HPVIII - INTERIM ARRANGEMENTS
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INTERIM ARRANGEMENTS FOR SUPPLY OF HPFVIII

THE BRIDGE

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HP FVIII SUPPLY - 1991 - 92 - THE BRIDGE

1.0 REQUIREMENT

The SNBTS development plan for H.P. FVIII has set a target date of February 1992 for initiation of clinical trials of product produced exclusively at P.F.C..

Subsequent operational targets are as follows:

(a) exclusive supply of HP VIII by January 1993

(b) receipt of product licence by mid 1994

The acceptability of this development and supply programme by Haemophilia Directors is based upon an additional requirement that the SNBTS initiates supply of HP FVIII with immediate effect for specific patient groups. Moreover it is anticipated that the demand for HP VIII during the interim period Jan'91 - Jan'93 will increase progressively throughout this 24 month period. For the purpose of planning the following HP FVIII demand has been estimated.

Jan 91 - Jan 92 - 4.0×10^6 iu
Jan 92 - Jan 93 - 9.5×10^6 iu

2.0 EXTERNAL FACTORS AFFECTING DEVELOPMENT/SUPPLY PROGRAMME

The most significant external factors affecting the supply capabilities of the SNBTS both in the short and longer term are:

(a) implementation of new organisational/shift arrangements within P.F.C.

(b) coincidence of the development programme with the major PFC building programme

In particular the impact of (b) requires PFC to stockpile significant (~ $8\text{-}10^6$ iu FVIII) stocks of FVIII to protect against building programme slippage. The product stockpile will require to be HP FVIII.

3.0 PRODUCTION AND SUPPLY PLAN 1991 - 1992

An outline production and supply plan has been developed. This is attached.

The main features of this plan are:-

(i) Immediate supply of HP FVIII purchased from Lille CRTS.

(ii) Contract manufacture of HP FVIII (at Lille) from PFC intermediate material (cryo or purified FVIII - S8) and supply of this material from July 1991.

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(iii) Routine manufacture of HP FVIII at PFC from January 1992.

(iv) Discontinued manufacture of Z8 from March 1992.

(v) Accumulation of approx 6.5 x 10^6 iu HP FVIII and 2.0 x 10^6 Z8 stock prior to Phase IV building programme.

(vi) Availability of 1.5 x 10^6 iu FVIII (or plasma equivalent) for development programme.

4.0 QUALITY ASSURANCE AND REGULATORY ISSUES

4.1 Supply of CRTS Material (Jan-June 1991)

It is necessary to establish whether this material will be supplied under CTX (cover) or named patient basis. The former arrangement will delay product availability by up to 3 months and it is therefore proposed that a named patient basis be adopted for the supply of Lille material.

In any event the SNBTS will require to notify the D.O.H. of importation of non-licensed material.

4.2 Arrangement for Contract Manufacture from PFC Cryo

The product supply programme calls for a proven and validated technology for the contract processing of PFC cryo or intermediate product to be available by April 1991. This technology is likely to differ in detail from that currently operated at CRTS, Lille.

This contract manufacturing arrangement requires detailed consideration of the following key issues.

(a) Responsibility for quality control of product and product release ie will the product be considered an SNBTS or CRTS product?

(b) Will the product carry an SNBTS or CRTS label?

(c) Requirement for manufacturing documentation to support chosen contract arrangement.

(d) Status of "clinical trial" for contract manufactured product ie CTX or named patient basis.

(e) Product dose size (ie 250 iu, 500 iu, 1000iu etc)

Proposal

The advantages of a contract arrangement which places the responsibility for manufacture with the SNBTS are significant.

- SNBTS will be seen to supply its own HP FVIII by mid 1991.
- SNBTS will be able to apply for a P.L. earlier than previously anticipated on the basis of contract material product.

The disadvantages are:

- requirement for SNBTS to audit manufacturing and QC arrangements at CRTS Lille.
- C.R.T.S. do not have a manufacturing licence and P.L. application for contract manufactured product would require UK inspection.
- design and implementation of such an arrangement would be a major distraction from the main development programme.

It is proposed that, for the likely duration of the contract arrangement, intermediate materials processed at CRTS be returned as CRTS product. This is considered to be the operationally simpler arrangement.

5.0 SPECIFIC ACTION REQUIRED

The following specific management actions is now required to facilitate the detailed planning for the interim product supply arrangements.

(a) Define customer requirements for HP FVIII during 1991 and 1992 (including N. Ireland).

(b) Determine product and contract processing costs at CRTS, Lille.

(c) Identify funds available during the next 24 months to support the required supply arrangements.

(d) Agree regulatory issues including clinical trial arrangements.

(e) Define technology and SOP's for contract manufacturing arrangements by April 1991.
Document from PF/R.McI attached.

(f) Subject to (a) to (e) above it may be necessary to modify the SNBTS production/supply plan. An initial draft plan is attached.

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