Issue 5:

The use of blood product materials in Scotland in the period between the introduction of NHS heat treated products in 1984 and the supply of NHS products sufficiently treated to inactivate Hepatitis C

Topics covered:

C3a – The use of blood product concentrates in Scotland in the period between the introduction of NHS heat treated products in 1984 and the supply of NHS products sufficiently treated to inactivate Hepatitis C.

Topic C3A

PENROSE INQUIRY

TOPIC C3A

Evidence was given on this topic by:-

(1) Professor Gordon Lowe (day 54: 13th October 2011);
(2) Professor Christopher Ludlam (days 54 and 55: 13th and 14th October 2011);
(3) Dr Robert Perry (day 74: 7th December 2011);
(4) Professor Brian Colvin (days 55 and 74: 14th October and 7th December 2011); and
(5) Dr James Smith (day 60: 2nd November 2011 in response to questions by Mr Di Rollo).

The relevant statements on this topic are:-

(1)	Professor Lowe	PEN.017.1471
(2)	Professor C Ludlam	PEN.017.1790 and PEN.017.1798
(3)	Dr Robert Perry	PEN.017.1244 and PEN.017.1843
(4)	Professor B Colvin	PEN.017.1674
(5)	Although primarily on C3 see also Dr J Smith	PEN.017.1130 and PEN.018.1408

TOPIC C3A

The use of blood product concentrates in Scotland in the period between the introduction of NHS heat treated products in 1984 and the supply of NHS products sufficiently treated to inactivate Hepatitis C.

Inquiry Counsel Issues Nos 1-5

1. **Given that, with effect from Autumn 1985, the Factor VIII concentrate 8Y, produced in England, was more severely heated than the Scottish product, could a supply of 8Y have been obtained to be held for the treatment of any Scottish patients with haemophilia who had received little or no previous exposure to concentrates and who required treatment before the equivalent Scottish product was available?**

2. **If the answer to question 1 is in the affirmative, should such a supply have been obtained (other than the small *ad hoc* supply procured by Dr Perry in the summer of 1986)?**

3. **If the answer to question 1 is in the affirmative, when and by whom should such a supply have been obtained?**

4. **In the absence of a supply of 8Y to treat patients with little or no previous exposure to concentrates, were the general approaches to blood product therapy for haemophilia in Scotland in the period 1985 to 1987 reasonable?**

5. **Were the arrangements for dissemination of general guidance to clinicians regarding haemophilia treatment during this period satisfactory?**

The first three questions essentially involve the questions of could or should a supply of 8Y have been made available for Scottish patients and, if so, who would/should have been responsible for this. It is difficult to answer these questions individually as the considerations that each question raises overlap with the other questions.

There appeared to underlie the questioning by Mr Di Rollo of witnesses on this topic certain assumptions which are to a lesser extent discernable in questions 11-20 of the issues proposed on behalf of the Haemophilia Society on this topic. These assumptions appear to be that (a) it was, or should have been, obvious that 8Y was the "safer" product (b) there existed or should have existed arrangements for the procurement of products for specific patients not available from the SNBTS, and (c) that correspondingly the failure to obtain a supply can be criticised.

Before addressing the specific questions it is again necessary to guard against the benefit of hindsight. It is now known that 8Y did not transmit any NANB Hepatitis. That was not known in the period in question. There were some encouraging signs in relation to the possibility of a greater degree of safety, *viz*:-

- PFC report for SHS Haemophilia/SNBTS Directors Meeting (March 1986) para. 3.1 … "Directors will be aware that BPL are issuing a Factor VIII product - and preliminary data indicates that this material is non infective with respect to HTLV III, NANB and Hep B" (SNB.001.5469).

- Addendum to development of new products 1986/1987 (written January 1986):- "The heat treatment now being applied to Factor IX concentrates (PFC and BPL) and to Factor VIII (BPL) may well be effective in ensuring non infectivity of products." (SNB.001.5484)

- Minutes of BPL/SNBTS meeting at PFC 17th March 1986 at page 3, para. 5:- "Dr Smith outlined the clinical trial results of the 8Y Factor VIII product so far. While results cannot be considered conclusive at this stage, he indicated that no cases of virus infection have occurred (attributable to 8Y material) after twelve months experience of 8Y in Virgin Haemophiliacs)." (SNB.001.5664)

However it is also necessary to recognise the general scepticism that was prevalent at that time in relation to dry heat treatment (see Professor Ludlam day 54 pages 107 and 117 and Dr Perry day 74 page 5). Evidence had suggested that pasteurisation was the option more likely to be successful in destroying the NANB virus. See SNBTS Briefing Paper on the development of heat treatment of coagulation factors by Dr P. Foster (PEN.013.1309) at page 9 (PEN.013.1317) and at page 17 (PEN.013.1325) and also the evidence of Dr Smith on day 60 at page 92. Heat treatment procedures devised by three commercial manufacturers had failed to destroy the NANB virus (see PEN.013.1328/9). As Professor Ludlam put it, medicine is full of examples of drugs which look promising to begin with but when the final results of study are published the drug is reported not to have any beneficial effect and in many instances patients have suffered from unpleasant and serious adverse side effects (see day 55 at page 99/100). Dr Smith talked of "a wave of NANB and even HIV failures in dry heated commercial products" (see Dr Smith's report PEN.017.1130 at 1140 and his evidence on day 60 at page 71, i.e. "the seemingly endless failures of dry heating between 1983-1985" and also Prof Colvin on day 55 at page 144/5).

Professor Ludlam's perception of 8Y appeared to be:- "I thought it was perhaps a little bit safer but not completely safe" (day 55 page 108). Dr Smith in evidence (day 60 page 69) told us that by early 1986 he would not have suggested 8Y would be effective. He would not indeed have expressed the same degree of optimism that Dr Perry had in his report (SNB.001.5484) - see Dr Smith day 60 pages 106-108. His own view as to the confidence one might have in 8Y is set out in his evidence at day 60 pages 109-110 i.e. "- the best we could say is that there may have been - the improvement may have been of the order of 30% but statistically speaking that does not give a very high probability of the product being safe". What is noteworthy is Dr Smith's suggestion that he can find no material difference between Professor Ludlam's and his own evaluation of the "safety" of 8Y in 1986 (see Dr Smith's supplementary statement PEN.018.1408 para. 1). It is of course true to say that during 1986 the picture was an evolving one but crucially clinicians would not have had access to that evolving picture. The picture, in any event, was still one of uncertainty (see Dr Smith's report PEN.017.1130, para. 4 at 1133). Even by

late 1987, the evidence was being described as “soft” - see minutes of meeting UKHCDO on 25th September 1987 (SNB.001.7768).

Also noteworthy is the evidence of Professor Colvin who is clearly of the view that there was no evidence in the period 1984-1987 that any Factor VIII concentrate was Hepatitis safe. See report PEN.017.1674 at page 5, i.e. PEN.017.1678. Professor Colvin enlarged upon this in evidence on day 55 at page 156, i.e. “at an objective level you couldn’t say that one product was better than another despite this encouraging information” and page 157:- “I think we were all extremely relieved when it became apparent that 8Y and the Factor 8 equivalent in due course actually were safe”. Perhaps most tellingly was Professor Colvin’s view that if, at the material time, he had heard that there was a more severely heat treated product available in Scotland in respect of which early results were optimistic, he would have taken no action but rather waited to see what further information might emerge (day 55 page 158).

It is against this background that matters of whether Scotland could or should have secured a supply should be addressed. Those representing the Haemophilia Society will no doubt say that during 1986 Scotland should have obtained a supply of 8Y. It may have been theoretically possible to have obtained a supply. However there was no direct evidence from an English perspective and from those who may have had the authority to agree such an arrangement of whether such a request for a routine supply would have been successful. Consideration of such a possibility would have taken place against a background of severe shortage of NHS product in England and Wales, the perception that Scotland was in a stronger position than other parts of the UK to protect patients from the risks of imported products and the absence of a UK-wide strategy to minimise the risk to untreated and minimally treated patients using 8Y. Dr Smith suggests that in a specific case for a specific purpose a request for a limited amount of 8Y may well have been viewed sympathetically (see supplementary statement last paragraph PEN.018.1408). Dr Perry’s request on behalf of Dr Ludlam was a carefully worded one pitched at a level which was perceived to have the best prospect of success.

Even if it were theoretically possible to obtain a limited supply of 8Y for Scotland as a whole, it is necessary to ask just how such a situation would have come about. It could not have been the responsibility of a clinician in one Scottish hospital to seek to obtain a supply for all Scottish haemophilia centres. Apart from the logistical problems, there remained the question of clinical autonomy. Professor Colvin spoke of this on day 74 at page 102/3, i.e. “… the responsible physicians acting within the spectrum of appropriateness sometimes came to different conclusions”. See also Dr Perry’s statement PEN.017.1244 and 1246 at his evidence on day 74 at pages 15 and 37/8.

The reason that Professor Ludlam channelled his request through Dr Perry is precisely because he thought that his chances as an individual clinician were limited. See Professor Ludlam day 54 at page 130. While there is evidence of one successful attempt, and other clinicians could have made similar requests whether by trading upon the goodwill that existed between BPL and PFC or not, it is unknown what the results of such requests would have been. Standing the views expressed by Professor Ludlam and Dr Smith about the awareness by Scottish clinicians of developments in England, it is entirely an exercise in hindsight to suggest that individual clinicians ought to have sought a supply of 8Y. As Professor Colvin put it, “There is a huge danger of using the

retrospectoscope to say one should have taken the particular view because it later turned out that that was the answer" (evidence day 55 page 157).

Standing that in 1986 8Y was not a licensed product and was far from completing its clinical trials, that it was in very short supply, that the letter of 24th July 1985 from BPL concerning the introduction of 8Y in September 1985 and ongoing clinical trials (DHF.003.0476) which was sent out to haemophilia directors in England, Northern Ireland and Wales but not to Scotland (DHF.003.0478), and the general scepticism prevalent in relation to heat treatment and its history of failure, it is difficult to see how Scottish clinicians were expected to "put their money on the 8Y horse" (see Prof. Colvin evidence day 74 page 100)

Given the separate arrangements for NHS product supply in Scotland and England and Wales, there would have been no reasonable expectation that 8Y could or would be available for the treatment of specific patients in Scotland.

Similarly it is difficult to see why the SNBTS in its role of manufacturer and supplier of its own products should have been expected to obtain a supply in the absence of a specific request to do so. The SNBTS had no role, authority, or funding for the central procurement and distribution of products manufactured by other organisations and it would appear that this position was understood by all interested parties. See Dr Perry day 74 at pages 38, 39, 43, 52 and 55. During 1986 the SNBTS was anticipating that its own product would be imminently available. It appears that on 2nd July 1986 Dr Perry was anticipating Z8 being available imminently (see SNB.007.5909 and Dr Perry's evidence day 74 and page 22). It is of course crucial to bear in mind (i) that it was not until May 1986 that it was known for certain that the SNBTS product transmitted NANB hepatitis in that it appeared to have done so on one occasion in about May 1986, (ii) that during this time the SNBTS, and general pre-occupation was with HIV safety and (iii) that NANB hepatitis was still perceived as being a much less severe infection.

For all these reasons it is submitted that no criticism can be made of either clinicians or SNBTS for not obtaining a supply of 8Y for Scottish patients for previously untreated patients in Scotland in the period prior to the introduction of Z8.

On the question of the general approach to blood product therapy for haemophilia in the period 1985-1987, the guidance document from the Haemophilia Centre Directors Organisation entitled AIDS Advisory Document dated 14th December 1984 (SGF.001.2388) sets out clear guidance, which guidance was followed. See Professor Lowe day 54 page 17 and Professor Ludlam statement PEN.017.1798 pages 1 and 2 and his evidence on day 54 at page 81. In relation to the choice between cryoprecipitate and concentrate, the need to personalise the treatment taking account of the number of treatments that may be needed was of great importance to clinicians (see day 54 page 66). Professor Ludlam also spoke of the importance of this guidance document and that the advice contained in that document was adopted for treating patients in Scotland. The advice from UKHCDO was issued directly to all the Scottish Haemophilia Centres (see Professor Ludlam day 54 page 147).

The dissemination of advice to clinicians working in hospitals in remote areas was a matter which was discussed with Professor Ludlam on day 54. In general terms, once a diagnosis of haemophilia was made, the patient was

referred to a reference centre which provided the high quality specialised care required. The appearance of a previously non transfused haemophilia patient was of course a very rare event. The local clinician if in need of advice had access to the expertise of the reference centres (see Professor Ludlam day 54 pages 148-154).

In conclusion the suggestion that Scotland should or could have sought to obtain a supply of 8Y for previously untreated patients pending introduction of its own Z8 is wholly unrealistic for the reasons outlined above.