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19th October, 1982

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Dear Jim,

I wonder if I could trouble you for some advice on a couple of points.

My first request concerns the paper that you presented at Groningen last November on the stability of FVIII.

We are looking yet again at our plasma quality (which is currently at pre 1975 levels) and we are trying to get some solid data on the rate of decay of FVIII in plasma and whole blood at different temperatures. I seem to remember that your study covered this at 20°C and 4°C over 24 hours. My notes of the meeting are a bit of a scribble and if you do have something written-up, a copy would be most welcome.

The second point concerns AT-III preparation. We are now pushing ahead with scale-up but I'm still a little worried about the hepatitis situation. In the published chimp study (Thromb. Res. 22, 233) HBsAg was inactivated at a titre of $10^{3.5}$ CID/ml. But this was on a Wickerhauser preparation, which presumably included a PEG step. We do not have a PEG step at the moment and I'm reluctent to include one for obvious reasons. However, without it we may have more virus in our product than Wickerhauser. For HBV it could be argued that pasteurisation is proven for a titre up to $10^{3.5}$ and if the contamination is greater it will be picked up by RIA. My worry is NANB; could the PEG step be cleaning up what would otherwise be a NANB level too high to be inactivated by pasteurisation?

On the FVIII front we are still grinding away at the yield problem and have started to look again at the high purity situation. We are currently pursuing precipitation by metal-ions, which is something we stumbled on with Milan Bier a few months ago. The early results are interesting but its going to be stuck on the lab bench for a long time yet. Everyone is getting very hot about pasteurisation/

pasteurisation, especially since Budapest. The little work that we have done suggests that higher purity material is needed and so far FVIII (using Duncan's CAG assay) has always gone into the solids phase!

Supernine has at last entered into some serious clinical study with early results very promising; so we are now reviewing production yield and I'm hopeful that we can make some significant improvements now that the clinical interest is catching on.

Best wishes.

PETER R. FOSTER