THE SPEYWOOD GROUP

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HUMAN PROTEIN PLANS

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SPEYWOOD LABORATORIES LIMITED

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INTRODUCTION

Over the past seven years Speywood Laboratories have spent large sums of money researching and developing new protein fractionation techniques. Approximately two thirds of the funds have been expended on animal plasma fractionation, the remaining third on human plasma processes. In the last few years a new technique, the "polyelectrolyte process", has emerged as a practical and exciting alternative to the 40 year old Cohn process.

Whilst the polyelectrolyte animal fractions have far less eventual potential than the human fractions, they are unique to Speywood and offer an ideal base for a small, highly specialised business. To maximise on their potential, Speywood have committed to a new 10,000 sq. ft. facility for production and research purposes, and a comprehensive and costly development programme for the next five years. This plan does not allow for any major expenditure in the human fractionation area.

The human polyelectrolyte process has not been practised on the same scale as the animal process. However, recent production yields, clinical trials and hepatitis tests have adequately demonstrated that the major protein, Factor VIII:C, can be produced economically, is very efficacious and is most probably free of hepatitis infectivity. Other human proteins, which have a vast therapeutic potential and cannot be produced via the classical Cohn fractionation process, have also been successfully isolated. To exploit these developments Speywood originally planned to licence this technology and the products thereof to a major American plasma fractionator. In the light of these recent findings and in view of a new EXCLUSIVE licence from Monsanto, Speywood now proposes to raise the necessary finance to fund the advancement of 'human proteins' through a new venture.

THE NEW VENTURE - MOLECULAR BIOLOGY LIMITED (MBL)

Outline Plan:-

To form a new division, adequately financed to undertake the following:

1) The establishment of a new manufacturing unit for the production of human biologicals, using polyelectrolyte fractionation technology and continuous centrifugal electrophoresis.

2) A research and development programme aimed at providing further therapeutic proteins from plasma and servicing the development of fractionation/purification skills.

3) An external research and development programme, designed to investigate the viability of producing therapeutically proven proteins via the recombinant DNA route.

This highly specialized company will have a base of products from the outset. It should become one of the leading protein fractionation companies in Europe with unique technology that can be applied to natural or synthesised product separation. The research and development plan is intended to provide a second generation of products which do not rely on the finite source - plasma.

Financial Support

£4-5M will be required to fund MBL through the first four years. The National Enterprise Board, Prutec and Celltech are evaluating Speywood's proposals with a view to providing this requirement in the form of equity and loans.

OPERATIONS

1) The Manufacturing Unit

Speywood Laboratories Limited have just spent two years designing and constructing a 10,000 sq. ft. production and research facility for commercialisation of the animal fractions. This unit, on the Wrexham Industrial Estate, is to Medicines Inspectorate standards and should be fully operational by September 1981. → Bovine unit.

It is proposed that this operation be repeated for the human fractions, with the additional facility of a sterile filling and finishing unit. The factory would be on its own site, but also situated on the Wrexham Industrial Estate and leased from the Welsh Development Agency.

The approximate cost of equipping this facility to full D.H.S.S. specification, and providing research laboratories would be £1.25 million.

By the end of year four this unit will employ 61 people. Production.

a) The Raw Materials

The first four products to be manufactured have been developed by Speywood Laboratories and are all derived from cryoprecipitate (the cold precipitated fraction of plasma). Conventional fractionation techniques produce only a crude concentrate of Factor VIII from cryoprecipitate. The other products MBL will produce are normally either denatured by the alcohol process or lost in the purification process.

A supply of cryoprecipitate has been arranged direct with a United States plasma collection company, on a long term contract. Each shipment will have full donor information and the plasmapheresis centres will be open to inspection by the U.K. Medicines Inspectorate.

When the Wrexham manufacturing unit and the products are fully licensed it is anticipated that Speywood will undertake 'contract' manufacture for other European commercial fractionators and transfusion services, who will provide the raw material to be processed.

b) The Products — The markets value/vol.

Factor VIII:C	For the treatment of haemophilia A. - 20 times purer than any competitive product. - Substantially free of hepatitis. - Free of isoagglutinins. - At greater yield than conventional Factor VIII. - Potentially less antigenic.
Factor vW	For the treatment of von Willebrands disease. - 50 times purer than existing treatment - cryo. - Substantially free of hepatitis. - Unique - A vWf concentrate has never been produced before.
Fibronectin	For the treatment of traumatic septic shock & anti-cancer therapy. - Unique - A fibronectin therapeutic concentrate has never been produced before.
Fibrinogen	Hypofibrinogenaemia. - Ultra pure. - Substantially free of hepatitis. (Fibrinogen is in very short supply, it is not produced in the U.S.A. because of the severe hepatitis risk when made via Cohn method).

The Factor VIII:C and vWf are fully developed products. The Fibronectin and Fibrinogen still require considerable development effort to scale up to commercial production scale.

Factor VIII:C will initially be the major product. After 'product licensing' it is envisaged that MBL will be able to capture a large share of the commercial U.K. Factor VIII market. This should drastically reduce the volume of imported finished product from the major U.S. fractionators. Despite the planned increased production throughput at the Blood Fractionation Laboratories, Elstree, it is envisaged that the total requirement for commercial Factor VIII will increase by 5-10% per annum. — for how long?

2) The R & D Programme To Provide Further Therapeutic Proteins

This will be a comprehensive in-house and collaborative programme covering the following:-

a) Polyelectrolyte development - to give greater yields and wider application.

b) Continuous Electrophoretic Centrifugation - to develop this new technique in conjunction with the Atomic Energy Authority, Harwell.

c) Isolation of other proteins - to develop and produce new fractions with therapeutic value using combined polyectrolyte/ continuous electrophoretic techniques.

d) Monoclonal Antibody Research - to produce monoclonal antibodies for diagnostic and therapeutic use.

e) Clinical Research - to test and validate existing and new fractions produced using polyelectrolyte techniques.

f) Product and Process Research - to improve products and processes.

This programme will employ 29 full time in-house and external people at the end of year four.

3) The Genetic Engineering Programme

There are four elements to this programme:-

a) Academic Institute Studies.

b) Scale-up Expression Studies.

c) Industrial Pilot Plant Production.

d) Industrial Production.

a) Academic Institute Studies

A team in Oxford, headed by Professor Brownlee, a team in London, headed by Professor Bevan plus a group at the Royal Free Hospital and the Hallamshire Hospital will be co-ordinated by four MBL employees working in each unit. Dr. Peter Esnouf of Nuffield Biochemistry Department, Oxford will provide coagulation research support.

Objective:- Investigational studies to produce the gene clones and laboratory expression of the following proteins.

Factor VIII:C
* Factor IX
Fibronectin
* Albumin
Fibrinogen
Apo Lipoproteins
* α 1 Antitrypsin
New proteins developed by the in-house research

* Gene clones already available.

This programme will employ directly and indirectly, 32 people by the end of year four.

b) Scale-up Expression Studies

Celltech will be contracted to undertake the expression scale-up development and will be advising through all three stages of research. At least one MBL scientist will be seconded to Celltech.

c) Industrial Pilot Plant Production

This will be undertaken by a British pharmaceutical firm who are well experienced in fermentation techniques and supervised by an MBL scientist. In return for the research the company will be offered the genetically engineered products on reduced licence terms.

d) Industrial Production

MBL will recall its industrial scientists working in the R & D programme, to set up production plant for the manufacture of viable products which have successfully progressed to pilot plant production.

Marketing of proteins produced via the polyelectrolyte process, from conventional sources, will be MBL's responsibility alone. Genetically engineered proteins will be jointly marketed by the collaborating pharmaceutical company and/or other major pharmaceutical houses, under licence, providing always that MBL can first replace its market share of conventional proteins with the synthesised products.