Summary of discussions of the meeting held at Excelsior Hotel, Heathrow Airport, on 24th January 1983

Professor A.L. Bloom in the Chair.

Mr. Berry welcomed all who were present and outlined the arrangements made.

Dr. Eibl then explained that two methods were being studied whereby the risk of transmitting non A, non B hepatitis by Factor VIII or IX concentrates could be removed or at least very greatly reduced. Unfortunately, as patenting procedures were not complete, he could not reveal full details. This would be possible within three months by which time treated concentrates would be available.

Method I

This is carried out at 4°C and is suitable for use with Factor VIII concentrate. The substance used is frequently employed in the food industry. The process is applied to the final product so other products from the fractionation scheme are not affected.

There is a 25% loss in yield.

No significant change has been observed in Ristocetin co-factor, Cag or Rag.

There is no loss of protein as shown by immunoelectrophoresis and chromatography, and no change in proteins.

It can be shown by chemical tests that less than 1% of the additive remains.

It was not yet known if all other viruses would be destroyed but certain animal disease viruses had been inactivated.

Factor VIII concentrate known to have transmitted non A, non B hepatitis was treated by Method I and 250 units in 10 ml (>100 infective particles) given to each of four chimpanzees. No increase in transaminase level occurred during six months observation. The animals were then challenged with untreated material and non A, non B hepatitis occurred in each as shown by elevated transaminase level and biopsy samples.

Method II

This method had been shown to be more suitable for treating partial prothrombin complex, whereas Method I caused too great a loss of yield. The process is carried out at 37°C using substances which are present in normal body metabolism.

../2

Method II has been shown to be more powerful than Method I for inactivating animal disease viruses, but experiments with non A, non B hepatitis in chimpanzees have not yet been completed.

Dr. Eibl then said that guidance was required from the meeting as to the correct procedure as far as future use of these products were concerned and the following points were made:

1. Young children could not be used for trials as neither they nor their parents could give consent.

2. Adult haemophiliacs with an established immunity to non A, non B hepatitis would not benefit from a trial, but it was thought that they would be sufficiently public spirited to agree to these materials being used on them to shown haemostatic effect and absence of toxicity due to remnants of additives.

3. All batches of NHS and US commercial concentrates had been shown to be capable of transmitting non A, non B hepatitis. It is believed that a one in fifty chance of transmission from cryoprecipitate occurs.

4. Because of 3, many thought it would be difficult to justify carrying out a prospective controlled trial. However, it was generally agreed that sufficient susceptible adult patients needing high level treatment, e.g. for surgery, could be identified to warrant uncontrolled prospective trials of this and other virus inactivated products. It was agreed that such trials should be instituted.

5. Aggregates are not formed by processing.

6. It was not practical to test every batch in animals. In fact, it is hoped that the requirement to test batches of HB_s vaccine in chimpanzees will soon be discontinued. However, it is intended that three consecutive batches will be tested in animals.

7. Maximum effort so far had been to show clearance of non A, non B hepatitis which is regarded as the main problem. Later on tests will be made on the effect of both methodson hepatitis B and possibly other viruses.

   It will be necessary to show separately that B and non A, non B can be removed and then in practice remove them together.

8. Testing for effect on poliomyelitis and canine hepatitis could be done on tissue cultures without resorting to chimpanzees.

9. Residual additive will be minimal but the amount will be declared.

10. Test concentrate will be made from infected chimpanzees treated and re-injected to indicate absence of antigen formation.

11. Clinical trials are planned in other areas including USA, Japan and Central Europe.

12. Within three months, the patent will be released and information on the additives will be released. By this time five batches of concentrate will be available.

13. The possibility of reducing the risk of AIDS was not known at this stage. In any case, it is not known if AIDS is caused by a virus or an attacker inimical to T cells.

Professor Bloom then summarised as follows:

(a) Clarification should be sought from DHSS as to whether the treatment of the final product could be covered by a Product Licence variation or if a Clinical Trial Exemption Certificate was necessary. It was agreed that the best procedure would be to seek a Product Licence, if necessary via Clinical Trials in preference to use on a named patient basis.

(b) Haemostatic activity in terms of in vivo recovery and half life and absence of toxicity should be ascertained in adult haemophiliacs.

(c) The material should then be assessed in the treatment of adult haemophiliacs susceptible to non A, non B hepatitis by a properly conducted trial in susceptible patients in appropriate need of treatment. It was agreed that it should be possible to identify sufficient U.K. patients for such trials.

(d) The material could then be used on newly diagnosed children.

(e) Trials could be arranged by the Committee of the Haemophilia Directors, and it would be best to use five separate batches with two patients receiving each batch.

Professor Bloom then closed the meeting with thanks to the participants and Immuno, then Mr. Berry thanked the Chairman.