



## SCOTTISH NATIONAL BLOOD TRANSFUSION SERVICE

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JDC/EP

22nd April 1983

Mr J G Watt  
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PROTEIN FRACTIONATION CENTRE	
Re: 26 APR 1983	
File No: 2167	
<i>John Watt</i> <i>or Factor</i>	

Dear John

Heat Treated Factor VIII

Thank you for your letter of the 18th April.

I think the position, which is one I would support, of Dr Ludlam is that if any evidence could be generated that suggested the immunogenicity of the heat treated product might be different from existing products (which are immunogenic to about 10% of haemophiliacs) then he would be much more cautious with regard to the speed at which the phase I clinical studies were implemented.

Dr Ludlam's approach is a well known one. You take the antigen and compare its reactivity, with known antibodies, with the other antigen. If you discovered there was no difference then, as far as this test allowed - inevitable lack of sensitivity and specificity - you would assume the two products were likely to be immunogenically indistinguishable, and press on, post haste, with the trial. If the new product behaved differently then you would assume that the material had been damaged in some way. This would lead to a cautious approach (not post haste) and a second patient would not be infused until the first had probably had a second (or third) dose and studies were completed with regard to the generation of an antibody to the new product. This second patient would go through the same laborious process - because the first may be a genetically poor responder.

I do not, therefore, regard the study proposed by Chris Ludlam to be either unnecessary or premature. It's partly about medical ethical considerations and also the time required to complete the phase I trials. The problem is even more complex for the clinician because he will infuse patients who are already pre-selected (the 90% who don't develop antibodies). Even greater care will be required on infants who have not been exposed to factor VIII. The 10% who develop antibodies to normal VIII may react in very unusual ways to the heat treated product.

Kindest regards,

Yours sincerely

John D Cash