REPORT ON THE POLYELECTROLYTE BLOOD FRACTIONATION PROJECT

- SECOND QUARTER 1982

(1)a. The project has not been completed on schedule i.e June 1982. More non-cryo precipitation studies must be completed before this process can be considered as a replacement for our conventional cryo process. A six month extention has been applied for.

Unit No. 9, Wrexham Industrial Estate

The preparation of Hyate:C from cryoprecipitate continues. The pilot plant processing area has been 'unofficially' inspected by Dr. Sloggem and Mr. Haythornethwaite who have both made recommendations for improvement. These recommendations have been implemented where possible; we are studying the feasibility of upgrading our autoclave to comply fully with D.H.S.S. standards. If this cannot be achieved in a cost effective manner we will replace it with the same type as that approved for our 'human' fractionation facility.

- In-House Research & Development

a) Porcine Plasma

The salting out precipitation of Factor VIII:C is very satisfactory at bench level and encourages us to believe that we have a cryo replacement method. However, on scale-up we have found that our capacity to centrifuge out the fine precipitates is limited. We have ordered a new large volume continuous centrifuge which will deal with this problem. The process will then be run through our pilot plant to produce sufficient material for animal studies. This new product will not be used on humans until adequate analytical, biochemical and animal toxicity data is available.

b) Human Plasma

Pilot plant production from human cryo continues. Factor VIII:C direct from plasma will not be attempted until the porcine process is proven. In vivo patient proof that polyelectrolytes remove hepatitis B virus from human preparations cannot proceed until our Clinical Trial Certificate is granted (submission has now been made).

c) Other Research

i) Sterile filtration of either porcine or human Factor VIII preparations usually results in a considerable loss of activity (and therefore yield). An intensive research programme to minimise this loss is now underway The first report from Dr. Robinson is attached.

ii) Hyate:C has now been granted I.N.D. status in the United States. Ten cases will be studied with parallel analytical work being conducted in-house.

iii) Human and porcine fibronectin products are now being produced in our R & D facility for cell culture use. Sales of this type of by-product will automatically improve the economics of fractionating Factor VIII.

iv) Porcine transferrin, another by-product useful for cell-culture, has been successfully purified from porcine plasma.

v) A new topical formulation of porcine fibronectin, fibrinogen and Factor XIII has been prepared for the treatment of surface wounds. Birmingham Accident Unit have helped in the formulation and after animal studies are completed they will conduct a pre-clinical trial, using severely burned patients.

- External Research & Development

i) C.N.T.S.

The C.N.T.S. have indicated their willingness to enter into a sub-licence arrangement with Speywood in order to introduce, on a commercial scale, polyelectrolyte fractionated human Factor VIII. They are well satisfied with their clinical and toxicological findings.

ii) The Royal Free - Liver Unit

Dr. Thomas has proposed a hepatitis study using marmosets. This will begin in the last quarter of 1982, using human Factor VIII 'salted' with hepatitis B prior to purification over polyelectrolytes.

The United States Bureau of Biologicals have also offered to do free chimpanzee studies in 1983.

iii) The Royal Free Hospital

Further batches of 'pure' Factor VIII:C have been prepared using monoclonal antibodies raised to Speywood's antigens. We are now confident in reporting that the single band protein we have produced has a molecular weight of approx. 360,000 and is adequate for amino-acid sequencing studies to begin.

Dr. Goodall has now produced monoclonal antibodies to porcine Factor VIII:C.

Using Dr. Goodall's monoclonal antibodies we have now prepared, in-house, Factor VIII and Factor IX depleted plasmas. For assay purposes these are preferred to naturally deficient plasmas since they provide an absolute zero as the standard. The N.B.T.S. are prepared to conduct controlled trials.

iv) Clinical Research Centre, Harrow

The oral liposome trial, using haemophilic dogs has not yet started.

- Clinical Trials & Licensing

Inveresk Research Laboratories have now completed the LD 50 testing of the amines that could potentially leach from the polyelectrolytes. The results were entirely favourable. (See enclosed). We believe we now have sufficient well documented clinical data to apply for a full product licence. This will be submitted before the end of 1982 along with a Manufacturing Licence Application.

(1)b Change in Nature or Scale of Project

There has been no further change in nature or scale of project since that reported in the first quarter.

(1)c Change of Ownership

There has been no change in ownership of or beneficial interest in the assets provided for the project.

(2) Audited Accounts

1981 already provided
1982 draft accounts enclosed

(3) Project Costs

As per our application.

SIGNED_____

D. HEATH
Managing Director

DATE_____