James K.Smith. Supplementary statement in C3.

Having had time to reflect on the transcripts of my oral testimony on 2 December, I realise that I was poorly prepared for some fair but "unseen" questions, particularly from Mr.Di Rollo and Mr.Mackenzie in follow-up, and was not nimble enough to give satisfactory responses. I would therefore be grateful if my more considered opinions could be taken into account.

1) Perceptions of 8Y by clinicians, to 1986

One focus of my written statement in C3 was the question "should PFC have considered adopting the 8Y process in 1986?" My position on that should already be clear. "Should clinicians have believed in the relative safety of 8Y in 1986? " is not quite the same question. This was brought out by Prof. Ludlam's testimony on 13 and 14 November, which I have now read carefully. I wish to make it clear that Prof. Ludlam's evaluation of the emerging clinical trial data was entirely in the mainstream of clinical opinion at the time. Although the "Oxford" protocol had been first in the field [Fletcher *et al* 1983], by 1985-86 it had become the renegade holding out against the stricter ISTH protocol. In my reviews, e.g., to the HCDs, I had already adopted the practice of presenting ALT data in patient groups according to the extent to which their inclusion in the trial and frequency of testing would have met the ISTH protocol. This allowed all factions to count the number of patients they would consider "compliant" and informative. Although I do not have transcripts, the short paper I presented in Sydney in May 1986 (and possibly in poster form at a London BBTS meeting) and the updated version presented by Mary Fletcher in Milan in June 1986 [?SNB.007.5955] would have been pitched in the same non-committal terms. Especially if a severe view were taken of compliance with the ISTH protocol, the number of clean follow-ups at the end of 1986 was too small to either support or disprove the proposition that 8Y was statistically significantly safer from NANBH transmission than commercial concentrates heated less severely. That was my own expressed position throughout 1986 and, save for his views on the Oxford and ISTH protocols, I can find no material difference between Prof. Ludlam's and my evaluation of the "safety of 8Y" in 1986. Although always ready to explain my views on the relative merits of the competing protocols, I do not recollect doing so in Prof. Ludlam's presence. These arguments may have appeared in print for the first time, albeit severely edited, in the 1988 publication [LIT.001.0330].

Mr. Di Rollo also detected that my own assessment of 8Y seemed to become more positive during the course of 1986. Any optimism would have been founded, not on any great accumulation of clinical data, but on the hard evidence presented by Dr. Cuthbertson at PFC that our heating conditions were hitting some tough viruses appreciably harder than were those of Hyland, Armour and Cutter. As I recall, the difference was about 100-1000-fold, quite significant in terms of the maximum concentration of virus which might be expected to be present in the plasma pool and in the concentrate before dry heating. Prof. Ludlam did not, as far as I know, have access to these data, nor would one expect a clinician to have been much impressed by such evidence.

I should have made it plainer that in the course of 1986 I became disillusioned with the goal of proving non-infectivity of a concentrate by means of liver enzyme tests. Our trial had already collected some bizarre "interesting ways to get an elevated ALT" - the examples the Inquiry encountered in investigating surrogate tests being by no means the only ones illustrating the hopeless non-specificity of ALT elevations. It had become clear that the twin pillars of the inflexible ISTH protocol - insistence on zero previous exposure, and an arbitrary grid of test frequency - were not sufficiently supported by published evidence to justify elevating it to a "gold standard". However, it was also increasingly clear that a number of authority figures had invested heavily in that protocol and

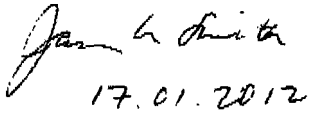
were not susceptible to quantitative, statistical argument (especially from irreverent non-medics). As my C3 statement confirms, I came to believe in the next few years that 8Y was probably safe, by sheer weight of good follow-ups and in particular the exposure of many batches of widely different provenance. However, I would not assert its safety until application of the highly-specific anti-HCV test, published only in 1993 [SNB.004.5996], vindicated our earlier data.

2) Scottish use of 8Y supplied to PFC in 1986.

I cannot now be sure that no Scottish clinician contributed patients to our 8Y trials published in 1988 and 1993. Especially in the period between availability of 8Y for virus transmission trials (March 1985) and general release (September 1985) my first priority was to provide any patient who had not yet acquired NANBH with "the best we can offer", even if we had no hard evidence that it would be safer than earlier intermediate-purity concentrates. The policy was to accept the requesting clinician's assessment that his patient had a sporting chance of still being free of infection; supply 8Y; decide later whether he met at least the more flexible Oxford entry criteria; and when publishing give everyone enough information to stratify patients according to their own convictions. In some cases it would take weeks to discover all the material an infrequently-treated patient had received. Although this policy was open to abuse, I believe that all our users acted in good faith, whether the patient ultimately proved to be countable or not.

On reflection, in my answers to Mr.Mackenzie I was over-hasty in suggesting the list of contributors in our various reports and publications as a means of excluding the use of 8Y by a clinician. It is certainly my recollection that in my reviews for HCDs and in the 1988 publication we agreed to acknowledge all clinicians who had offered a patient, whether we had been able to use his data or not. However, it was a long time ago and I have to admit that my answer was unsafe. Secondly, the 1993 publication appeared when I was no longer employed, and there was no author from BPL. Although I remember making certain contributions to a draft before departing, the style suggests that I had much less input in the final script than I had had in 1988. It follows that I cannot be sure that the previous policy was maintained in 1993 [SNB.004.5996], i.e., listing as a contributor every clinician who had offered a patient. On balance, my conclusion today would be that the authors acknowledged only those whose patients were considered in the publication. This leaves the possibility that the 8Y provided to PFC in 1986 was used in good faith by Scottish clinicians but that the data had not been considered suitable for that publication.

For completeness, I should add that, had BPL received a Scottish request for a limited amount of 8Y for a patient not eligible for NANBH trial, but who might, e.g., be suffering serious reactions to the home product, I am sure that the request would have been considered sympathetically. However, that would have been a decision for Dr.Lane to make; I would probably not even have known about it.



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