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Dear Chris,

Many thanks for your comments on the calcium manuscript.

1. Use of Different Standards. I am re-writing this to try and explain the point more clearly. It would be possible to convert the results derived using the plasma standard to "concentrate equivalent" values but this might be even more contentious - what do you think? How would we spell this out in the methods section?

2. VIII:C Assay in the Presence of Heparin. No special treatment was used as the heparin concentration was only 1 u/ml. I think you advised me that this would be OK.

3. Titration End-point. This was done by monitoring changes in voltage (see p10). To get an ionised calcium value it is necessary to calibrate the instrument with a standard solution. We have this data, but it is probably not very accurate as it is close to the limit of sensitivity of the equipment. Hence the direct monitoring of small voltage changes was more accurate and does not strictly require any knowledge of absolute values of ionised calcium. Do you think we still need to quote some Ca\(^{2+}\) value?

4. Two-stage Assays. The assays quoted in table IV were all done at your lab. The omission of alumina is mentioned in the discussion (page 18).

5. Thrombin-activation Potential. We still have samples of the two types of material tested clinically. If you think there are further tests that could be done to address the question of potential activation I could send some vials to you.

I have not quoted VIII:Ag values simply to try and keep the size of the manuscript down.

Best wishes,

Yours sincerely,

PETER R. FOSTER