SPEYWOOD LABORATORIES LIMITED

CORPORATE PLAN 1983-85

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FROM: THE CHAIRMAN

SPEYWOOD LABORATORIES LIMITED

CORPORATE PLAN 1983-85

INTRODUCTION

The original plans for the development of therapeutic blood proteins, projected Speywood establishing a viable operation based on porcine FVIII in 1982/3. The company would then develop a highly purified human FVIII, and this product would become a major profit earner in the mid nineteen eighties. These two products would generate adequate funds to finance extensive research in genetic engineering. In this way a synthetic human FVIII would be marketed at the end of the decade as the forerunner of a range of therapeutically useful proteins derived from genetic engineering.

The majority of the Board now recognise that the original plans were unrealistic and that the rate of sales growth projected was unattainable whilst the resources required to establish production, technical support and marketing were underestimated. In 1982 management priorities were poorly selected with funds being diverted to prestige projects, whilst inadequate attention was devoted to the necessities of technical support date for Product Licences, essential production plant and facilities.

During the first quarter of 1983 priority has been given to correcting the matters indicated above. A reappraisal has also

been undertaken to ascertain whether the original plan for Speywood is still viable but on an extended timetable, or whether the company must change its direction and concept in order to ensure future profitability.

There is little doubt that with standard management practice a radical improvement can be achieved so that a loss in 1982 approaching £1.5 million need not reoccur.

The factors that should effect an improvement in profit in 1983 are:-

1. The promotion for Hyate:C that has been sustained in Europe and the U.S.A. since 1981 is now producing results, and sales in March and April at £80,000 for each month will exceed the average level achieved in 1982. Growth is now being demonstrated in those countries where porcine FVIII therapy has become accepted i.e. U.K., Italy and France. In 1983, Hyate:C sales should reach £850,000 demonstrating an increase of £266,000 over the previous year.

2. Research expenditure has been examined in detail, and the projects classified under three broad headings:

   a) Necessary for support of current and future porcine derived products. The external cost is £40,000 in 1983 as back up to Wrexham Internal R & D costs. See Appendix 13.

   b) Projects not directly relevant to current products or Genentech support, which are therefore being terminated as soon as contractually possible. A provision of £100,000 is made in the 1982 accounts, but the cash outflow is being met throughout this year.

   c) Support for the Genentech project. The long term success of the company must be linked to having genetically engineered Factor VIII:C, but providing

the input necessary to support Speywood's side of the Genentech project is going to cost between £100,000 and £200,000 p.a., a cost which cannot be firmly established until the two Chairmen meet in May.

The project is set out in Dr. Wheatcroft's report on Genetically Engineered Factor VIII:C which accompanies this Corporate Plan, and shows that the work is mainly at academic centres like The Royal Free Hospital and Oxford University, with some support from Speywood research scientists.

This is a 5 year programme which is beyond the resources of the Speywood core business.

It has therefore been proposed that a Research Partnership be set up to provide the long term funding and share the anticipated success. B.T.G. and Prutec have both shown an interest in this proposal but it is too early to have a firm plan agreed.

The figures on Schedule 1 of the Appendices contain all the costs which are presently considered necessary, but with a credit of £10,000 per month to represent the contribution made by the Research Partners. The cash flow shows the company cannot support a genetic engineering programme without long term investment.

3. A concentrated effort is to be made to promote the sales of Laboratory and Industrial products which should become commercial in late 1983, contributing sales of £51,000 in the year.

4. Sub-contract work will be considered in the new filling plant and if economically viable could generate an income of £15,000 per month, but this is by no means certain.

5. Administrative costs will be reduced by the closure of the Bingham office, estimated savings of £15,000 in a full year.

6. Wherever possible, Speywood development projects will be supported by P.P.D.S. grants and in this way a further contribution of at least £26,000 will be obtained in 1983.

These factors will have the major impact on Speywood's current losses by increasing the contribution to profit by a sum in excess of £0.5 million.

Certain other action will be necessary in 1983 to ensure the continued efficiency and profitability of Speywood in the longer term.

D.H.S.S. LICENCES

7. It will be necessary for Speywood to obtain a Manufacturing Licence for its plant and a Product Licence for Hyate:C. The first should be available within weeks, the second months - perhaps up to 18 months. Capital investment of £160,000 for additional plant will be essential to ensure compliance with D.H.S.S. requirements. This capital can to a degree be phased but Speywood have tested the patience of the Department to the limits in the past, and would be well advised to now attempt compliance and co-operation. The application for a Hyate:C Product Licence cannot be made until an acceptable blood collection system is in operation at the abattoir.

The capital expenditure considered essential is indicated in Appendix 14 and reflected in the cash flow calculations.

PRODUCT REGISTRATION - APPLICATION

8. These must be submitted to all European territories with the minimum of delay in order to retain our exclusive position under the Monsanto Licence. The Product Licence application for the U.K. Authorities is scheduled to be completed in June and will form the basis of Speywood's application to overseas territories. See Appendix 28 for details.

DEVELOPMENT

9. Internal development expenditure in 1983 will amount to £172,000. The majority of this will be concerned with the improvement of the Hyate:C process. Details of the development programme are given in the Appendix, pages 15 to 21.

MANAGEMENT METHOD AND STYLE

10. A Management Committee has been established and the use of Departmental Budget and Management Accounts to progress and control activities is being introduced. In time this should create greater awareness of a cost/effective approach to decision making.

1983 SUMMARY AND CONCLUSION

The measures outlined should reduce the 1983 loss to £752,000 with a nett cash outflow of £1,014,000. It will be appreciated that creditors for capital and external research expediture at January 1983 were high and will reduce during the year. Capital expenditure in 1983 will be minimised and confined to that essential to obtaining a Manufacturing Licence.

As at December 1983 it is projected that gross profit will have risen from nil at the start of the year, to £57,000 per month. At the same time the monthly expenditure apart from interest and depreciation, will have declined from £100,000 per month to £67,000. However, Speywood will not have attained breakeven. The projected December 1983 loss is £31,000 improving to a £17,000 loss in March 1984.

It is however projected that the company can stay within its cash limit in fact only £900,000 of the £1 million loan stock will have been utilised by the year end.

PRODUCTION OF HUMAN MATERIAL

The fundamental reason for Speywood failing to achieve a breakeven in the next 12 months is the absence of any revenue from products resulting from the processing of human cryoprecipitate.

Such products are considered to be uneconomical due to a high price of imported cryoprecipitate, and impracticable due to the inevitable licensing problems that would arise in employing U.S.A. plasma raw materials, and their association with viral diseases.

Experience to date has also indicated that the FVIII content of this material and the yield achieved after processing is so variable that no reliable commercial forecasts are possible.

It is, of course, possible that a source of cryoprecipitate acceptable to the D.H.S.S. could be identified and that various products, high purity FVIII:C, von Willebrand Factor and Fibronectin could be extracted from this material in adequate quantities to ensure a financial return providing an acceptable (above 50%) gross profit on the total operation. Significant process and clinical development is required prior to these products becoming commercial realities. If this work was initiated it is quite clear that the investment necessary would

exceed any return in the years 1983/4.

The possibility of contract processing human plasma or cryoprecipitate from third parties has been considered, but on first sight this also appears to be uneconomical. A further investment of £150,000 will be required for the human products area. The maximum processing fee likely to be obtained would be 10p per unit, with a marginal cost to Speywood of 3.5p per unit. In addition the plant once having used plasma would have to be dedicated exclusively to this activity. The D.H.S.S. now consider the risk of A.I.D.S. so great, that they have reversed their previous decision to permit a multi-function plant. This is a change of the greatest significance, since the original plans were prepared.

No firm proposals are made at this time, but obviously the Board of Speywood must consider the future handling of human blood products most carefully. Outside advice will be sought. It is appreciated that Speywood originally allowed for human Factor VIII to be its main product from 1984 onwards. However, since that time the exchange rate of sterling to the U.S. dollar has changed so that the price of commercially available cryoprecipitate has effectively increased by 50%. Also the advent of A.I.D.S. has changed the D.H.S.S. attitude towards processing as mentioned previously.

THE FUTURE 1984-85

Sales of both therapeutic and non therapeutic lines should improve in 1984-5. The Appendix contains a summary of the products and their projected performance in the future. Certain interesting new product possibilities exist but as the gestation period of new therapeutic agents is lengthy it is unlikely that they will contribute anything to profit before 1986/7.

To project revenue three to five years ahead for products where development is only just being initiated is highly speculative. At this time an assessment of market potential adequate to justify the deployment of development resources is all that is justified.

Sales in 1984 can be projected at £1,818,000 with a modest improvement in gross profit. Expenses can be controlled and demonstrate only a minor increase over the previous year. However, with the company continuing to operate on a narrow product base losses will continue, even though for the year they are only forecast to amount to £96,000.

Depreciation should balance capital expenditure, so that use of the final £100,000 of the £1,000,000 of loan stock can finance Speywood to December 1984.

In 1985 sales should grow to £2,980,000 with a further improvement of gross profit and providing expenses are controlled Speywood could demonstrate a profit of approximately £250,000. However, any projection for 1985 is somewhat speculative, particularly in view of Speywood's modest record and vulnerability due to its restricted product range.

CONCLUSION

This detailed review demonstrates that as Speywood has been equipped and staffed as a multi product company, it will remain in a loss or marginal profit position while its product range is restricted to porcine products. The prospects for supplementing these with products derived from human plasma are not currently favourable and would require an investment beyond current resources. Genetically engineered products will be available in the future but during the interim period of up to 7-10 years the company as presently constructed will be unable to provide an effective return to its shareholders.

Production is, however, highly volume sensitive and with higher levels of throughput gross margins should improve. Development work presently in train can lead to greater efficiencies, while the plant has been designed for a capacity greatly in excess of volume currently projected for 1985.

Marketing, administration and clinical support expenses are, however, excessive for a company of less than 2.5 million pounds sales. If a rapid increase in volume were to be attempted then, these resources and their cost would have to be increased. This course of action is not recommended.

A possible solution to this problem could be for Speywood to seek any association with a licencee distributor or, preferably a marketing partner. Such an organisation should be able to supply international marketing and health registration resources. These would save Speywood some revenue expense and provide the commercial strength to facilitate more rapid growth.

Although the projected future financial prospects may force a decision of this type it should not be considered a retrograde step.

To date Speywood has relied heavily on its own personnel to promote Hyate:C and the industrial products. This was inevitable as the lines were little known without health registration or major medical reputation.

The question of commercial leverage is also important. A single product company is very limited in its ability to maintain regular stocking of its product. For these reasons distributors for Hyate:C are being sought overseas. A licencee for the U.S.A. appears essential for reasons of F.D.A. acceptance and product liability assurance. It is likely that if this principal of appointing distributors is followed Speywood could eventually develop a wide range of associations with different companies for various territories.

Alternatively, a partnership relationship with an International Organisation able to offer commercial and technical marketing strength in the hospital field is a preferable alternative.

It is accepted that these arrangements will involve some sacrifice of margin but providing this is more than compensated by increased volume there will be no adverse effect on profit. Virtually all production costs are fixed and the present plant is operating at a fraction of capacity.

These ideas are, therefore, to be explored and in the interim any increase in marketing resources or expense will be avoided.

It is accepted that a long term agreement with a marketing partner may be a prelude to a partial or full acquisition, but based on the views recently expressed by the present shareholders this is not a move they would discourage.

FINANCIAL IMPLICATIONS OF A PARTNERSHIP

It is unlikely that negotiations for any arrangement would be completed in time to have a material effect on 1983.

However, if and when beneficial arrangements are concluded we will look for the following changes:

Sales volume to increase to maintain margin.

A saving on Marketing, Administration and Clinical Trials of over £100,000 p.a.

It is too early to be certain that such a partner can be found, or to evaluate the precise benefits, but it is an area which will be investigated.

Improvement in cash flow with lower debtors could be a significant factor.

FINAL SUMMARY AND CONCLUSION

The introduction of good business practice, with financial discipline, will reduce Speywood's loss within the next 12 to 18 months. Effective control of revenue and capital expenditure with tight credit supervision should enable the company to survive on its planned cash resources. The application of routine pharmaceutical practice with essential quality assurance and development back up should ensure lower production costs, higher quality products, and D.H.S.S. approval in the foreseeable future.

The company that evolves from the proposed re-organisation will, however, fall short of the aspirations of the original management. It is unlikely to have a significant role in the supply of high purity Human FVIII:C and certainly will

be unable to fund University Research at a seven figure level as was originally projected. An interest can be maintained in genetically engineered FVIII:C however, providing this is progressed as a co-operative venture.

It would be most unfortunate if the Speywood team, both staff and shareholders, lost sight of the long term aims. If Speywood fails to obtain continued support, its liquidation appears inevitable. Time is inadequate for the company to obtain other backing. It is also apparent that both Monsanto and Genentech have something to gain if they are released from their obligations to Speywood following a liquidation. The know-how Speywood has developed would immediately be lost from the U.K. to the U.S.A.

It is now generally accepted that the performance originally projected for Speywood was unattainable from the outset. The current prognosis is, however, far from mundane as in the pharmaceutical area the opportunities for new therapeutic substances are decreasing rapidly while Speywood has original innovations.

The technology Speywood is developing for the extraction of purified proteins from clean animal blood is proving of significant value in Hyate:C, PDGF, and fibronectin. One can be confident that additional areas will arise.

The superiority and value of human plasma proteins have significantly declined in the last months due to the increasing incidence of fatal serum transmitted diseases. The set back faced by Speywood in the development of human FVIII:C is therefore, of much reduced significance in the longer term.

The reduction of Speywood's external research budget has little relationship to the genuine and productive research effort which has probably not declined at all. With a

greater emphasis being placed on internal development and standards, Speywood in 1983 is likely to evolve as a true high technology company.

If the decision to move towards marketing via a partner is confirmed then this is progressive rather than retrograde. Syntex demonstrated some 20 years ago that early in its life a company involved in high technology therapeutics should concentrate its resources in development and manufacture, leaving sales and marketing to established professionals in the field.

The credibility of Speywood and staff morale are obviously major problems in the immediate future. Providing the support of the shareholders is obtained, these difficulties can be overcome. Products of quality and value are an effective answer to disparaging press reports. Staff, if disillusioned, can seek alternative positions, nobody is indispensable.

The Chairman and General Manager recommend that the Corporate Plan be accepted, and the funding as planned be made available.

Mr. D. E. Seymour
19th April 1983

SPEYWOOD LABORATORIES LIMITED

CORPORATE PLAN 1983-85

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SPEYWOOD CORPORATE PLAN

EXTERNAL R & D 1983 COSTS PER MONTH

RE: GENETIC ENGINEERING PRODUCT	£
Nuffield - Esnouf	3,000
Royal Free - Tuddenham	3,000
Goodall	1,700
Sir William Dunn	7,000
Travel - Sundry - say	1,000
	15,700

SPEYWOOD R & D	
Cambridge - dogs	280
Liver unit - Dr. H. Thomas	1,000
Southampton - Dr. C. Lowe	1,200
I.C.R.F. - Dr. Waterfield (from May)	1,300
	3,780

TOTAL EXTERNAL R & D - PER MONTH	£19,480

NOTE: Genetic costs will also include a proportion of Internal R & D costs.

SPEYWOOD CORPORATE PLAN

CAPITAL EXPENDITURE 1983 - 84

ALL £000's

	NEW EXTENSION	WREXHAM PLANT	ABATTOIR	R&D & Q.C.	TOTAL
1983					
March Quarter	110	-	-	-	110
April	29	5	3	-	37
May	29	6	7	1	43
June	-	4	4	-	8
July	-	13	9	-	22
Aug		15	27	5	47
Sept		5	3	-	8
Oct		8	9	11	28
Nov		8	10		18
Dec		6			6
Total 1983	168	70	72	17	327
	OTHER CAPITAL				
1984					
Jan			1		23
Feb			3		20
March			10		26
Plant modifications (Human)	70				
Depleted plasmas	32				
PDGF	49				
Vehicles & Sundries	24				
Total 1984	175	82	76	17	350

S P E Y W O O D L A B O R A T O R I E S L I M I T E D

Internal Research and Development

Schedule

1.0 Hyate:C Process Development.

1.12 Anticoagulant 1 person 12 weeks

1.13 Determination of Variability of Blood Collection.
1 person ?

1.2 Precipitation of Factor VIII from plasma.
Effect of rate of freezing and thawing on
yield of Factor VIII precipitated from plasma.
1 person 12 weeks

1.3 Polyelectrolyte.

1.31 Autoclaving and Washing.
1 person 2 weeks

1.32 Distribution of Active Group.
1 person 1 week

1.4 Ultrafiltration.
1 person 2 weeks

1.5 Final product stability over sterile filtration
and freeze drying.
1 person 4 weeks

1.6 Optimisation of novel solid phase reagent.
1 person 10 weeks

2.0 Fractionation of Human Cryoprecipitate von Willebrand
Factor Concentrate.
1 person

3.0 Deficient Plasma Development.
1 person 24 weeks
including pilot scale production

4.0 Porcine Fibronectin.
1 person 2 weeks
pilot scale production
awaiting marketing

5.0 Porcine Fibrinogen.
Awaiting pilot scale production
and marketing.

6.0 Porcine Transferrin.
1 person 8 weeks

7.0 Miscellaneous Activities.

1.0 Hyate:C Process Development

In the longer term, it is anticipated that a new solid phase ion exchange resin will be developed to replace the existing EMA polyelectrolytes. A monoclonal antibody purification procedure for the production of a high purity concentrate Hyate:C Mk II is scheduled for pilot scale development in June 1984. However, it is recognised that optimisation in certain areas of the present Hyate:C production process will still be applicable in the event of the adoption of either of the foregoing procedures.

1.1 Blood Collection and Anticoagulant Development

1.11 Optimisation of Blood Collection

This is imperative in order to achieve optimal yield and stability of Factor VIII in the final product. It is anticipated that the introduction of the new knife system, in which anticoagulant is introduced into the blood immediately after collection, should result in considerable improvement in plasma quality.

1.12 Anticoagulant

An anticoagulant will be developed to achieve optimisation in the following:

(a) control of proteolytic activity;

(b) maintenance of physiological pH and osmomolarity of the blood.

Anticoagulants will be assessed by fractionating the plasma through the polyelectrolyte procedure in order to determine yield and purity of the Factor VIII:C.

Proteolytic Activity

Non toxic proteolytic inhibitors eg Heparin, Trasylol, EACA, will be investigated, in addition toxic but 'diagnostic' inhibitors eg PMSF and Benzamidene will be used.

Maintenance of Physiological Ca^+ Levels

The use of Heparin as anticoagulant in the absence of citrate will be investigated. It has been reported by some workers that maintenance of physiological levels of Ca^+ will stabilise Factor VIII:C.

Maintenance of pH and Osmolarity

Better control of pH can be achieved by the use of a more adequately buffered anticoagulant. In addition, the use of Dextrose may serve to maintain the integrity of the red blood cells preventing haemolysis.

1.13 Determination of Variability of Blood Collection. Effect on Yield and Stability of Hyate:C

With optimisation and standardisation of blood collection and anticoagulation, variability in plasma collection throughout the year will be assessed by screening a number of different parameters in the plasma. Subsequently, follow up through the processing of the plasma will determine any trends in variability in yield and stability of the Factor VIII:C.

1.2 Precipitation of Factor VIII from Plasma

Cryoprecipitation is inefficient in terms of recovery of Factor VIII:C and is difficult to control in a large scale procedure. We aim to optimise the precipitation of Factor VIII from plasma by investigating the following:

(a) Salt precipitation using ammonium sulphate;

(b) The use of macromolecules for the specific precipitation of Factor VIII, including

  i Hydroxyethyl starch

  ii Ficoll

  iii PVP

  iv Dextrose

(c) Optimisation of cryoprecipitation eg continuous controlled thawing procedure.

(d) Optimisation of rate of freezing and thawing of plasma.

Each precipitation method will be investigated with relation to yield, purity and stability of Factor VIII over the polyelectrolyte procedure, and also with respect to yield

and purity of other potentially valuable proteins eg fibronectin, fibrinogen.

1.3 Polyelectrolyte

Due to the longer term strategy of replacement of the EMA PE's, minimal work will be carried out on the present material.

1.31 Autoclaving and Washing

To complete the study on PE leakage, experiments are to be carried out to determine the effect of autoclaving and prolonged storage at acid pH on ligand leakage and deterioration of the PE as seen by GC analysis.

1.32 Distribution of Active Groups

Titration of the active group will be examined in several batches of PE in order to determine inter-batch variation. A further project may result from this work concerning optimisation of PE equilibration time during fractionation procedures.

1.4 Ultrafiltration

At the present time, recovery of Factor VIII from the high salt PE eluate is achieved by precipitation with polyethylene glycol. This procedure is not only inelegant but results in contamination of the final product with PEG 4000, a material which is difficult to quality control adequately.

The Millipore cassette ultrafiltration system has already been used effectively for the recovery of Human Factor VIII:C. The same system will be evaluated for Porcine Factor VIII:C.

1.5 Stability of Final Product

Stability of Hyate:C in the freeze dried formulation is not optimal. The product is found to deteriorate at +5°C. Instability may be due to physical instability of the highly pure Factor VIII:C or proteolytic degradation. The inclusion of stabilisers over the final

sterile filtration and freeze drying process is to be investigated. A selection of polysaccharides and pharmaceutically acceptable proteolytic inhibitors and also toxic but diagnostic proteolytic inhibitors will be tested.

The yield of Factor VIII will be determined both over filtration and subsequently in the freeze dried state, in an accelerated degradation study at 37°C. It is anticipated that stabilisers may serve to stabilise FVIIIP:AgF activity over freeze drying, this will also be investigated.

1.6 Development of Novel Ion Exchange Resin

The production of possible resins will be undertaken at the University of Southampton. Testing of promising reagents will be carried out at Wrexham. Gels will be tested with respect to yield and specificity for Factor VIII:C.

2.0 Fractionation of Human Cryoprecipitate

At the present time, Wrexham does not have the facilities to fractionate Human Cryoprecipitate for potential clinical use. It is believed that the risk of contamination of porcine products with Hepatitis B or an AIDS causative agent cannot be risked.

In order to determine the clinical efficacy of von Willebrand Factor, it will be necessary to negotiate with an outside agent to carry out the fractionation of 2 Kg of cryoprecipitate using polyelectrolyte.

To this end, we are optimising a procedure for the isolation of von Willebrand Factor from PE supernatant using an ion exchange procedure. We are aiming to achieve an improved product to that already developed in that it will be isoagglutinin free, and of higher purity. If possible, demonstration of clearance of Hepatitis B surface antigen by the procedure will be demonstrated, in addition the material can be heat treated by the method already developed at Speywood.

It is anticipated that data will be available defining such a process by the end of May.

3.0 Deficient Plasmas

3.1 Factor IX

A Factor IX deficient plasma is now available for marketing.

3.2 Factor VIII

The Factor VIII deficient plasma is still under development. It will be necessary for suitable plasma to undergo screening using both haemophilic and von Willebrand plasmas, in order to demonstrate the suitability of Factor VIIIR:Ag free plasma as a substrate.

Considerable input from R and D will be required during pilot scale development for preparation of immunoadsorbants.

4.0 Porcine Fibronectin

Porcine fibronectin has been isolated to two levels of purity. A precipitation method to achieve 60% purity for tissue culture grade, and a higher purity of more than 85% by affinity chromatography. The materials are undergoing assay for cell spreading and then the methodology will be introduced into the pilot plant.

5.0 Porcine Fibrinogen

A methodology is available for scale up in the pilot plant. Awaiting marketing.

6.0 Porcine Transferrin

This project has been low key up to the present time. Emphasis on this fractionate will be increased.

7.0 Additional Services

R & D staff are involved in providing continuous back-up to both Quality Control and Production.

7.1 Production of antibodies for the QC of Hyate:C and other products.

7.2 Iodination of antibodies for CRP Kit.

7.3 Hyate:C - trouble shooting.

7.4 Factor VIII Assay - R & D has been involved in the whole saga of unit definition and is currently involved in the development of a standard assay reagent.

7.5 Pilot Plant development - all R & D staff are involved in pilot plant development where appropriate.

SALES OF CURRENT PRODUCTS

1. HYATE:C £000's

Forecast	1983	1984	1985
Sales	780	1,500	2,400
Gross Profit	45%	50%	60%

It is projected that a U.K. product licence will be issued in the first half of 1984 which should lead to wider acceptance of the product in both U.K. and overseas. With increased sales the margin will improve, as costs for Hyate:C are particularly volume sensitive. Significant development is currently being undertaken to improve the Hyate:C process which should result in higher yields and an improved quality product.

Prices in Europe should be held or moderately improved. The appointment of a licencee for the U.S.A. will involve the supply of material at a reduced price, and this will to some extent offset the benefits of cost reductions.

INDUSTRIAL AND RESEARCH PRODUCTS

2. P.D.G.F. (Platelet Derived Growth Factor)

This is obtained from Porcine platelets that are seperated from plasma at an early stage after blood collection at the abattoir. The I.C.R.F. (Imperial Cancer Research Fund) have devised a process for extracting P.D.G.F. in relatively pure and stable form. The product accelerates growth in cell tissue cultures, can be used in synthetic alternatives to foetal calf serum and as a research tool.

The present source is from outdated platelets from blood banks and is of unreliable quality. Speywood should obtain a position of a reliable commercial supplier of a high quality product.

23

£000's

Forecast	1983	1984	1985
Sales	22.5	80	150
Gross Profit	60%	60%	60%

In fact the marginal gross profit is virtually 100% as the raw material is currently wasted. Production employs current resources, and requires negligible additional plant.

3. FIBRINOGEN

This is the Porcine supernatant at the end of the Hyate:C process. It would form a replacement for Bovine Fibrinogen currently used by manufacturers of microbiological culture media. We have a firm enquiry from Oxoid and a positive response to our samples. A trial order has been supplied.

£000's

Forecast	1983	1984	1985
Sales	21	60	120
Gross Profit	50%	50%	50%

As in P.D.G.F. the marginal contribution is virtually 100%.

4. FIBRONECTIN

Human fibronectin is an article of laboratory commerce at £5000 per G. but in short supply. We are to develop a market for a porcine product. It is used as a research tool.

£000's

Forecast	1983	1984	1985
Sales	7.5	18	40
Gross Profit	60%	60%	60%

Marginal contribution - 100%.

5. DIAGNOSTIC PRODUCTS

No increase in this area as forecasts on new product availability from Hybritech and Speywood have proved unreliable. Unless a financially attractive disposal can be negotiated the products

will be retained, but with promotion limited so that a breakeven is assured.

As and when new lines become available additional margin will be obtained, but it is considered unwise to forecast any increased revenue. The problem with these products is that whether they are Speywood originals or Hybritech they make little if any contribution to production - overheads.

NEW SOURCES OF REVENUE

6. ROYALTY INCOME

Sub licensing of our polyelectrolyte technology for the fractionation of human cryoprecipitate or plasma is permitted under the Monsanto licence. This could provide a route for the preparation of a highly purified FVIII possibly free of risk from hepatitis and A.I.D.S. It is unlikely to have general application, but a demand has been identified for special patients.

It is necessary for Speywood to perfect the method of fractionation, but to do this on "bought in" human cryoprecipitate would be expensive. It is planned therefore to work with B.P.L., Elstree who are interested in obtaining access to polyelectrolyte technology. In this way Speywood can acquire know-how for subsequent licensing to third parties.

The returns to be obtained from such arrangements could be significant as total usage of human FVIII in Europe amounts to hundreds of millions of units per annum. Even if only 10% of the market was converted to high purity material a royalty of 1 or 2 pence per unit could add in excess of £100,000 to Speywood revenue.

This matter is to be pursued but is currently too speculative for the provision of a firm forecast.

NEW PRODUCTS

7. THERAPEUTIC

The safety of Hyate:C, in addition to its value in treating inhibitor patients, is now becoming accepted. This follows the improvements made in purity over the last 6-12 months. Further progress is planned, but it is also theoretically possible to produce a product of ten-fold improvement in quality by the application of a monoclonal purification system.

A "super pure" porcine FVIII would be completely free of hepatitis or A.I.D.S. risk and could well be an acceptable alternative to human FVIII in selected patients. Further marketing and technical feasibility studies are necessary before committing research funds to this project. It is however highly attractive economically as it would maximise the added value to be obtained from the present porcine production investment both in the plant and at the abattoir. The only additional capital investment would be at the purification stage.

The product is unlikely to be available commercially before 1985, so no projected sales have been included. However it is reasonable to assume that such a product would achieve sales equal to those of Hyate:C. An addition of £250,000 to £500,000 to profit in 1987/8 would therefore be quite possible.

8. FIBRONECTIN

There is clinical interest in the application of Fibronectin as a wound healing agent and in the treatment of D.I.C. (Disseminated Intravascular Coagulation). Clinical feasibility studies are to be undertaken. If therapeutic value is identified potential sales could be in excess of £1,000,000 so that minor development expenditure is justified.

9. INDUSTRIAL

There is a considerable gallonage of porcine cryoprecipitate supernatant going to waste at present. We have several commercial possibilities:-

An ingredient in specialised cosmetics.
(Firm enquiry from Boots)

Specialised animal feedstuff supplement.

Ingredient for a foetal calf serum substitute.

None of these have progressed to the stage where firm sales projections can be made. However trials would be minimal and no health registration required.

In general it will be our policy to capitalise on our clean blood collection resource and exploit our animal blood fractionation technology.

NEW PRODUCTS SUMMARY

There is considerable room for commercial expansion within the area of porcine blood fractionation, adequate to ensure Speywood's growth over the next 5 to 7 years prior to the availability of genetically engineered FVIII:C. The areas selected are synergistic to current production technology and will therefore demand little additional capital investment.

The products will be novel and suitable for marketing via distributors, licencees or partners enabling Speywood to concentrate on its true role as a development and production company.

SPEYWOOD CORPORATE PLAN

GRANTS 1983

£000's

R.D.G.

CAPITAL BALANCE from period to 31st Dec 1982 £175K

Release 20% average in 1983	35
New Capital 1983 £396	
22% R.D.G. £87. CASH INCOME	
Release 20% average half year	8
Total R.D.G. P&L Release	43

P.P.D.S.

Old Claims Capital Balance £53K	
Release 20% in 1983	10
Revenue released 1982	
NEW P.P.D.S.	
Total R&D 300	
Claims - say 100 at 33% = 33	
100 at 25% = 25	
58 annual rate	
In 1983 half year average	26
Capital will be spread - insignificant	—
TOTAL P.P.D.S.	36
TOTAL 1983 GRANT RELEASE TO P&L	79

Research grants will be diligently persued wherever possible against the necessary expediture, and the above figures are considered a conservative minimum.

HYATE:C - DISTRIBUTOR AND PRODUCT LICENCE STATUS BY TERRITORY

Territory	Distributor	Target Appointment Date	Product Licence Application Date	Target Registration Date	Local Clinical Trial Requirement
U.K.	Speywood Labs.	Appointed	July 1983	Oct. 1984	Yes
U.S.A.	Armour or Cutter	Dec 1983	April 1984	April 1985	Yes
CANADA	Armour or Cutter	Dec 1983	Feb 1985	Oct. 1985	Yes
FRANCE	Brocades	Dec 1983	Not required	-	No
SWITZERLAND	Speywood GmbH.	Appointed	Dec 1983	Dec 1984	No
W.GERMANY	Speywood GmbH.	Appointed	Dec 1983	Dec 1984	No
AUSTRIA	Schwab or Germania Pharmaz-eutika	Dec 1983	Not required		
ITALY	Kabi-Lang	Appointed	Oct. 1984	Oct .1985	No
SPAIN	Hemoresearch Labs.	Appointed	Oct.1985	Oct. 1986	Yes
DENMARK	Danapharm	June 1983	Oct. 1984	Oct. 1985	No
SWEDEN	Pharmacia	June 1983	Oct. 1984	Oct. 1985	No
NORWAY	Collett Marwell Hauge	June 1983	Oct .1984	Oct. 1985	No
FINLAND	Orion	July 1983	Oct. 1984	Oct. 1985	No
HOLLAND	C.N.Schimdt or Tramedico or Brocades	Dec 1983	Dec 1983	Dec 1984	No
BELGIUM	C.C.P. or Brocades	Dec 1983	Dec 1983	Dec 1984	No
AUSTRALIA/ NEW ZEALAND	C.S.L. or Protea	Dec 1983	Oct 1984	Oct. 1985	No
JAPAN	Tashin Mitsui or Chugai Boyeki	Dec 1983	June 1986	June 1991	Yes
S.AFRICA	Bioclones	Dec 1983	Feb 1985	Feb 1986	Yes
ISRAEL	Migada	Dec. 1983	Dec. 1984	Dec 1985	Yes

It should be noted that discussions on the appointment of distributors are still at an early stage in the following territories: U.S.A., Canada, France, Holland, Belgium, Japan, S. Africa, and Israel.

Furthermore, sales can be made in all of these territories (with the possible exception of Japan) on a named patient, or similar, basis. i.e. before registration is applied for or granted.

Information on local clinical trial and registration requirements is our current best guess, and based on limited information. Each licensing authority has been contacted to determine precise requirements and distributors will also be able to advise on requirements, feasibility and costs.

ALL £000's

SPEYWOOD LABORATORIES LIMITED - CORPORATE PLAN

PROFIT & LOSS 1983 - 1985

	1982 ACTUAL	3 MONTHS TO MARCH 1983	1983 APRIL	MAY	JUNE	JULY	AUG.	SEPT.	OCT.	NOV.	DEC.	TOTAL 1983	1984 JAN.	FEB.	MARCH	TOTAL 1984	TOTAL 1985
TURNOVER																	
Animal	584	150	80	80	60	75	75	75	75	90	90	850	90	110	110	1500	2400
Diagnostic	18	12	5	5	5	5	5	5	5	5	5	57	5	5	5	60	60
Research & Industrial	10	-	-	-	2	2	3	6	8	12	18	51	10	15	15	158	310
Contract Manufacture	-	-	-	-	-	-	15	15	15	15	15	75	15	15	15	100	120
	612	162	85	85	67	82	98	101	103	122	128	1033	120	145	145	1818	2890
COST OF SALES																	
Animal	335	82	44	44	33	40	40	40	40	49	49	461	45	52	52	680	1080
Diagnostic	12	9	3	3	3	3	3	3	3	3	3	36	3	3	3	36	36
Research & Industrial	6	-	-	-	1	1	2	3	4	6	9	26	5	7	7	78	160
Adverse Production Variance + Contract	232	70	10	10	15	10	10	10	10	10	10	165	10	10	10	100	120
	585	161	57	57	52	54	55	56	57	68	71	688	63	72	72	894	1396
GROSS PROFIT																	
Animal	17	(2)	26	26	12	25	40	40	40	46	46	299	50	63	63	820	1320
Diagnostic	6	3	2	2	2	2	2	2	2	2	2	21	2	2	2	24	24
Research & Industrial	4	-	-	-	1	1	1	3	4	6	9	25	5	8	8	80	150
	27	1	28	28	15	28	43	45	46	54	57	345	57	73	73	924	1494
OVERHEADS																	
Marketing:																	
Therapeutic UK & Europe	107	21	9	10	10	7	7	7	7	7	7	92	7	7	7		
Therapeutic USA	25	6	3	3	3	3	3	3	3	3	3	33	3	3	3	210	280
Other Products + Diagnostics	122	15	6	7	7	5	5	5	5	5	5	65	5	5	5		
Administration	271	60	20	20	20	18	18	18	18	18	18	228	19	19	19	240	260
Development - Internal R & D + Pilot	137	46	15	15	15	15	12	12	12	15	15	172	12	12	12	160	180
Clinical Trials, Registration & Licences	148	20	5	5	5	5	5	5	5	5	5	65	5	5	5	80	60
Depreciation	108	36	18	18	18	20	20	20	20	20	20	210	22	22	22	270	320
Interest	55	15	6	7	8	9	10	10	11	12	12	100	12	12	12	150	150
TOTAL OVERHEADS	973	219	82	85	86	82	80	80	81	85	85	965	85	85	85	1110	1250
Grants Receivable	82	12	4	5	6	7	8	8	9	10	10	79	10	10	10	150	150
Profit/(Loss) Trading	(864)	(206)	(50)	(52)	(65)	(47)	(29)	(27)	(26)	(21)	(18)	(541)	(18)	(2)	(2)	(36)	394
External R & D	(380)	(67)	(18)	(19)	(19)	(19)	(19)	(19)	(19)	(19)	(19)	(237)	(15)	(15)	(15)	(180)	(150)
Genetic Eng. Contribution	-	-	10	10	10	10	10	10	10	10	10	100	10	10	10	120	120
Exceptional Costs	(110)	(10)	(10)	(4)	(10)	(10)	(4)	(4)	(4)	(4)	(4)	(64)	(4)	(4)	-	-	-
TOTAL LOSS	(1354)	(283)	(68)	(65)	(84)	(66)	(42)	(40)	(39)	(34)	(31)	(752)	(27)	(11)	(7)	(96)	364

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SPEYWOOD LABORATORIES LIMITED - CORPORATE PLAN

BALANCE SHEETS 1983-1985

All £'000	DEC. 1982	MARCH 1983	1983 APRIL	MAY	JUNE	JULY	AUG.	SEPT.	OCT.	NOV.	DEC 1983	1984 JAN.	FEB.	MARCH	DEC. 1984	DEC. 1985
FIXED ASSETS																
N.B.V. Opening	260	1028														
Net Additions	867	110	37	43	8	22	47	8	28	18	6	23	20	26	350	300
Depreciation	99	36	18	18	18	20	20	20	20	20	20	22	22	22	270	320
	1028	1102	1121	1146	1136	1138	1165	1153	1161	1159	1145	1146	1144	1148	1225	1205
CURRENT ASSETS																
Stock and Work in Progress	191	200	205	210	220	225	225	225	225	225	225	225	225	225	240	320
Debtors - Sales	341	230	250	260	240	260	275	275	275	290	300	300	325	335	360	520
Grants	217	200	135	100	60	40	35	30	15	15	20	20	20	20	30	30
	749	630	590	570	520	525	535	530	515	530	545	545	570	580	630	870
CURRENT LIABILITIES																
Creditors - Revenue	477	357	360	372	351	352	350	330	330	330	330	320	320	330	350	400
Capital	192	78	48	33	23	34	51	48	56	54	52	55	55	41	50	50
Hire Purchase Creditors	65	50	46	43	40	37	33	30	30	30	30	30	30	30	50	50
Bank Overdraft	100	396	376	354	314	280	250	201	227	178	214	257	299	332	399	245
	834	881	830	802	728	703	684	609	643	592	626	662	704	733	849	745
NET CURRENT ASSETS	(85)	(251)	(240)	(232)	(208)	(178)	(149)	(79)	(128)	(62)	(81)	(117)	(134)	(153)	(219)	125
TOTAL	943	851	881	914	928	960	1016	1074	1033	1097	1064	1029	1010	995	1006	1330
Loan Stock	-	100	200	300	400	500	600	700	700	800	800	800	800	800	900	900
Share Capital	160	190	190	190	190	190	190	190	190	190	190	190	190	190	190	190
Preference Shares	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000
Share Premium Account	1383	1453	1453	1453	1453	1453	1453	1453	1453	1453	1453	1453	1453	1453	1453	1453
Revenue Reserves	(725)	(2079)	(2079)	(2079)	(2079)	(2079)	(2079)	(2079)	(2079)	(2079)	(2079)	(2831)	(2831)	(2831)	(2831)	(2927)
Profit(Loss) to Date	(1354)	(283)	(351)	(416)	(500)	(566)	(608)	(648)	(687)	(721)	(752)	(33)	(50)	(63)	(96)	364
W. Alexander Loan	250	250	250	250	250	250	250	250	250	250	250	250	250	250	250	250
Preferred Revenue	229	220	218	216	214	212	210	208	206	204	202	200	198	196	140	100
FUNDING TOTAL	943	851	881	914	928	960	1016	1074	1033	1097	1064	1029	1010	995	1006	1330

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SPEYWOOD LABORATORIES LIMITED - CORPORATE PLAN
CASH FLOW 1983-84

All in £'000

	3 MONTHS TO MARCH 1983	1983 APRIL	MAY	JUNE	JULY	AUG.	SEPT.	OCT.	NOV.	DEC.	TOTAL 1983	1984 JAN.	FEB.	MARCH	
INCOME															
Sales	141	65	75	87	62	83	101	103	107	118	942	120	120	135	
Regional Development Grant	17	67	-	40	25	6	8	7	8	3	181	8	8	8	
P.P.D.S. Grant	15	-	38	4	-	5	3	15	-	-	80	-	-	-	
V.A.T. Recovery only	34										34				
CAPITAL LOANS - BTG/PRUTEC	200	100	100	100	100	100	100	-	100	-	900				Total 900 leaving 100 for 1984
TOTAL	407	232	213	231	187	194	212	125	215	121	2137	128	128	143	
PAYMENTS															
Revenue	545	115	133	174	115	94	148	131	146	152	1753	151	150	136	
Capital	158	97	58	17	38	70	15	20	20	5	498	20	20	40	
TOTAL	703	212	191	191	153	164	163	151	166	159	2251	171	170	176	
Net Flow	(296)	20	22	40	- 34	30	49	(26)	49	(36)	(114)	(43)	(42)	(33)	
Opening Bank O/D	100	396									100				
Closing Bank O/D	396	376	354	314	280	250	201	227	178	214	214	257	299	332	

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SPEYWOOD LABORATORIES LIMITED - CORPORATE PLAN

ALL IN £000's

CASH FUNDING 1983 TO 1985

	1982 ACTUAL	3 MONTHS TO MARCH 1983	1983 APRIL	MAY	JUNE	JULY	AUG.	SEPT.	OCT.	NOV.	DEC.	TOTAL 1983	1984 JAN.	FEB.	MARCH	TOTAL 1984	TOTAL 1985
PROFIT (LOSS)	(1354)	(283)	(68)	(65)	(84)	(66)	(42)	(40)	(39)	(34)	(31)	(752)	(33)	(17)	(13)	(96)	364
ADD BACK DEPRECIATION	99	36	18	18	18	20	20	20	20	20	20	210	22	22	22	270	320
CAPITAL	(867)	(110)	(37)	(43)	(8)	(22)	(47)	(8)	(28)	(18)	(6)	(327)	(23)	(20)	(26)	(350)	(300)
STOCK	(26)	(9)	(5)	(5)	(10)	(5)	-	-	-	-	-	(34)	-	-	-	(15)	(80)
DEBTORS- SALES	(158)	111	(20)	(10)	20	(20)	(15)	-	-	(15)	(10)	41	-	(25)	(10)	(60)	(160)
GRANTS, ETC.	(220)	17	65	35	40	20	5	5	15	-	(5)	197	-	-	-	(10)	-
CREDITORS - REVENUE	274	(135)	(1)	9	(24)	(2)	(6)	(23)	-	-	-	(182)	(10)	-	10	40	50
CAPITAL		(114)	(30)	(15)	(10)	11	17	(3)	8	(2)	(2)	(140)	3	-	(14)	(2)	-
NET FLOW	(2252)	(487)	(78)	(76)	(58)	(64)	(68)	(49)	(24)	(49)	(34)	(987)	(41)	(40)	(31)	(223)	194
BANK O/D MOVEMENT	324	296	(20)	(22)	(40)	(34)	(30)	(49)	26	(49)	36	114	43	42	33	185	(154)
DEFERRED GRANTS	188	(9)	(2)	(2)	(2)	(2)	(2)	(2)	(2)	(2)	(2)	(27)	(2)	(2)	(2)	(62)	(40)
	(1740)	(200)	(100)	(100)	(100)	(100)	(100)	(100)	-	100	-	(900)	-	-	-	100	-
SHAREHOLDERS LOANS	-	200	100	100	100	100	100	100	-	100	-	900	-	-	-	100	-
SHARE CAPITAL	1740																

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