IIth January, 1984

Dr. J.D. Cash,
Blood Transfusion Service,
Ellen's Glen Road,
Edinburgh.

Dear John,

Heat Treated Factor VIII Batch NY761

I write to let you know the outcome of infusing the heat treated factor VIII. The above batch of material was given to a single severe haemophiliac on three separate occasions. I enclose a copy of the results that Chris Prowse obtained but we have confirmatory studies from our own Department. As you can see the recoveries and survival times were reasonable.

Infusions were accompanied by reactions on all three occasions. On the first the recipient had a short episode of diarrhoea beginning an hour after the infusion. On the second and third occasion he felt ill towards the end of each infusion. He developed transient central chest pain, pallor and wretching. There was no change in his pulse, BP or temperature. To ascertain whether this was likely to be an organic reaction to the concentrate we gave him a 'placebo' infusion of ordinary SNBTS factor VIII. He was told that it was the heated material and the infusion protocol was identical. He had no adverse reaction to this standard product. I therefore have to conclude that this batch of material genuinely gave rise to significant and unacceptably adverse reactions in the recipient.

I hope this information is of use to you in the further development of hepatitis reduced factor VIII concentrates.

With best wishes,
Yours sincerely,

C.A. Ludlam
Consultant Haematologist

cc. Dr. C.V. Prowse
    Dr. F.E. Boulton
    Mr. J. Watt
    Dr. C.D. Forbes
SUMMARY OF IN VIVO STUDIES ON NY 761 (HEAT TREATED) FACTOR VIII CONCENTRATE

(Haematology, RIE have independent data)

<table>
<thead>
<tr>
<th>Date</th>
<th>Issued</th>
<th>Infused</th>
<th>Dose Assay</th>
<th>In Vivo Recovery</th>
<th>Extent First Phase of Decay</th>
<th>Half-Life</th>
</tr>
</thead>
<tbody>
<tr>
<td>7/9/83</td>
<td>10 vials</td>
<td>192 mls</td>
<td>6.9 u/ml</td>
<td>92%</td>
<td>-3 h</td>
<td>12.2</td>
</tr>
<tr>
<td>5/10/83</td>
<td>10 vials</td>
<td>240 mls</td>
<td>6.9 u/ml</td>
<td>55%</td>
<td>none</td>
<td>8.3</td>
</tr>
<tr>
<td>2/11/83</td>
<td>210 vials</td>
<td>240 mls</td>
<td>5.2 u/ml</td>
<td>99%</td>
<td>-3 h</td>
<td>12.1</td>
</tr>
</tbody>
</table>

in SD 23 ± 4 u/ml 6.3 ± 1 u/ml 82 ± 34% 10.9 ± 1

PES:

Previous Results in this Patient (All Patients) Using Concentrate Standard for Factor VIII

Frozen Cryoprecipitate 99 ± 16 (97)% 8.8 ± 2 (10)
Glasgow Freeze Dried Cryoprecipitate (n=1) 144 (125)% 9.5 (9.3) h
Factor VIII Concentrate (unheated) 122 (152)% 10.5 (10.4)

Laboratory

(1) Samples for factor VIII:C were assayed against a plasma standard, concentrates prediluted in haemophilic plasma.

(2) NY 761 comes in 25 ml vials with a label potency of 145 iu.

(3) This patient had basal levels of VIII:C < 0.015 u/ml, VIII:Cag < 0.01 u/ml, VIIIR:RCF and VIIIR:Ag about 1.2 u/ml. After infusion VIII:Cag was recovered quantitatively. VIIIR:Ag and VIIIR:RCF rose after infusion.

Clinical

(1) The patient weighed 59.5 Kg consistently and this gives an estimated plasma volume 2,440 ml (41 ml/Kg). His date of birth is 010754.

(2) On each occasion the patient experienced some reaction (eg diarrhea, pallor, etc.) in cases requiring Piriton cover). This appears to be real, since on 071283 he required further infusion of unheated material (25 u/Kg NY 727) the only symptom of which was faint paraesthesia.

Rowse/G McKay 1283)