Response to the Penrose Inquiry to the request of 21st December 2011 concerning the reports of Dr Hay (of 31st December 2011) and Professor Nathanson (of 4th November 2011) by

Professor Christopher Ludlam

The Inquiry has sought my opinion on two topics in relation to the Reports by Dr Hay and Professor Nathanson.

The first invites me to 'comment on whether or not I (they) agree or disagree with what has been said by Dr Hay about HCV testing and the provision of results'.

The general content of this report reflects my impression, recollection and the documentation of arrangements for hepatitis assessment and communication of information to patients from 1974 to 1995. The general discussion on hepatitis, evolution of knowledge and what would have been intimated to patients during the period is very reasonable. The following are my specific observations (which are of a relatively minor nature);

1. Dr Hay's report refers to the situation in England in relation to clotting factor concentrate availability (e.g. in Appendix page 35 para 3 refers to 'unavailability of UK virally attenuated concentrate until the autumn of 1985' refers to the situation in England as Scotland offered virally attenuated concentrates from December 1984 onwards.

2. In para 47 Dr Hay summarises the response amongst haematologists to his 1985 Lancet paper. What he writes is accurate and although the conclusions in his paper related to those with persistently elevated liver function test results (which was only half of the patients assessed by liver biopsy) a selected minority of these patients revealed serious and progressive disease. As he correctly points out his paper stirred controversy and he states that 'There was initial widespread reluctance to accept that non-A, non-B hepatitis was progressive in a significant minority of patients'. When other studies were subsequently published the general view amongst haematologists shifted towards viewing non-A non-B as a progressive type of hepatitis which could, in some patients, result in cirrhosis.

   He continues in paragraph 50 by stating that 'It was still felt that the majority of patients would have non-progressive or very slowly progressive disease and this has proved to be the case, by and large'.

3. Para 52 is a reasonable assessment of the situation as I remember it at the time.

4. Para 53 is also reasonable although I do not remember counselling the majority of patients to 'minimise alcohol intake' at this time. I had patients under my care with non-A non-B hepatitis who clearly consumed an amount of alcohol which was detrimental to their health (and some had clinical evidence of liver disease) and I certainly tried to persuade them to consume less. But I do not recall any advice at this

time suggesting that all patients with non-A non-B hepatitis should 'minimise' alcohol intake.

5. Paras 54-59 coincide with my recollection and the available documentation

6. Para 60 Dr Hay states that 'condoms were not required' however in Scotland we had advised all patients to use condoms from December 1984 onwards because of the risk of HIV which was known to be sexually transmitted. From evidence presented to the Inquiry earlier all patients were advised to use condoms (and they were given out routinely at the Haemophilia Centre) because it was unclear until sometime after 1985 that HIV antibody negative individuals were truly not infected with the HIV virus.

7. Para 62 contains an error. In line 6 it should read 1992 (not 2002) otherwise this para is accurate if it refers to 1992.

8. Paras 63-66 are a reasonable reflection of what was happening from 1992 onwards.

9. Para 67 states that in 1992 only an antibody test was available, however in Edinburgh because of our research activities in conjunction with Professor Peter Simmonds, who had developed an HCV PCR test (which detected HCV RNA and therefore the presumed virus in 1990) we were able to assess the viral carriage of Edinburgh patients earlier than elsewhere. (Simmonds et al, Lancet 1990, 336;1469-72)

10. Para 67 states that interferon use started in 1995/6. In Edinburgh we started initial treatment with interferon in about 1988 in symptomatic patients with non-A non-B hepatitis (after the publication of the paper by Hoofnagle et al in 1986). It was not until about 1992/3 that we systematically reviewed all patients with HCV in close collaboration with Professor Peter Hayes with a view to offering interferon to those who we considered might benefit. As Dr Hay indicates treatment of HCV in HIV positive patients is not so straightforward.

11. Para 68 reasonably states the position in the early 1990s.

12. Para 69 states in (a) that patient 'who had never been treated with blood products would have been known to have no higher risk of HVC than the general population and would be reassured and not tested'. As a minor point we wanted to be certain that in addition to 'blood products' we would wish to be reassured that the patient had not received any 'blood component', e.g. cryoprecipitate, before recommending that a test was not necessary. Patients are not always clear about what treatment they have previously received and therefore in Edinburgh we had a very low threshold for testing individuals, i.e. if there was any uncertainty in either the doctor or patient's mind HCV testing would be offered.

The second question to be addressed is to 'comment on whether or not I (they) agree or disagree with what has been said by Dr Vivienne Nathanson about HCV testing and the provision of results'.

Professor Nathanan's Supplementary report does not specifically address the questions related to HCV. Much of her response relates to good general medical practise rather than HCV specifically. She appears to be equating HCV testing with HIV testing from 1990 onwards and for reasons set out below I think this is entirely inappropriate. In my view it also seems quite inappropriate to equate HCV with Serious Communicable Diseases as set out by the GMC in 1997.

My more specific comments are set out below;

13. In her Supplementary Report Professor Nathanson, in response to **question (1)** in relation to what is explained about HCV testing **currently** to patients quotes from general GMC guidance and her own views about any investigation or treatment but she does not give any specific guidance in relation to HCV.

The information which is given today will depend upon the circumstances but if a patient is being investigated for the cause of abnormal liver function tests a large number of investigations will probably need to be initiated including for hepatitis B as well as hepatitis C. For an individual with active hepatitis B infection the implication of infection are probably more severe than for hepatitis C in that the risk of cirrhosis and hepatoma are greater. But in addition to these two hepatitis viruses there are many other causes of abnormal liver function tests and the causes include; primary or secondary cancer, chronic active hepatitis, chronic persistent hepatitis, primary biliary cirrhosis, gall stones, parvovirus, CMV, EBV and toxoplasma infection, alpha 1 anti-trypsin and caeruloplasmin deficiency, although the commonest cause is probably alcohol excess. To explain all the implications of all these possible causes, as Dr Nathanson is suggesting, is unrealistic in everyday clinical practice. It is appropriate to ask what the patient thinks the cause might be, enquire if they have particular diagnoses that were of special concern to them and potentially offer some suggestions as to the most likely cause if pressed or it seems appropriate.

If a patient **today** presented solely for HCV testing then it would be appropriate to outline the implications if PCR or antibody positive and what treatment could be on offered (and its side effects). Much more is known about HCV now compared to 20 years ago so it is possible to offer reasonably reliable information.

14. In her response to **question (2)** about HCV testing between 1991 and 2000 she quotes from the BMA publication on Philosophy and Practice of Medical Ethics of 1988. She states that there was an absence of GMC guidance at this time. In addition she quotes from the 1997 GMC advice on Serious Communicable Diseases (this document was withdrawn by the GMC on 13th November 2006) and it is noteworthy that by 1997 virtually all haemophiliacs had been tested for HCV.

As in response to the answer in para (1) above she responds by quoting what she considered would have been good medical practice in general rather than what should

have been told to patients specifically about HCV prior to testing. Furthermore she implies that there are serious non-medical consequences of HCV testing. Whilst I accept that patients should be well informed about their condition and investigations, an HCV antibody or PCR test was only confirming what was presumed to exist already, i.e. non-A non-B hepatitis. Most patients were very conversant with this situation.

In my view it is quite inappropriate to equate an anti-HCV test with an HIV test and to suggest that the Serious Communicable Diseases guidance was applicable to HCV.

HIV prior to about 1995 was an infection which appeared to be fatal in the majority of those infected, there was no effective treatment, it was relatively readily sexually transmitted and a significant risk to health care workers from needle stick injuries. Also being known to be HIV positive had major implications affecting all types of life insurance, sexual and marital relations, ability to travel (e.g. USA ban on travellers who were HIV positive) and possible (by implication) disclosure of sexual orientation.

By contrast HCV was known to be a slowly progressive disease in some individuals, treatment was effective in some, the chance of death was small, in the early 1990s it was not known to be sexually transmitted (and even with current information sexual and needle stick transmission is rare), it rarely affects the type of employment, it does not affect the ability of individuals to travel and does not reflect sexual orientation.

There are not, in general, serious non-medical consequences for a haemophiliac being known to be HCV positive. It is possible that a haemophiliac seeking life insurance might be asked about HCV and if he indicated he had not been tested the potential insurer would enquire about blood product therapy and liver function test results and with an appropriate history would assume he was HCV positive (and possibly load the premium). The individual might have been better off for being HCV tested because there is a 30% chance if antibody positive that he was PCR negative and he was therefore not at risk of progressive liver disease.

The implications, therefore, of HIV and HCV infection are very different. Although the whole of medicine, including issues related to consent, had been changed by the consequences of HIV infection in the 1980s, it was inappropriate to equate the arrangements for pre-HCV testing, particularly in those with haemophilia, with pre-HIV testing in after 1988 for the reasons set out above.

15. In response to **question (3)** Dr Nathanson refers to her answer in her previous report which was in relation to HIV. Again the issues are very different between HIV and HCV testing. A patient **currently** requesting HIV testing is usually very anxious (particularly if the individual is at significant risk) and it is appropriate to make the result available to the patient as soon as possible after the blood sample has been taken. In our clinical practice we have gone to considerable lengths to try and get the result back the same day and to inform the patient as soon as possible in person. In the context of HCV antibody testing the result usually confirmed that the patient had been exposed to the virus causing their non-A non-B hepatitis and this was anticipated to be positive. There was no benefit to be gained by giving the patient a rapid result (as described above for HIV) and therefore the patient was usually given the result at the

subsequent clinic visit. If a patient wished the result sooner arrangements would be made to provide it.

16. In response to **question (4)** Dr Nathanson makes reference to 'paternalistic' doctors but it is unclear why she makes this reference because I am not aware of any doctors not giving HCV results to patients for 'paternalistic' reasons. She very correctly outlines that in 1991 not a lot was known about the natural history of HCV infection and this only evolved over the succeeding decade. Again she correctly points out the difficulty of patients and relatives understanding risk and dealing with uncertainty.