APPENDIX VI

0009

NOTES FOR HAEMOPHILIA DIRECTORS' MEETING (FEBRUARY 1987)

1. INTRODUCTION OF NEW FACTOR VIII PRODUCT (Z8)

Plans are now well advanced for the introduction of a new Factor VIII preparation which compares with the existing (NY) product as follows:

	Existing Product (NY)	New Product (Z8)
Specific Activity	0.3 IU/mg protein	0.7 IU/mg protein
Fibrinogen Content	2.3 mg/IU	1.0 mg/IU
Heating Regime	68°/24 hrs	80°/72 hrs (initial supplies will be heated at 75°/72 hrs)
Yield	190 IU/litre plasma	300 IU/litre plasma
Solubility	Variable	Improved

- It will be noted that the new product is of higher purity, virucidally safer and paradoxically substantially higher yielding (improvement of >50%).

- Product development has required that initial batches of product are heated to 75°/72 hours. All batches manufactured since January 1987 are heated to 80°/72 hours.

- Virus inactivation studies, using live HIV and a range of model viruses are underway.

- Subject to satisfactory clinical trials (T 1/2 and recovery) it is hoped to obtain full regulatory approval for this product by late April '87.

- Assuming a continued fresh plasma input to PFC of 60,000 kg per annum (Scotland and Northern Ireland) the potential product output from PFC will be 18×10^6 IU FVIII.

  This equates to 2.57×10^6 IU/10^6 population and provides a comfortable margin in respect of National Self-Sufficiency.

- Product stocks at the present time are as follows (Jan '87):

  NY (68°/24 hrs) - 3.15×10^6 IU

  Z8 (75°/72 hrs) - 1.2×10^6 IU

  Z8 (80°/72 hrs) - 0.3×10^6 IU

- It will be necessary to agree a plan for phasing out NY product and phasing in Z8. PFC has discontinued the manufacture of NY since July '86 enabling a reduction of National FVIII stocks (NY) and opportunity to build up stocks of Z8.

2. FACTOR IX

There appears to be an inexorable increase in the usage of FIX in Scotland and Northern Ireland.

Issue trends for FIX (Scotland and Northern Ireland are as follows:

Year	Vials	IU x 10^6
82/83	3,646	1.10
83/84	4,782	1.43
84/85	3,800	1.14
85/86	6,100	1.83
86/87*	10,000	3.00
87/88**	13,000	3.90

*Estimate based on first 3 quarters of 86/87.

**Estimate based on previous trends.

- Increased demand together with significant losses on heating continue to place increasing pressure on the supply situation for this product. At the present time PFC can only supply this material for the treatment of Haemophilia (A and B).

- Batch dedication remains impracticable.

3. NEW PRODUCT DEVELOPMENTS

(a) FVII

It is hoped that pilot batches of this material will be available for in-vitro and animal studies in the Spring of '87. This product will eliminate the need for PPSB (4 factor concentrate).

(b) AT III

The technology for this product is similar to that used for FVII manufacture. It is hoped that pilot batches of product will be available for study before December '87.

(c) Product for Treatment of Inhibitor Patients

Anecdotal reports have emerged (locally and internationally) which suggest that heat treatment of FIX preparations have reduced their efficacy in the treatment of FVIII inhibitor patients.

Preliminary studies (SNBTS) suggest that FEI8A heated at 80°/72 hrs retains its in-vitro biological activity and it may be that the reports of the failure of heated IX to control bleeding may be batch related or associated with the presence of AT III in the PFC FIX product.

It is suggested that Haemophilia Directors continue to use FIX (DEFIX) for the treatment of those patients and attempt to establish whether "reduced efficacy" is indeed batch related.

Such information is likely to contribute to our ability to develop a specific product for inhibitor patients.

4. PRODUCT PRESENTATION

PFC are exploring the possibility of introducing a 500 IU dose vial within the next 12 months and also hope to standardise the existing vial content at 250 IU.

It is understood that these "packaging" developments would be regarded as very desirable by Haemophilia Directors and would also reduce storage space requirements by Haemophiliacs themselves and RTC's.

R J PERRY
15 January 1987