



SCOTTISH NATIONAL BLOOD TRANSFUSION SERVICE

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MEMORANDUM

SNBTS PRODUCT DEVELOPMENT GROUP

FACTOR VIII CONCENTRATES : INTO THE 1990s

REQUIREMENTS

- (a) I would suggest that most of us would share my view - that the marketplace will demand a high purity Factor VIII product in the very near future. I would judge that a useful working definition of high purity should be a product with a specific activity of at least 50 iu/mg.
- (b) The objective (a) above needs to be achieved with a final product yield of not less than 200 iu/kg of FFP processed.
- (c) I would suggest that this high purity product needs to be available for clinical trial purposes before September 1991.
- (d) We will need to incorporate into the planning for (a) above a product for the management of VWF deficient patients.
- (e) The safety of the new product (with respect to viral transmission) must be considered to be no less than current products. But we should ultimately seek to incorporate into this product a "belt and braces" approach.

VIRAL INACTIVATION

It is my view that our terminal dry heating programme has served us extremely well and that we should give very careful thought before abandoning it. I'm thinking of our existing product licences, the ongoing PUP studies, the repercussions internationally (headlines - "SNBTS finally accepts demise of dry heat treatment") and "better the devil you know etc etc"!

On the other hand we need to be careful and realistic in charting our way into the 1990s, and because we have an open invitation to acquire the CRTS (Lille) technology, the time has come for us to consider very seriously the solvent detergent (SD) approach.

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PLEASE GIVE BLOOD

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Christopher P has kindly undertaken a recent survey (see enclosed) of those fractionators who have now embraced the SD approach. I am bound to conclude that the vast majority of the world's major fractionators have gone down this path. Thus, if we were to opt to go SD we would be in good company.

Of course, the SD approach is not a terminal one and as a consequence most fractionators have introduced product dedicated facilities. I cannot escape the conclusion that we must not at this stage reject this technology on this basis alone. We need to think positively! We need to remind ourselves that we've been in this position with IVIG for several years. Moreover, against a background of a "belt and braces" philosophy, I could still envisage a terminal dry heat programme being our ultimate goal - particularly if we were able to introduce a higher yielding purification process. CVP has already produced data which indicates that the Lille product can be dry heat treated (80°C for 72 hours).

PROCESSING

Purification

I'm sure we all agree that the task before us (a high purity product) must lead us to abandon precipitation technology in favour of chromatography. I suspect that we would also agree that immunopurification, at least in this context, is not acceptable (very high cost, low yielding, toxicity and unacceptably rigid contractual arrangements). Thus we are led - as was foreseen by PFC (RD) colleagues - to non-immune purification systems. We now know that these have been developed in France, to the point of clinical use and acceptability and we have been offered this technology by CRTS (Lille).

We need to remind ourselves that the PFC (RD) team has been working in this area for several years. As a consequence, very considerable critical expertise has been acquired which will be of substantial benefit to us over the next 12 months. In the light of the market time constraints (we need to be on stream before September 1991) and the many other product development pressures on the PFC team, I conclude that it would be unwise and unreasonable to pursue the introduction of what we call the "Johnson option" and that the best approach would be to pick up what is on offer from CRTS (Lille). The very considerable

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investment made by the PFC team in this field should result in a more rapid and effective transfer of the CRTS (Lille) technology and could be of considerable further value if and when we give consideration to products beyond the Lille process (third generation Factor VIII products).

Virus Inactivation

I would suggest that we "bite the bullet" and accept the total Lille package and thus our immediate goal is an SD only treated product for September 1991. However, because we should be in a yield area of around 250iu/kg I believe we should also aim to bring on stream either in September or in January of 1992 a "belt and braces" product - SD and dry heated product.

It can be argued that, if our ultimate aim is terminal heating, then we shouldn't build a small dedicated SD downstream area (waste of money). I would suggest that the financial rewards of bringing in the Lille technology are so great that this concern should be set aside. Moreover, this SD dedicated area could be used in the future for other products which cannot be terminally heat treated (IVIG) and, in any event, we are likely to see further developments in the chemical approach to product "sterilisation" which may prove to be very attractive to us in the future.

BEYOND FACTOR VIII

I would suggest that the team going to Lille make every effort to look at the "total package". David McIntosh will bear the burden of any trading exercises but I think our visiting team should define the total package for product technology transfer as follows:

Factor VIII
VWF
Fibrinogen
Factor IX

If we can get all this in exchange for our haemoglobin programme then I will be content! Beyond this is α , PI and growth factors for fibrin glue - perhaps - and a lot more!

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WHAT ABOUT S8?

We need to think carefully about this. My gut reaction is to continue as planned (double belt and braces) but perhaps we should not give this serious consideration until the team reports back from Lille - in sober mood!

LILLE VISIT PLANNING

I have no doubt we should expedite this proposed visit. I would suggest that the visit is co-ordinated by CVP (he has good relationships with Dr Burnouff) and that in addition to CVP the team would be Bob Perry, Peter Forster, Ron Mac. and Duncan Pepper.

SOME FINANCIAL THOUGHTS

If we assume we can achieve a consistent increased yield of 40 iu/kg over existing technology, and this difference has a commercial value of 27p/iu, then we get £10.80/kg fractionated. This would amount to over £650,000 per annum. This must surely give the SNBTS a lot of future options - not least the RTCS and their plasma procurement.

J D CASH

22nd May 1990.

cc Dr D Pepper (for information)