M E M O R A N D U M

TO: Mr. J. Watt H.O.D.'s Section Managers Dr. A. Macleod	FROM: Dr. P. Foster
SUBJECT: Heat Treated FVIII	DATE: 11th January, 1983

It is now considered that a number of companies will be making heat treated factor VIII concentrate available to clinicians in the very near future.

This could well have major implications for the NHS users and suppliers of concentrate and it is therefore recognised that there is some urgency in demonstrating that the NHS has the capability to manufacture products of this kind.

The PFC R & D programme on this topic is advancing well and in view of this we have been given a target by Dr. Cash to prepare a small quantity of heat treated material for clinical test within 3 months.

It has been agreed that this product will be prepared by the zinc fractionatio method also under development in R & D; hence the clinical test will involve a test of the zinc product both heated and unheated.

Dr. Cash has indicated that the quantity of product required is 1500 iu/patien with 6 patients for each test. That is:

(1) 9000 iu ZFVIII (non-heated)

(2) 9000 iu HTZFVIII (10hr 60°C)

To estimate the scale of manufacture involved I suggest we assume that the yie for (1) will be the same as the NY process and that the yield for (2) should b 50% of this. This is a conservative estimate to ensure that we do meet the ta quantity.

A rough approximation of the NY process is that 1 kg plasma will produce 40ml TE1 or 1 dose of FVIII (200 iu). Hence test (1) will require 45kg plasma or 1.8 litres TE1 while (2) will require double this quantity. If we want to carr out a full QC we will have to include extra material. I therefore suggest we aim for (1) 70kg plasma or 2.8 litres TE1 and (2) double this.

The pasteurisation conditions have not yet been established precisely but the quantity of stabiliser required is expected to double the volume of solution.

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The approximate volumes will therefore be:-

TEST 1 Z FVIII		TEST 2 HTZ FVIII	
STAGE	QUANTITY	STAGE	QUANTITY
Plasma	70 kg	Plasma	140 kg
TE1	2.8 litres	TE1	5.6 litres
ppt 1mM Zn 1u/ml heparin pH 6.7		ppt 1mM Zn 1u/ml heparin pH 6.7	
Zn Super + Citrate	3 litres	Zn Super	6 litres
		+Sorbitol/Glycine	12 litres
Diafilter (x7)	3 litres		
		10 hr 60°C	24 x 500 ml
Ultrafilter		Dilution ultrafiltration	24 litres + 12 litres
		diafilter (x7)	12 litres
Dispense	? 20ml fill		
		ultrafilter	
Approx no. vials	70	Dispense	? 20ml fill
		Approx no. Vials	70

For this exercise it has been agreed that pasteurisation should be carried out using the spray cabinets. We must also ensure that diafiltration and freeze drying equipment carry no risk of hepatitis infection.

In view of the phase II shut-down (beginning Feb 12) it might be useful if we could agree a tentative date (? 1st week Feb) for this exercise. This would allow a repeat in mid-March if necessary.