Appendix VI 0010

PFC REPORT FOR SHS HAEMOPHILIA/SNBTS DIRECTORS MEETING (MARCH 1986

1.0 SUPPLY AND DEMAND (FACTOR VIII)

1.1 Demand

Best estimates (from RTC's) for FVIII demand in Scotland and Northern Ireland in 85/86 are as follows:

Table I

Centre	Vials At 230	IU x 10^6 At 230
Aberdeen	1,900	0.44
Belfast	12,500	2.8
Dundee	1,800	0.41
Edinburgh	9,000	2.07
Glasgow	18,000	4.14
Inverness	2,000	0.46
Total	45,200	10.32

THUS THE ESTIMATED DEMAND FOR 85/86 IN SCOTLAND AND NORTHERN IRELAND IS 1.58 x 10^6 IU/10^6 POPULATION.

1.2 FVIII Stock (March 86) and Production Output 85/86

TABLE II

Plasma Stock March 86	Product Stock at March 86			Plasma Intake kg 86/87	Production Output 86/87	PFC+RTC Stock March 87
	PFC	RTC	Total			
5,000	5.9	1.84	7.74	60,000	11.40 x 10^6 IU	9.25

1.3 See Table III.

TABLE III

TRENDS IN FVIII MANUFACTURE AND SUPPLY

Year	Fresh Plasma Delivered to PFC kg	Fresh Plasma into Process kg	Process Yield IU/kg	Factor VIII Production IU x 10^6	FVIII Issued to RTC's IU x 10^6	PFC Finished Product Stock IU x 10^6	Plasma in Stock at 31 March kg
1983/84	54,520	60,120	270	13.9	12.5	1.6	3,567
1984/85	57,750	53,000	265	13.41	7.9	6.54	8,609
1985/86	56,000	60,000	190	11.40	(9-10)**	5-9	5,000
1986/87*	60,000	60,000	190	11.40	(11-12)	5.3	5,000
1987/88*	70,000	70,000	>190	13.3 - 17.5	17-18***	1.6-4.8	5,000

* Estimates.

** PFC issue figures to RTC's in 85/86 are estimates because:

(a) Batch dedication system introduced.
(b) Product recall, rework and reissues.
(c) No stable supply period during which meaningful calculations of product issues could be made.

*** Figure assumes that demand will reach 2.75 x 10^6 IU/10^6 population.

1.4 Comments on FVIII Supply and Demand

(a) It is estimated that current demand (9-10 x 10^6 IU) is now approaching the limit of production output on the basis of existing plasma supplies (11.4 x 10^6 IU from 60,000 kg plasma).

This situation has been reached earlier than anticipated as a result of substantial yield losses (25-30%) on heating product and significant increases in demand.

(b) While substantial National stocks of FVIII exist (9-12 months supply), Haemophilia Dirctors are asked to comment on the validity of the assumption that demand may begin to exceed production output in 1986/87 ie demand will rise to 1.75 x 10^6 IU/10^6 population.

(c) In the light of (b) above, plans are in hand to increase output by:

(i) Improved manufacturing technology.

(ii) Improvements in plasma quality.

(iii) Increased plasma input to PFC commencing in 1987/88.

It is likely that (iii) will make the major contribution to this development and it has been calculated that an additional 30,000 kg of plasma will be required to achieve a production output equivalent to 2.75 x 10^6 IU/10^6 population (assuming existing yields and plasma quality).

2.0 SUPPLY AND DEMAND (FACTOR IX)

2.1 Estimates of usage of this product are as follows:

TABLE IV

	Factor IX	
	Vials @ 300 IU	IU x 10^6
1982/83	3,646	1.10
1983/84	4,782	1.43
1984/85	3,800	1.14
1985/86	8,000	2.4
1986/87	10,-12,000	3.6

2. Comments on FIX Supply and Demand

(a) There is no doubt that demand for this product has increased markedly over the past 3 years.

(b) Haemophilia Directors are invited to comment on the assumption that demand will escalate further now that FIX is heated and probably non-infective.

In particular, the author is aware of trials of this product in the treatment of liver disease and anticoagulant reversal therapy. These applications combined with an anticipated increased use in the treatment of Haemophilia A and B suggest that demand in 1986/87 may reach 12,000 vials per annum (3.6×10^6 IU).

3. HEAT TREATMENT OF COAGULATION FACTOR CONCENTRATES

3.1 Factor VIII

In January 1985, PFC distributed heat treated FVIII (68°/2 hr) to all centres in Scotland and Northern Ireland and this material was used until September/October 1985 when a new formulation product, heated at 68° for 24 hrs was issued. At the time of writing there have been no reports of HTLV III seroconversion following the use of either of these products although equally it is recognised that the current heat treatment regime is unlikely to produce a non-infective product with respect to NANB or Hepatitis B.

These encouraging results are reinforced by the absence of reports (internationally) of HTLV III seroconversion following the use of commercial products which have been subjected to similar heating conditions.

Most recently unconfirmed reports have emerged which suggest that HTLV III may be less susceptible to heat inactivation that was originally thought. In response to these reports, PFC has recently recalled all residual stocks of 68°/2 hr material.

Directors will be aware that the Blood Products Laboratory are currently issuing a FVIII product which has been heated at 80°/72 hrs and preliminary clinical data indicates that this material is non-infective with respect to HTLV III, NANB and Hepatitis B. While it is unlikely that the current PFC product could be successfully treated under these conditions, a major development programme has been underway for 12 months with a view to the production of a high purity FVIII product which can be formulated and heat treated, under conditions which give comparable levels of viral inactivation. Such treatment may not require such vigorous heating conditions.

A collaborative scientific programme has now been established with Professor Robin Weiss so that viral inactivation (HTLV III) procedures can be validated using live HTLV III. This contrasts with our previous reliance on published data from other organisations and control authorities.

3.2 Factor IX

Heat treated FIX (80°/72 hrs) is now at routine issue. Extrapolation of the clinical data derived from the BPL FVIII (80°/72 hrs) product would suggest that PFC FIX is likely to be non-infective. Extensive animal studies (dogs) indicate that heated PFC FIX carries no additional risk of thrombogenicity.

4. BATCH DEDICATION OF FVIII

A system of batch dedication of FVIII has now been in operation since early 1985 and has operated successfully. This system of product issue will continue until a safe non-infective product is at routine issue.

5. DEVELOPMENT OF NEW PRODUCTS IN 1986/87

5.1 Factor VIII

Directors will be aware that PFC has been pursuing the development of a new FVIII product which is high yielding, high purity and non-infective. This programme of work has been afforded the highest priority over the past twelve months.

A pharmaceutical manufacturing process has now been developed which gives access to FVIII with a purity of >50 IU/mg protein and in high yield. Work is now in hand to formulate this material into a form suitable for a viral inactivation process which gives comparable levels of viral kill to the current BPL product which so far has proven to be non-infective.

A programme of in-vitro characterisation and animal studies has been initiated and it is likely that the product will be ready for Phase I clinical studies in April 1986.

5.2 Von Willebrand Factor

The technology used for the manufacture of FVIII above is equally applicable to the isolation of VWF as a pure fraction.

Directors are invited to comment on the potential demand for such a product if it were to be made available.

5.3 Factor VII

PFC currently produces a four factor concentrate (PPSB) to meet the small but significant demand for FVII. This product cannot be heat treated and consumes substantial RTC and PFC resources in its production.

A specific FVII concentrate is now under active development as a replacement for PPSB and Directors are invited to comment on the potential demand for such a product in the treatment of both FVII deficiency (congenital) and in the treatment of liver disease in conjunction with DEFIX concentrate (II, IX and X concentrate).

5.4 Anti Thrombin III (AT III)

This product is now included in the formulation of Heat Treated DEFIX. Hitherto supplies of AT III have been obtained from BPL for this application and also for the treatment of congenital AT III deficiency.

The strategic importance of this material is now such that PFC is actively developing an AT III concentrate and Directors are invited to comment on the potential demand for this product specifically in the context of congenital AT III deficiency.

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10 January 1986

WP Ref: rjp.imm S/DFVIII.DOC - DOC 002