Witness Statement Request in relation to Topic C3: Heat Treatment 1985-1987
Statement – Professor Christopher Ludlam (CAL 30)

'Does Professor Ludlam consider that the lack of appropriate compensation arrangements resulted in any delay in the introduction of Z8 and, if so, by how many weeks, months etc was the introduction of Z8 delayed because of the lack of such arrangements?'

From the accompanying narrative derived from the available documents the following facts appear to be particularly relevant. *Comments are in italics*

1. There was considerable uncertainty about when samples of Z8 would be available for clinical assessment in the second half of 1986.

    a. Although it was hoped to undertake test infusions in patients of Z8 in about September 1986, when it was anticipated that appropriate material might be available, difficulties were encountered with its freeze drying. This led to a substantial delay and it appeared that the product might not be available until December 1986.

    b. The initial Z8 product was heat treated at 72 degrees in September 1986, although it seems that it subsequently became policy, in perhaps October, that it should be heated to 75 degrees. Thus it was the 75 degree material that was not available in September. It seems that it was anticipated that it would be the 75 degree material which would be ready in December.

    c. Although Dr Cuthbertson wrote on 26th November 1986 to Dr Boulton with a specification of the 75 degree/72 hour product, there is no evidence that this product was ever despatched or received by Dr Boulton. I have no recollection of any

communication to indicate that it had been received at the Royal Infirmary. (SNB.007.6268)

2. Dr Boulton had SNBTS responsibility for liaising with clinicians over arrangements for the test infusions of Z8 in patients. In his letter of 1st December 1986 to Dr Perry, Dr Boulton indicated that he had received a letter from Dr Mayne 'saying that she will be very pleased to enter into the trials as soon as the material is available'. His letter continues by stating 'I think it would be best if I wait until the material is actually in our cold room (at the Royal Infirmary Blood Bank) before I tell Dr Ludlam'. The letter ends by Dr Boulton indicating that he will get in touch with Dr Forbes directly to arrange Z8's assessment in patients (SNB.007.6270). Subsequently, Dr Cash wrote to me on 13th January 1987 reporting that 'Charles Forbes has agreed to look at the 75 degree/ 72 hour product' (SNF.005.8713).

   It thus appears that both Dr Mayne and Dr Forbes were prepared to test the heat-treated Z8 by the beginning of January 1987.

3. On 5th December 1986 Dr Boulton wrote to Professor Cash indicating that I would be 'unwilling to agree to such trials unless there is specific commitment by SHHD ...to give appropriate compensation'. A P.S. to the letter states that 'I have heard from Dr Mayne that she (is) willing to participate in the trials of Z8 (SNB.007.6274).

4. Documentation is available which indicates that Dr Perry agreed to the release of the 80 degree/72 hour material to Edinburgh BTS for Clinical Trial on 22nd December1986 (SNB.009.4073).

   This is an unsigned memorandum. I cannot find any evidence that the Z8 was despatched from PFC, or was received at the Blood Bank at the Royal Infirmary Edinburgh, or that any of it was forwarded to Glasgow or Belfast for assessment in patients. I do not have any recollection of any communication from Dr Boulton to me that the

material had arrived in 'the cold room' at the Royal Infirmary as he indicated he would do. (Para 2 above)

5. Dr Cash, in his report for the Haemophilia/SNBTS meeting, which he compiled in January 1987 wrote (para 3d) (ii) 'We anticipate having sufficient evidence, indicating acceptable recovery and t/2, within 3 weeks and that as a consequence it will be generally acceptable for routine use.' (SNB.001.5496)

   When writing this he was aware that I was not prepared to test the Z8 (without indemnity) and must have based his understanding on the fact that it was being assessed in Belfast and Glasgow. No date for the introduction of material for therapeutic use is stated.

6. Indemnity by SHHD was offered, for non-therapeutic infusions, by way of a letter from Mr Murray (SHHD) of 6th February 1987 to Dr Cash. A similar offer was made at the Haemophilia/SNBTS directors meeting three days later on 9th February by Mr Macniven (SGH.003.1870) and (SGF.001.2261).

   Although there was subsequently a difference of opinion as to what had been offered by way of indemnity by Mr Macniven, there was agreement that ABPI guideline arrangements would cover test infusions. What was subsequently contested is whether or not ABPI indemnity was (at this meeting) offered for 'therapeutic infusions'

7. The 80 degree/72 hour Z8 was tested in 3 patients in Edinburgh probably in March 1987 (and additional patients in April) as Dr Howe wrote with results of initial infusions on 31st March to Dr Perry (SNB.006.5609).

8. My understanding is that it was proposed to phase in Z8 as the stocks of 68 degree/24 hour material NY ran down. My understanding of

events is that manufacture of 68/72 ceased in February 1987 and that there was only a small amount of stock.

9. If indemnity arrangements, for test infusions, had been in place by 1st January 1987 it seems likely that I would have been able to arrange such infusions in January 1987 (assuming also that the Z8 was actually available for assessment, see para 4 above).

10. The records indicate that Dr Mayne would have been prepared to arrange test infusions at this time in Belfast. There is nothing in the documentation that I can find which indicates that she was insisting upon having indemnity arrangements in place prior to test infusions. It seems likely that the test infusions could also have been carried out under Dr Forbes' supervision in Glasgow (see para 2 above). I presume that these infusions could have been carried out in January 1987.

11. As well as undergoing satisfactory test infusions prior to Z8 being released for clinical use, it would have been necessary for PFC to manufacture several batches to demonstrate that the production process could be replicated and was stable. These batches would need to be 'finished', i.e. undergo standard quality control tests including pyrogen testing, as well as being labelled and boxed etc. Furthermore before releasing any for clinical use, it would be necessary to have a stock of several batches, at least enough for 1-3 months' supply.

12. In conclusion, my refusal to give test infusions delayed Z8's assessment in Edinburgh for about two months. My interpretation of the correspondence is that both Glasgow and Belfast were prepared to test Z8 without indemnity arrangements being in place. Furthermore, without knowing more about the production schedules of batches and stock at PFC, it is not possible for me to draw a valid conclusion as to

whether the lack of indemnity delayed introduction of Z8 for clinical use.

13. If there was a delay of approximately 3 months (Z8 introduced for clinical use in May rather than February 1987) untransfused patients (PUPs), who would have been at risk of non-a non-B hepatitis, could have had access to 8Y (a small stock of which had been acquired in August 1986). Thus patients, therefore, should not have been disadvantaged if there was any delay in the introduction of Z8.

....12/9/11.....

Signed Date