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25 November 1985

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Dear Brian

F PRINCE PUBLICATIONS - HTLV III

Very many thanks for the pre-prints of Prince's papers. There seems little doubt that these will be accepted for publication in view of the quality of the reports and the potential significance of their findings and speculative conclusions. My initial reaction therefore is to contact Robin Weiss as a matter of urgency and convince him that it is a matter of strategic importance to the UK that we collaborate to evaluate both our IV IgG and FVIII manufacturing processes. We (PFC) are now equipped to handle virus but as you know, there is no assay expertise locally. I have already written to Robin Weiss with a view to an urgent visit to his lab to work out experimental protocols.

Prince's data on IgG certainly contradicts the views expressed to date that alcohol inactivates HTLV III and he goes on to argue for other defined inactivation steps in a manufacturing process - this is consistent with the view we recently expressed to the DHSS in the document we are now seeking to publish. We know that pH 4/pepsin inactivates a wide range of viruses but we have not quantified this process step for HTLV III. We are also looking at heat treatment but this is embryonic and probably produces molecular modification. I have been briefed by John on the Sandoz story and this <u>may</u> lead to a major crisis of confidence in pH 4/pepsin although if these reports evolve into proven cases of AIDS then I would be inclined to favour GMP failure. This observation does not diminish the need for urgent studies with Weiss.

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Princo's comments relating to the safety of IM IgG are of interest since the idea that liquid IgG may be virucidal over a period of time is no more than an ill-defined concept. The traditional view for hepatitis safety is preferential fractionation of virus into other fractions combined with the effect of neutralising antibody. In addition there is at least one manufacturer (Immuno) who produce a dried IM IgG product (presumably immediately after fractionation). There are no reports of viral transmission from this product which is likely to have been manufactured from paid donor plasma.

The pre-print on heat treated FVIII also conflicts with pre-existing knowledge in this area - the CDC/Cutter study suggested 37 log inactivation for 60° treatment. I'm not sure that this data conflicts with the Levy data (2.5-3.5 logs at 68°/24 hr) since in a sterilisation process 8° C can have very substantial effects on the kinetics of viral or bacterial inactivation especially if one is approaching the temperature at which a catastrophic event occurs in the viral particle. Nonetheless, the pressure will now be for local process validation and better processes - BPL hold the lead in this area with 80° C/ 72 hrs but PFC is not far behind.

With kind regards.

Yours sincerely

R J PERRY
Director

cc Dr John D Cash