Response from Dr Tait to the FURTHER QUESTIONS ON STATISTICS
relating to patients with bleeding disorders – HCV

Thank you for the opportunity to offer comment on the apparently discrepant statistics on HCV infection rates presented to the Inquiry by myself (on behalf of Scottish Haemophilia Directors), by Dr Hay from UKHCDO (reporting from the National Haemophilia Database) and Professor Goldberg (reporting from Health Protection Scotland data on positive HCV antibody tests from patients with bleeding disorders).

On review of the 3 sets of statistics, I believe the figures (accepting minor differences being explained by differing methodology and assumptions) are in fact broadly reconcilable as follows:

a. Using data from an updated UKHCDO database (April 2012), Dr Hay estimated the maximum total figure of likely HCV-infected patients to be 447. This is based on evidence of first exposure to clotting factor concentrates in Scotland and assumes that all patients not previously infected would have likely contracted HCV from their first exposure to concentrate during the period of risk. The UKHCDO database did not include information on known HCV status, and so this estimate does not take account of the known HCV status (antibody positive or negative) of some patients.

b. In contrast, Professor Goldberg’s data are based purely on the number of bleeding disorder patients in Scotland who have tested positive for HCV antibody (n=351) and who are likely to have acquired HCV through blood product exposure. These data do not take account of the country in which patients received the treatment which most likely transmitted HCV. Nor does it include any patients who were likely to have had HCV but who were deceased before antibody testing became available in ~1991.

c. Of relevance the ‘Scottish Haemophilia Directors 2007 review of HCV and its treatment in Scotland’ included in my previous statement (PEN-013-0016) was recently updated (February 2012) by Dr Henry Watson on behalf of Scottish Haemophilia Directors. Within the cohort of HCV positive bleeding disorder patients identified in Scotland there were 46 who were thought to have contracted HCV from prior treatment out with Scotland.
The estimate provided by myself, on behalf of Scottish Haemophilia Directors, takes account of treatment data (ie treatment with clotting factor concentrates, plasma or cryoprecipitate) provided by UKHCDO in January 2011 and HCV status data (as well as additional treatment data) from patient records held at Scottish Haemophilia Centres. We estimated that up to 459 patients likely contracted HCV through treatment in Scotland. This included 15 patients not present in the UKHCDO list (January 2011), but who were known to Scottish Haemophilia Centres as HCV positive most likely due to treatment in Scotland. If we add these 15 to Dr Hay’s estimate it would increase to 462 (very similar to our figure of 459).

Our total of 459 consisted 300 patients known to be HCV antibody positive and 159 patients whose HCV antibody status was unknown (although 14 of these patients were known to have had NANB hepatitis). Of the these 159 HCV antibody status unknown’ patients it is estimated that ~96 are now deceased and ~63 lost to follow-up, possibly deceased or moved out of Scotland. Our figure of 300 known HCV positives should be consistent with Professor Goldberg’s data on HCV positive bleeding disorder patients in Scotland (n=351). However, we know that the HPS figure of 351 will include patients HCV tested in Scotland but who may have contracted HCV from treatment out with Scotland. As noted in c (above) we are aware of 46 such patients. If these are subtracted from the HPS figure of 351 we reach a figure of 305 – similar to our figure of 300 for bleeding disorder patients known to be HCV positive from treatment in Scotland.

In summary then, I believe the statistics can be reconciled as demonstrating:

- A minimum figure of ~303 [300-305] bleeding disorder patients known to have contracted HCV (as assessed by HCV antibody positivity) through haemostatic treatment in Scotland.
- An estimated upper figure of ~460 [459-462] bleeding disorder patients who have or will likely have contracted HCV from haemostatic treatment (clotting factor concentrate, plasma or cryoprecipitate) administered in Scotland.
- We remain conscious of the possibility of a further small number of ‘unknown’ HCV positive, infrequently treated patients in the 1970s or early 1980s, whose treatment records no longer exist and who are no longer known to Scottish Haemophilia Centres.
As regards the five questions posed by the Inquiry to myself and Dr Hay, I would make the following additional comments:

1. What is the explanation for the discrepancy between these figures?

Key differences in methodology most likely explain the different statistics generated by the three authors.

Professor Goldberg's HPS data reflects the number of samples taken from patients within Scotland testing positive for HCV antibodies, and for whom the clinical history (presumably from HCV test request forms) states a bleeding disorder. This exercise cannot differentiate those patients whose HCV disease was contracted via treatment in or out with Scotland - in this respect it would appear to overestimate the true figure of known HCV positive patients contracting HCV via treatment in Scotland. However, because it will not include cases never having HCV testing in Scotland (e.g. who may have died or moved out with Scotland prior to 1991), it will underestimate the maximum figure of likely HCV infected patients.

Dr Hay's UKHCDO statistics and the data presented by myself are both based primarily on UKHCDO National Haemophilia Database (NHD) treatment records. However there are important differences in our assumptions and methodologies:

- Dr Hay's statistics are based on an updated version of the National Haemophilia Database (April 2012), whereas my submission is based on NHD data supplied by Dr Hay in January 2011.
- Dr Hay has allocated 'country of likely HCV infection' based on first treatment with coagulation factor concentrate. This contrasts to the exercise undertaken by myself which allocated likely country of HCV infection according to first treatment with factor concentrate, plasma or cryoprecipitate. Thus a patient who received cryoprecipitate in Scotland and subsequently factor concentrate in England would have been included in my statistics as possibly infected in Scotland, whereas Dr Hay would have excluded this patient. Conversely, a patient receiving cryoprecipitate in England and then factor concentrate in Scotland would have been excluded from my statistics but included in Dr Hay's numbers. This is likely to have led to at least small differences in the estimates of maximum numbers likely infected with HCV from treatment in Scotland.
- My data included 15 patients, known to Scottish Centres as HCV positive from treatment in Scotland, but whose treatment data were not present in the January 2011 NHD dataset. I am uncertain how many of these 15 cases would have been included in the updated (April 2012) NHD dataset used for Dr Hay’s most recent analysis.

- Dr Hay’s NHD dataset did not include any HCV antibody data. It was purely based on treatment records and the assumption that the first treatment with factor concentrate would transmit HCV. In contrast, my analysis included HCV antibody data where known.
  
a. Thus, if some patients exposed to small quantities of factor concentrate did not become HCV infected, Dr Hay may have overestimated the number of likely infected patients. This may be particularly true of patients receiving their first ever treatment as factor concentrate in 1987 & 1988, when concentrates were more effectively virally inactivated.
  
b. Conversely, Dr Hay’s estimates would ‘miss’ any patient receiving cryoprecipitate only. Admittedly the infection rate from cryoprecipitate is accepted as being lower than for factor concentrate. This potential limitation is accepted by Dr Hay in his submission.

2. Is one set of figures more likely to be correct and, if so, why?
As described above I believe the 3 sets of figures are broadly reconcilable, with the most reliable figure for the likely maximum number of bleeding disorder patients infected by HCV through treatment in Scotland being around 460.

3. The Inquiry is aware that the UKHCDO is in the process of collecting data from haemophilia centres on Hepatitis C test results. Do the currently available results of that exercise allow for a more accurate estimate to be made of the number of patients with bleeding disorders in Scotland likely to have contracted HCV as a result of treatment?
I believe this UKHCDO exercise is still ongoing, however Dr Hay will be in a better position to answer this question. This exercise may be able to clarify the HCV status of a few of the 159 ‘HCV antibody status unknown’ subset in d (above) – particularly
patients who moved to English centres in the 1990s and would have had their HCV status determine there.

Haemophilia centres in Scotland continue to seek out and assess patients who have or may have received coagulation treatments prior to 1989-91, and remain untested for HCV.

4. When is that exercise likely to be completed or, at least, reach a stage at which a more informed estimate can be made of the number of patients with bleeding disorders in Scotland likely to have contracted HCV as a result of treatment?

Dr Hay would need to answer this question.

As regards local activity in Scotland, this remains a slow ongoing exercise.

5. Has any further work been undertaken on the number of patients with bleeding disorders who were infected with HCV as a result of NHS treatment in Scotland who have died (including any further work in respect of the cause of death)?

Scottish Haemophilia Centres have found it impossible to undertake further work on the causes of death of our patients infected with HCV. However we continue to monitor the effects of HCV and particularly its response to therapy in our current patient cohorts.

This statement was prepared and submitted by Dr RC Tait on 8th January 2013.

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