IN CONFIDENCE

NOTES FOR SCOTTISH HEALTH SERVICE HAEMOPHILIA CENTRE/
TRANSFUSION SERVICE DIRECTORS' MEETING:
FEBRUARY 1987

January 1987

JDC/SHID/1/87/2
These notes have been produced to facilitate discussion with regard to future SNBTS planning for the production of blood products required for the management of patients with haemostatic or thrombotic disorders, within the Scottish Health Service. All annual figures contained in these notes refer to years ending 31st March and do not include Northern Ireland.

I am indebted to SNBTS Director colleagues who have been responsible for providing, through the national statistical returns, much valuable information, and in particular to Dr Perry for information on PFC's activities (Appendix VI).
FACTOR VIII CONCENTRATES

FRESH PLASMA PROCUREMENT FOR FACTOR VIII

The progress made in previous years has been maintained (see Appendix I). The total annual SNBTS figures (Kg) can be summarised as follows:-

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>35,748</td>
<td>40,739</td>
<td>51,017</td>
<td>52,480</td>
<td>53,005</td>
</tr>
</tbody>
</table>

Note: Attention of colleagues is drawn to the first recorded fall in FFP to PFC. This is regarded as significant and is likely to be due primarily to the impact of increasing platelet therapy support and the increased use of cryoprecipitate. At the present time the overall SNBTS blood collection programme has not been significantly affected by the AIDS publicity.

ISSUES OF FACTOR VIII CONCENTRATES

The figures below provide a summary position of trends since 1981 (details in Appendices II and III), and are derived from issues from PFC to RTC and cryoprecipitate from RTCs to Wards or Haematology Departments:-

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Cryoppt. (donations)</td>
<td>17,855</td>
<td>12,953</td>
<td>11,646</td>
<td>12,693</td>
<td>16,801</td>
</tr>
<tr>
<td>Intermediate VIII/ new formulation (m.i.u.)</td>
<td>4.70</td>
<td>4.86</td>
<td>9.26</td>
<td>7.40</td>
<td>5.52</td>
</tr>
</tbody>
</table>

COMMERCIAL FACTOR VIII CONCENTRATES

The information obtained by the SNBTS is summarised below (m.i.u.) (details in Appendix IV):-
1.40  1.04  0.11  0.03  0.13*

* This material was of porcine origin for an inhibitor patient in the West.

SUMMARY (Details in Appendix V)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Cryoppt.</td>
<td>1.78</td>
<td>1.27</td>
<td>1.16</td>
<td>1.27</td>
<td>1.68</td>
</tr>
<tr>
<td>P F C</td>
<td>4.70</td>
<td>4.86</td>
<td>9.26</td>
<td>7.40</td>
<td>5.52</td>
</tr>
<tr>
<td>Commercial</td>
<td>1.40</td>
<td>1.04</td>
<td>0.11</td>
<td>0.03</td>
<td>0.13</td>
</tr>
<tr>
<td>Total</td>
<td>7.88</td>
<td>7.17</td>
<td>10.53</td>
<td>8.70</td>
<td>7.34</td>
</tr>
</tbody>
</table>

COMMENTS:

1. Fall in Use of Factor VIII Concentrates
   The activities in 1984/85 of establishing batch dedication produced, we believe, some falsely high issue figures. Nevertheless, there is reason to believe that there has been a significant true fall in the use of factor VIII concentrates in the SHS in the last 12 months. This conclusion is supported by the most recent data from Oxford. We have assumed this relates to the AIDS problem.

2. Future Production Targets
   In the light of these trends SNBTS Directors have shelved all plans to further increase FFP production (for PFC) above the 1984/85 figures. At the present time it is proposed that should increased demands arise then these will be met by improved yields (see Dr Perry's report: Appendix VI).

3. HIV (SNBTS) Activities
   (a) New definitions of high risk donors have been made operational. A further revision is in the process of consultation.
   (b) Donation Screening Tests
       A SNBTS Group (Chaired by Dr Cuthbertson) has recently been established to assess, among other things, the new generation of donation screening kits. The group will also establish materials for RTCs which will enable them to check in-house if
their testing arrangements meet agreed (SNBTS) specifications with regard to specificity and sensitivity.

(c) PFC Heat Treatment Programmes
(i) It is noted that PFC has succeeded in producing coagulation factor concentrates (VIII and IX) which are dry heat treated at 80°C/72 hours.
(ii) PFC staff are currently engaged in the establishment of validation tests with regard to their fractionation processes and heat treatments in the context of HIV. This work did not begin until the summer of 1986. Progress is satisfactory.

(d) Z8 Product
(i) Product specification and comments are contained in Dr Perry's report.
(ii) We anticipate having sufficient evidence, indicating acceptable recovery and t/2, within the next 3 weeks and that as a consequence it will be generally acceptable for routine clinical use.
(iii) It is suggested that the Z8 product is phased into use via issues to the existing batch dedication system and that should Haemophilia Directors wish to have certain patients receive priority then these desires are made known to PFC via medical staff at local RTCs.
(iv) Efforts will soon be made to produce a 500 i.u. vial (see Dr Perry's report).

(e) High Purity Product
Once Z8 has been satisfactorily introduced PFC staff will return to the problem of producing a high purity product. There are no time scales available for this product at this time.

OXFORD RETURNS
We are again indebted to Dr Rizza and Miss Spooner for providing us with the relevant data.
These data reveal that there may be a consistent trend whereby the SHS use of factor VIII concentrates may be less than in England and Wales. It is of interest that there are no records of commercial factor VIII used in the SHS in 1985. It should be noted that the clinical use figures are significantly lower than corresponding PFC issue figures. This period was one in which efforts were made to establish batch dedication systems at RTCs. Moreover, in the latter part of 1984 and early 1985 large quantities were returned to PFC for reprocessing (heat treatment).

**FACTOR IX CONCENTRATES**

**SUPPLY TRENDS**

PFC issues to RTCs since 1982 are summarised below:

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DEFIX</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(m.i.u. of IX)</td>
<td>1.0</td>
<td>0.9</td>
<td>1.43</td>
<td>1.59</td>
<td>1.18</td>
</tr>
<tr>
<td><strong>PPSB</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(10^3 i.u. of IX)</td>
<td>44</td>
<td>20</td>
<td>35</td>
<td>30</td>
<td>22</td>
</tr>
</tbody>
</table>

**COMMENTS**

1. The figures in the above are somewhat misleading because in a period
in 1985/86 PFC declined to issue a dry heat treated product (80°/72 hours) for clinical use until its safety (thrombogenicity) had been validated by animal model studies. In this period substantial commercial purchases were made.

2. By the time PFC was in a position to issue validated product there was evidence that there had been a remarkable escalation in clinical demand which appears to have been sustained (see Dr Perry's report). It seems probable the original (SNBTS) conclusion that this escalation was due to the use of the product in non-haemophilia patients was wrong and that the primary reason was the increased use associated with the management of haemophilia A patients with inhibitors. Notwithstanding this reason PFC has had severe difficulties in maintaining supplies and significant difficulties remain.

3. Evidence is now to hand which would suggest that the dry heat treatment process at PFC does NOT reduce the efficacy of PFC's DEFIX in the management of haemophilia A patients with inhibitors. It can be concluded that the report from Belfast was related to the inevitable batch variations in efficacy: a well described phenomenon in commercial products.

4. In view of the rapid escalation in the purchase of commercial fractionated factor IX containing concentrates it has been decided that PFC will develop a programme designed to produce an "activated product".

NEW PRODUCTS

See Dr Perry's report

PFC SUPPLIES TO BELFAST

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor VIII (m.i.u.)</td>
<td>0.15</td>
<td>1.03</td>
<td>1.70</td>
<td>1.89</td>
</tr>
<tr>
<td>DEFIX (m.i.u.)</td>
<td>Nil</td>
<td>0.14</td>
<td>0.58</td>
<td>0.32</td>
</tr>
<tr>
<td>PPSB (m.i.u.)</td>
<td>Nil</td>
<td>0.008</td>
<td>0.018</td>
<td>0.024</td>
</tr>
</tbody>
</table>
GENERAL COMMENTS

It is arguable that the events of greatest importance in the area of the SHS activities referred to in this Report are those which have arisen after 31st March, 1986 and therefore outside the remit of this report. I refer to the question of clinical trials and product licences. These topics will be addressed at other points in the Agenda at the 1987 BTS/Haemophilia Directors' meeting.

Directors will wish to note that modest progress has been made with regard to establishing a long-term follow-up of haemophilia patients receiving heat-treated concentrates - a study being co-ordinated by Dr Forbes and Dr Dawes.