KW 5/4/95

Colindale 29-3-95

Minutes of a preliminary discussion on the potential scientific outcome of the NBA HCV lookback

Attending: Drs P Hewitt, L Williamson, JP Allain

1- Projected numbers for the SE zone

- Confirmed anti HCV donors:

		Now
Cambridge:	70	~~890~~
Brentwood	100	75
NLBTS	136	150
SLBTS	300	- 250
Total	606	570-580

- Anticipated number of corresponding products: 3030

- Assuming that 50% of the recipients are dead and 50% of those alive will be traced, a population from 680 recipients will be obtained.

2- A large number of techniques is available and could be applied to this unique set of samples. However, most are expensive so we considered acceptable to use them only if it was anticipated to answer a specific and relevant question.

3- We have essentially identified 6 such questions:

1. What is the rate of infectivity of HCV confirmed positive blood and blood products?

2. Is there any difference of infectivity between products? In particular between platelets, red cells and cryoprecipitate?

3. If any recipient has indeed been transfused with an HCV carrying product, is seronegative and HCV RNA negative, can we identify some explanation? ie below threshold of infectivity? host factor protective of infection? less infectious subtype etc.

Any such recipient will be submitted to intense research.

4. What is the respective proportion of chronic vs recovered post-transfusion HCV infections? The presence or absence of HCV RNA does not seem to be a sufficient criterion. Liver biopsy will be the most decisive criterion provided the reference hepatologist agrees with this concept. This is the case in Cambridge but may not be with other consultant ie H Thomas or Dusheiko. The HCV research group in Cambridge has developed a panel of peptides from the E1 and E2 regions. They can be used to detect specific antibodies which might correlate with recovery or chronicity.

5. What is the impact of host factors on the natural history of HCV infection? This critical question could be addressed in a nearly experimental fashion by in-depth study of clusters of recipients from a given donor. Such donor ideally should present the following characteristics: archived serum or plasma samples to follow by sequencing of the E2 hypervariable region the genetic drift of the reference virus; a number of traceable recipients in

particular who have received products from any given date; if at all possible to obtain, in addition to today's sample, some archived samples taken in hospital between the time of transfusion and 1995. If several such clusters can be identified, it would be desirable to compare clusters from different HCV subtypes in particular 1a, 1b, 3.

6. What is the rate of sexual transmission of HCV from infected recipients to their sexual partners and of vertical transmission? These questions are not directly part of the look-back study, require recipients' informed consent as well as of partners and are therefore not considered as priorities.

In practical terms, the answers to the first four questions could be obtained with the serology and the RNA detection required from PHLS laboratories involved with the exercise. The clinical side, in particular liver biopsies, should be discussed with the appropriate hepatologists. The antibodies to E1/E2 peptides could be done within the routine in Cambridge. Only project from question 3, if any is found, and the last project would require special funding.

Next meeting is scheduled for 26 April, the time remains to be determined.