CVP/JL

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Dear Peter

Many thanks for sight of the paper on the effect of calcium on the factor VIII process. My main concerns would be that I suspect the referees will require it to be shortened and that it is unfortunate that frozen and freeze-dried samples were assayed against different standards. Were it not for the 2-stage results I would be tempted to suggest dropping the freeze-dried results from Table II. Is there any way that a conversion factor (e.g. by local assays of plasma vs concentrate standard or by inspection of NIBS concentrate standard calibrations vs plasma standard) could be arrived at to convert everything to 'concentrate units' -- including the 100% figure for untreated extract (presumably assayed against plasma standard). If possible this would also, presumably, get round the problem of recoveries greater than 100%.

Additional points are:

1. Legend to Fig. 2 needs symbol definition.

2. The method enabling VIII assay in the presence of heparin needs stating (? protamine sulphate neutralisation).

3. To what end point (uM ionised calcium) is titration mode (e.g. p.8, 15)?

4. Two-stage assays were presumably done without alumina adsorption.

5. Spelling of 'disappearance' on pages 15 & 16.
6. On p.16 would 'less' rather than 'non' infective be more appropriate?

To predict other comments by referees I suspect there may be queries on the thrombin-activation potential of the products and their VIII:Ag content. The latter, at least, would probably be of little help in determining te 'correct potency' unless the VIII:C/VIII:Ag ratio was close to 1.0.

Hope these comments are helpful.

Best regards

[Signature]

pp C. Prowse

(Dictated by Dr. Prowse but signed in his absence.)