Response to request received from the Penrose Inquiry and dated 28 November 2012 for further information on statistics

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The following is my response to the Inquiry's request about my contribution to the assumptions stated in the paper on estimates of HCV infections by Dr Christian Schnier and Professor David Goldberg.

Assumption i

Proportion of recipients of HCV contaminated units that develop HCV infection. We assumed that every recipient of a contaminated unit (independent of the type of unit) subsequently developed HCV infection. It is theoretically possible that a unit obtained from an infectious donor might not be infectious as a consequence of viral inactivation incurred during the donation/storage process.*

* ie an RNA (virus) positive unit

1 What data did I provide*? I did not provide data on this point.*

2 What opinion(s) did I express*? I would have agreed with this assumption, being familiar with data from the HCV lookback study*

3 To what extent did my information form the basis of the assumption? *I do not know*

4 Do I have reservations about reliability of the data and opinion(s) that I provided? *No*

5 Do I consider that further steps could be taken to improve the reliability of data and opinion evidence that I provided? *No*

Assumption ii

Proportion of HCV antibody positive donors who are RNA positive (infectious).

It was assumed that 75% of HCV-antibody positive donors were RNA (virus) positive and therefore infectious (The Global Burden of Hepatitis C Working Group, 2004).

1 What data did I provide*? I did not provide data.*

2 What opinion(s) did I express*? I would have agreed that published papers support the view that this assumption is reasonable*

3 To what extent did my information form the basis of the assumption? *Not at all*

4 Do I have reservations about reliability of the data and opinion(s) that I provided? *No*

5 Do I consider that further steps could be taken to improve the reliability of data and opinion evidence that I provided? *No*

Assumption iii

Reduction in the number of HCV-positive donors in the donor population as a result of deferral policy. Deferral policy, introduced by SNBTS in 1984, was assumed to have reduced the HCV prevalence in the donor population constantly by 66%. This assumption was based on limited local data and expert opinion.

1 What data did I provide? *Dr Gillon and I referred to the published SNBTS information on the prevalence of HCV antibody among donors in the 6 months from September 1991 (0.09%). However I was fully aware of the absence of reliable prevalence data either for donors or for a properly defined sample of the general population for the years in question. I therefore agreed with the decision to make a very conservative estimate of the possible effect of donor selection on HCV prevalence in donors over the period in question.*

2 What opinion(s) did I express? *The data from the lookback study was compared with the prevalence estimates for the wider population that had been published by Balogun et al (2002) who estimated that the population prevalence in England and Wales peaked in 1986 at about 1%. We also took account of the 0.67% prevalence (adults) in 2005, reported by the HPA (Hepatitis C in the UK. 2011 Report). My opinion on this information was that it could be interpreted to suggest that HCV prevalence was of the order of 10 fold lower in donors than in the general population. Dr Gillon also provided data indicating that the prevalence of HIV in donors was very substantially less than that among non donor populations for which data were available. I gave the opinion that the donor deferral measures introduced in 1983/4, although directed at AIDS, can reasonably be expected to have had some impact on another infection such as HCV that can be transmitted by blood and other body fluids.*

3 To what extent did my information form the basis of the assumption? *I do not know*
4 Do I have reservations about reliability of the data and opinion(s) that I provided? *I was fully aware of the absence of reliable prevalence data either for donors or for a properly defined sample of the general population for the years in question. I therefore agreed with the decision to make a very conservative estimate of the possible effect of donor selection on HCV prevalence in donors over the period in question.*
5 Do I consider that further steps could be taken to improve the reliability of data and opinion evidence that I provided? *No*

Assumption iv
HCV prevalence in the donor population between 1970 and 1990.

The first available observed data on the prevalence of HCV antibodies among the Scottish blood donor population applies to September 1991 to February 1992. The HCV prevalence in the donor population for each year between 1970 and 1990 was assumed to be proportional to the estimated number of HCV infected injecting drug users (IDU) alive during each year of the period, as above (Hutchinson, 2005). The rationale of assuming proportionality is that it is estimated that 90% of HCV-infected individuals in Scotland acquired their infection directly through injecting drug use and that an appreciable proportion of the remainder will have acquired infection indirectly as a consequence of injecting drug use (e.g., being born to an infected IDU or having unprotected sex with an infected IDU) (Hutchinson et al., 2006).

1 What data did I provide? *I did not contribute any data*
2 What opinion(s) did I express? *I did not express an opinion as I do not consider that I could add further information that I would expect to improve the reliability of that already provided*
3 To what extent did my information form the basis of the assumption? *Not at all*
4 Do I have reservations about reliability of the opinion(s) that I provided? *No*
5 Do I consider that further steps could be taken to improve the reliability of data and opinion evidence that I provided? *No*

Assumption v
Number of units generated from one blood donation. Each unit of donated blood was assumed to have been split into 1.25 units. This assumption was based on limited local data and expert opinion.

1 What data did I provide? *I did not provide any data in addition to that provided by Dr Gillon*
2 What opinion(s) did I express*? I gave the opinion that the most relevant evidence on this point was that from the HCV lookback studies.*
3 To what extent did my information form the basis of the assumption? *I do not know.*

4 Do I have reservations about reliability of the data and opinion(s) that I provided? *I pointed out that during the period under consideration the NHS in Scotland did not have a system to provide reliable data about the number of patients receiving blood components and the number of units that each patient received in a given period. A system has now been introduced that provides this information reliably on a routine basis (NHS Scotland Account for Blood).*

5 Do I consider that further steps could be taken to improve the reliability of data and opinion evidence that I provided? *No*

Assumption vi

Proportion of units transfused. Approximately 56% of the donated blood was assumed to have been transfused, with all units having the same probability of being transfused. Assumptions were based on limited local data and expert opinion.

1What data did I provide*? I did not provide data. I referred to the fact that during the period under consideration the NHS in Scotland did not have a system to provide reliable data about the number of patients receiving blood components and the number of units that each patient received in a given period. A system has now been introduced to provide this information.*

2 What opinion(s) did I express? *I agreed with the view of Dr Gillon that the most reliable data was that from the HCV lookback studies conducted in SE Scotland region following the start of HCV testing of blood donations*

3 To what extent did my information form the basis of the assumption? *I do not think that I contributed relevant information.*

4 Do I have reservations about reliability of the opinion(s) that I provided? *No*

5 Do I consider that further steps could be taken to improve the reliability of data and opinion evidence that I provided? *No*

Assumption vii

Number of recipients expected to receive more than one HCV contaminated unit. The risk of receiving two or more contaminated units is approximately 0.0007% – a risk which is negligible. Accordingly, it was assumed that all HCV-contaminated units were transfused to different patients.

1What data did I provide? *I made no contribution to the formulation of this assumption*

2What opinion(s) did I express*. I do not recall that I expressed an opinion on the final assumption. I did question whether it was important to consider the possible effect on risk estimates of the fact that patients receive different numbers of blood components, but eventually accepted the expert opinions that this was not relevant.*

3 To what extent did my information form the basis of the assumption? *Not at all*

4 Do I have reservations about reliability of the data and opinion(s) that I provided? No

5 Do I consider that further steps could be taken to improve the reliability of data and opinion evidence that I provided? *No*

Assumption viii

Age at transfusion of a contaminated unit. The age distribution of people receiving a blood transfusion was assumed not to have changed drastically between the years 2010/2011 (for which data were available, (Table 10 in the Appendix)) and 1970. This assumption was based on limited local data and expert opinion.

1 What data did I provide? *The data about the age distribution of blood recipients in 2010/11 was transmitted by me having been provided by colleagues from the NHS Scotland Account for Blood*

programme.
2 What opinion(s) did I express? *That the assumption was reasonable.*
3 To what extent did my information form the basis of the assumption? *I believe that this was the only data used*
4 Do I have reservations about reliability of the data and opinion(s) that I provided? *No*
5 Do I consider that further steps could be taken to improve the reliability of data and opinion evidence that I provided? *No*

Assumption ix
Effect of HCV infection on post transfusion survival rate. We assumed that the survival rate of recipients of HCV contaminated units did not differ from the survival rate of recipients of non-contaminated units. This assumption was based on Harris et al. (2006), who showed that for the first 16 years post transfusion, all-cause mortality in 924 HCV-infected transfusion recipients (cases) and 475 anti-HCV negative transfusion recipients (controls) did not differ significantly. Information about later survival of that cohort was not available.

1 What data did I provide? *None*
2 What opinion(s) did I express? *I do not remember but I think it is probable that I would have expressed the view that the assumption is reasonable in the light of published reports.*
3 To what extent did my information form the basis of the assumption? *Not at all*
4 Do I have reservations about reliability of the data and opinion(s) that I provided? *No*
5 Do I consider that further steps could be taken to improve the reliability of data and opinion evidence that I provided? *No*

Assumption x
Survival rate post transfusion to 2011. Age-stratified 5-year survival after transfusion was assumed to be similar to 5-year survival in North England (Wallis, 2004). Survival after those 5 first years post transfusion to 2011 was assumed to be similar to the survival of the general population in Scotland and that life expectancy for the period between 1970 and 2011 did not change enough to significantly influence survival in the context of the size and the age, at transfusion, of the infected cohort; life expectancy data for 2000-2002 were used in the model.

1 What data did I provide? *I did not provide data about this assumption.*
2 What opinion(s) did I express? *I expressed the opinion that it is reasonable and that the NHS Scotland Account for Blood system will in a few years begin to provide data but has not been in place for long enough to explore relationships between transfusion and survival.*
3 To what extent did my information form the basis of the assumption? *Not at all*
4 Do I have reservations about reliability of the data and opinion(s) that I provided? *No*
5 Do I consider that further steps could be taken to improve the reliability of data and opinion evidence that I provided? *No.*

Brian McClelland, 13 January 2013