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CONFIDENTIAL

The Chairman and Managing Director of Porton International.

SPEYWOOD LABS JULY, 1984

1) CURRENT STATUS

During the April - June 1984 quarter SPEYWOOD Labs achieved a virtual financial "break even" due to bouyant sales in May and a significant improvement in production efficiency. A useful base from which to progress to full commercial viability has now been established. Certain steps should be taken in the second half of 1984 to ensure continued progress in later nineteen eighties.

a) DISTRIBUTION

The present state of discussions with possible distributors was outlined in the paper "General Managers Report" of June 29th. My advice in this connection would be to reach a satisfactory understanding with Cutter for the U.S.A. and Canada which would involve a 20pence per unit C.I.F. floor price for Hyate C. Then proceed with a further round of negotiations, involving presentations by the potential distributors for the E.E.C. Spain and Scandinavia. The first priority for potential distributors being, Immuno, Armour and Cutter. A decision in respect of the Western European countries is urgent, but action for Africa India Japan and S.East Asia can be deferred.

Speywood has no sales or marketing staff, and this situation should be rectified after the distributors commence selling and produce adequate revenue to fund additional management. A single London or Wrexham based executive should be adequate to monitor performance in the U.K. U.S.A., Canada, Latin America, Eastern Europe, Africa and Asia. A European based executive with linguistic ability is essential to ensure optimum performance in European territories. Appendix 1 provides an outline of these executives functions.

It is assumed that the European distributor will also have a francise for the U.K., as it will be uneconomic to establish a sales and marketing organisation for just one country. The U.K. based sales executive can however, maintain direct contact with key haemophilia specialists.

b) PRICE

18 months ago Hyate C was priced at 16 pence per unit to U.K. and European hospitals. The previous management considered that a low price in comparison with the two competative products F.E.I.B.A. and Autoplex was appropriate. This policy was a disaster. When distributors are employed then any price to hospitals has to be discounted by 30% - 50% to arrive at the net return to Speywood. The company's operating expenses with the utmost economy are unlikely to be less than £150,000 per month. It follows, therefore, that a 16 pence list price involves a less than 10p net return and a monthly sales performance in excess of 1.5 million units is necessary to achieve break even. If Speywood was only to move into profit after sales of 1.6 units per month say 20 million units a year had been achieved then an operating loss was inevitable until Speywood had made a significant penetration of the U.S.A. market. Hyate C cannot be sold in the U.S.A. until F.D.A. approval has been obtained which is likely to be 12 months after D.H.S.S. clearance in the U.K.. In fact it is doubtful whether the company could have ever been profitable on a 16p list price.

In view of the above, considerable emphasis in 1983/4 has been placed on increasing the price of the product to hospitals. This has not been easy as many of the major users had been conditioned to the low prices. The policy adopted has been to :-

Raise prices at 3 / 4 month intervals by increments of 5 pence per unit.

Allow major users discounts for quantity purchases over a 6/12 month period to soften the blow of the price increase.

It is planned over future months to raise the minimum quantity to qualify for the discount.

It is also current policy to allow potential customers free material for so called "CLINICAL TRIALS" to satisfy themselves of the products efficacy prior to attempting a commercial sale.

FOR SPEYWOOD TO BE PROFITABLE HYATE C MUST HAVE A U.S.A. LIST PRICE OF OVER $0.60 per unit A EUROPEAN LIST PRICE OF £0.40 OR MORE.

It should also be a clear policy to set list prices at the above levels or greater, but in line with F.E.I.B.A. or AUTOPLEX who ever is the market leader in a particular territory.

It is unwise to expect a distributor to pay for stock which he has to give away for clinical trials. He will only want to take a larger margin which costs Speywood more in the long run.

The accepted policy in the pharmaceutical industry is to provide free stock to capture the major customer, and then use confidential discounts to retain the big user.

There is a considerable reluctance amongst the technical staff, Sarah Middleton and Anne Walton particularly and Lewis and Heaf to a lesser extent to accept the necessity for realistic prices. In particular Sarah and Anne feel most embarrassed at negotiating increased prices. Lewis will also resist the appointment of a sales executive, but such a man is fundamental to study, plan and negotiate prices and other commercial terms.

Dennis Waine and David Jones are very sound commercially. There are no other employees in the company capable of making proper decisions on prices or contract terms. The women in particular are very muddled in their thinking on the morality of increased prices, rather than the immorality of operating a company at a loss.

Advice on Hyate C commercial policy from all staff other than Waine and Jones is based on an unlimited fund of inexperience. There appears to be a feeling that marketing small quantities of Hyate C at a loss will ensure investment and diversification into other products which will in some way improve their job security.

If Speywood is to be viable it is essential that the Management of Porton International become closeley involved in Hyate C pricing policy.

c) PRODUCTION

It should now be possible to produce 1 million units of Hyate C a month on a regular basis. This is more than is required for immediate sale, however, production at this level should continue : -

1) To provide stock for the 2 month hold period which is necessary if we are to be allowed a 10 month shelf life in our product licence.

ii) To create a 4 to 6 week inventory of finished goods. This is essential to cover for emergencies.

iii) When i and ii have been completed then clinical trials can be extended via distributors, should sales not have advanced sufficiently to absorb all production. It is quite normal in the pharmaceutical industry to establish the use of a product by clinical trials with free material and then move into commercial sales after 6 months.

iv) After i to iii have been achieved changes should be made to tighten the limits on the product. The D.H.S.S. expect a continued improvement in standards over the first 3 years of a products life. Efforts made in this connection involve the risk of batch rejection and so it is wiser to make changes when production is surplus to sales requirements.

d) QUALITY CONTROL

Chris Ilott the quality control manager should be given the maximum support. It is normal for production procedure and practice to be somewhat flexible during the development phase of a plant or product. However, once a product licence is issued a higher degree of discipline is essential. At this stage of Speywoods development it would be quite normal for 1 or 2 batches to be rejected each month. Production should be pressed on their technical standards up to, and occasionally beyond their capability.

The Q.C. manager must have immediate, direct and confidential access to top company management. A situation must never arise when production management can "pull rank" on Q.C.

e) DEVELOPMENT

David Heaf currently reports to Dr. Lewis. He is fully engaged on Hyate C. production improvement schemes. It is doubtful if he can be profitably diverted from this work before the end of the year. This fact may cause some frustration.

2) FUTURE ACTION

a) R. D.N.A. FVIII

The Genentech / Cutter situation requires to be progressed. Different distributors for different E.E.C. markets for R. D.N.A. FVIII is likely to be untenable. This implies that the European Hyate C distributors may not obtain the franchise for R.D.N.A FVIII when it becomes available. This could be a problem when negotiating the Hyate C distribution rights.

b) Production

i) Filling and freeze drying should be transferred into Speywoods plant and out of C.P. Pharmaceuticals. Hand filling in the sterile area should be avoided as the more personnel inside the area, the more the risk of contamination. Ideally the mechanised filling line should be capable of generating a full freeze drier load in one shift (i.e. half a day). It is essential that Q.C. sampling and work be reduced, this can best be achieved by sterilizing and filling the largest batch in one day.

Currently 10% of Hyate C is lost in Q.C.sampling. This is excessive but each shift comprises a batch demanding a specific quantity for sampling, hence small batches greatly inflate Q.C. work and expense. If Speywood achieves £5 million sales of Hyate C per annum via distributors, the capacity of the sterile area will only be utilized to 1 week a month or less.

ii) A scource of porcine plasma adequate for 20 million units per year should be made secure. This implies the establishment of a permanent blood processing plant at a major abattoir where the pig thoughput is ensured. The present portacabin installations can only be considered temporary facilities. Detailed study of possible sites and alternative blood processing methods needs to be undertaken over the next six months, to ensure that any new establishment can come into operation at the end of 1985.

A continuous supply of porcine plasma is essential to the viability of Speywood. This raw material cannot be purchased in the open market, and the labile nature of the product implies that the holding of a 6 month reserve stock is impractical.

Doctors and patients now depend on Hyate C. An inability to supply could result in death, as patients now live a less protected life style. If Speywood could not supply Hyate C for a month doctors and Haemophilics would never trust the company again. Hyate C and Speywood would be finished. Porton would lose £4. million in just four weeks.

c) Future Development and new products.

In mid 1985 it will be generally recognised that porcine FVIII represents the ideal treatment for haemophiliacs with inhibitors and also the one off treatment of normal haemophiliacs when special precautions are essential to eliminate any risk of hepatitis or AIDS. The potential market for the product will be 30 - 50 million units per annum at a net price to hospitals in excess of 25pence. A product of this £10 million p.a. potential with a gross profit of 75% will attract competition.

The Monsanto patent on the polyelectrolyte provides no real protection to Hyate C, as an alternative way of employing affinity chromatography to purify porcine FVIII could be devised.

In view of this Speywood should develop an improved MK II Hyate C, as a defence against any alternative porcine FVIII. This can be achieved by employing a new polyelectrolyte and/or a monoclonal purification.

The polyelectrolyte must be outside the Monsanto patent as otherwise it will be considered an improvement and they will have rights to it. It is inadviseable to use the Monsanto polyelectrolyte plus a monoclonal as the improved product will still be subject to the Monsanto and Johnsons royalties.

The new product objective will be to create a purer product having 5x - 10x the specific activity of Hyate C. This will reduce the incidence of side effects, lower the risk of allergic reactions and probably reduce the incidence of amenestic response. It is generally accepted that the amenestic response , that is the production by the patient of inhibitors to porcine FVIII, is exacerbated by the totalchallenge to the system of foreign protein. The higher specific activity will automatically reduce the total protein being injected.

A product with higher specific activity will tend to be unstable, so that formulation development will be essential.

The interesting feature of this research project are the related benefits that could arise. A new polyelectrolyte could be used to extract human FVIII from human plasma. (ELSTREE?) or the purification of R. DNA FVIII from fermentation broth (GENENTECH). Also the formulation studies could be useful for the formulation of R. DNA FVIII as and when this becomes available.

Sarah Middleton has already written an outline of the development project for the polyelectrolyte. David Haef has certain ideas on formulation studies.

APPENDIX I

MARKETING EXECUTIVE.

DUTIES

Assist management in negotiating distribution agreements, become the accepted point of contact with the distributor

Negotiate and agree with each distributor a Hyate C marketing plan for each country. Matters to be included in the marketing plan : -

a) Projected local sales to be achieved by units, price and hospital on quarterly basis.

b) Agree distributors purchase plan quantity time and price and incorporate into a production requirements forecast.

c) Check promotional activities by representatives visits, agree actual hospitals to be visited, special group meetings, promotional clinical trials congresses and exhibitions.

d) Monitor performance (In view of the specialised nature of the products there would be little difficulty in centralising copies of each distributors local invoices and so obtain a precise record of prices and usage).

e) Study the activity of competitors, determine Autoplex and FEIBA sales, price usage in each territory and hospital.

f) Maintain direct personal contact with every key specialist in haemophilia (Opinion Leaders) in each country.

OTHER DUTIES

The marketing executives will also be required to survey the market potential for possible new products. They should be capable of defining the product profile, possible price and project likely growth rate and avenues of distribution.