

8) Investigations

a) Blood samples will be collected at the following times

Before treatment	9.00 a.m.
15 mins	9.15 a.m.
3 hours	12.00 p.m.
6 hours	3.00 p.m.
12 hours	9.00 p.m.
24 hours	9.00 a.m.
36 hours	9.00 p.m.
48 hours	9.00 a.m.

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b) The samples will be tested as fresh specimens at each Centre.

b) Each sample will be tested "blind", i.e. the laboratory staff will not be aware of the product used.

d) Each sample will be subjected to two tests of Factor VIII activity

i) a 1-stage assay
ii) a 2-stage assay

(Note: the 2-stage assay is considered the more reliable, but the one-stage assay is that used by American BOB-FDA)

e) The labelled potency of the products used will be validated by laboratory assay. The same batches of each product will be used throughout the study.

f) All samples will also be tested for CAg by two methods.

9. Analysis of Results

It is considered that a difference of 20% in the half-lives of the two products will indicate a clinically significant difference. It is thought that the small numbers of cases is not likely to produce a statistically significant result.

10. Ethics

Informed consent will be obtained from all patients, who will have the right to refuse or to withdraw consent without prejudice to their routine treatment.

The investigators undertake this pilot study on their own responsibility and do not need the agreement of an Ethical Committee. There is no Regulatory implication in this study.

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