Minutes of the 31st Meeting of Haemophilia Reference Centre Directors held at the Royal Free Hospital on Monday 13th Febraury 1989.

Present: Dr. C.R. Rizza (Chairman)
Professor A.L. Bloom
Dr. J. Craske
Dr. G.D.O. Lowe
Dr. C.A. Ludlam
Dr. E.E. Mayne
Professor F.E. Preston
Dr. G. Savidge
Dr. I.D. Walker
Dr. R. Wensley

1 Apologies for absence were received from:-

Dr. I Delamore, Dr. P. Jones and Miss R.J.D. Spooner. The Chairman welcomed those present. He indicated that Dr. Delamore had written to him informing him of his (Dr. Delamore's) early retirement in March 1989. He sent apologies and said he had always enjoyed attending the meetings.

2 Minutes of the Thirtieth meeting were approved and signed by the Chairman.

3 Matters arising from the Minutes

3a. Revision of Document giving Recommendations for Safety and Usage of Factor VIII

The second draft of the document was presented and introduced by Dr. Kernoff. Dr. Savidge and Professor Bloom felt that the Travenol monoclonal product, Hemofil M, should be included under para. 5.2.1. if it had obtained a CTX. Dr. Craske felt that UK material should be recommended where products were of equal merit. It was agreed that "Virgin" or "PUP" patients should be treated with 8Y. It was stated that Hemate (Behringwerke) had been used safely in many more patients than any monoclonal factor VIII. It was regretted that it was not more freely available in the UK. Dr. Wensley indicated he had found that patients who had experienced reactions to 8Y had no difficulty when treated with monoclonal factor VIII. Professor Bloom indicated that Profilate HT (Alpha) had the largest share of UK commercial market and that the company were probably to change from Heptane - slurry to solvent/detergent treatment. Dr. Mayne expressed some reservations regarding the longterm toxicological effects in patients of traces of infused solvent/detergent. Members agreed to write to Dr. Kernoff before the end of the month (February) with any recommendations for changing the docuemnt. There were differing opinions expressed regarding the efficacy of factor VIII concentrates (including 8Y) in

managing von Willebrand patients.

3b. **Collection of data on Factor VIII usage on a Regional Basis**

Members had been requested to write to Dr. Rizza regarding the collation of Factor VIII usage on a regional basis. There had been no input from members.

The Chairman reported that Dr. Gunson had requested information regarding the Regional Factor VIII usage and the numbers of patients treated per annum. He stated that it would help estimate future distribution of factor VIII. Dr. Ludlam indicated that Professor Cash had requested similar information within Scotland.

Dr. Savidge questioned the confidentiality of sending information to Dr. Gunson. Professor Bloom was apprehensive that the information might be misused especially with the implementation of cross charging. Dr. Mayne suggested sending at least three years' statistics to Dr. Gunson so that he could see the variability in usage in each region. Dr. Savidge requested a formal letter from Dr. Gunson outlining precise requirements before the members sent any deatils. This was agreed. Dr. Rizza stated that he would write to Dr. Gunson and that he would circulate the subsequent reply. He requested members to respond promptly and write comments to him. It was agreed to include data regarding Factor IX usage.

3c. **Shortfall of factor VIII in Scotland**

Dr. Mayne and Dr. Ludlam stated that many bureaucratic problems had been overcome and a successful interchange of material had beeen achieved between Scotland and Northern Ireland.

3d. **Newsletter**

There had been no input from Directors. The principle of a News Letter was accepted but the matter was deferred in the meantime. Members were reluctant to devote valuable time to it at present.

4a. **Reference Directors Meetings - Participants**

The Chairman had received a letter suggesting that the Director of Blood Transfusion (England and Wales), Dr. Harold Gunson, should be invited to the meetings on a regular basis. Discussion ensued. There would be a need to invite Professor John Cash in addition, in his capacity as Director (Scotland). Dr. Wensley thought it would be of mutual benefit to have regular transfusion input to meetings. Dr. Mayne thought 'ad hoc' invitations would be of greater benefit; Dr. Lowe agreed. Dr. Savidge suggested invitations to appropriate sub-committees after the regional reorganisation. The Chairman agreed to write to both, extending regular membership.

4b. **Annual General Meetings's**

The Chairman had received several letters subsequent to the September meeting in Dublin, proposing future combined meetings, e.g. with 'haemophilia doctors' in France or Holland. The proposal was accepted in principle and will be put to the AGM. Various venues were suggested, e.g. Jersey or Leiden. Dr. Rizza agreed to contact the former to ascertain costs and feasibility. David Watters had written suggesting holding a much larger UK meeting - a "mega meeting" with poster session and simultaneous seminar/lecture session. It was decided not to change the format of alternate year meetings at present. Dr. John Leslie had written proposing that peripheral haematologists be invited to the scientific meetings and AGM. It was agreed that this suggestion should be placed on the agenda at the next AGM. Dr. D.H. Evans wrote commenting on the lack of variation in the Haemophilia Nurses participants. It was agreed that that the Reference Centre Directors had no remit to offer suggestions in this respect.

5. **1987 Annual Returns**

These were presented and discussed. The increased number of deaths related to HIV was noted. Professor Bloom felt that clear guidelines should be established regarding referrals to the Coroner. In Wales all transfusion-related HIV cases must be referred to him. This action is not general throughout the UK. It was observed that there were more deaths from cancer in the HIV negative patients. Dr. Rizza drew attention to his final paragraph of introduction to the report om the 1987 Annual Returns; he made the point that other causes of death could have been related to HIV infection, e.g. septicaemia, etc.

6. **Factor IX Gene Mutation - Proposals for a UK data base**

Doctor F. Giannelli and Dr. David Bentley from Guys Hospital were introdued by the Chairman. Dr. Giannelli outlined his proposal. He requested the help of the committee in the establishment of his data base as outlined in his document circulated prior to the meeting. A wideranging discussion followed. Professor Bloom inquired as to the total number of kindreds in the country with Haemophilia B. There were approximately one thousand patients. Dr. Giannelli intended to utilise PCR (polymer chain reaction) techniques on each exon. His "running time" was estimated to be three days. He estimated that compilation of the Data Base would be completed within 3-5 years. He intends to correlate the molecular defect obtained from his methodology with the functional defect. Dr. Giannelli stated that he would provide a service and that the patients results would be sent back promptly to the referring doctor. He thought his technique would be more accurate than the present RFLP technique, the chances of positive error would be minimal and if the result was negative, he would return to reinvestigate

the affected relative. The time estimated for investigation was between 48 and 72 hours. He admitted difficulty when there was a single patient with no family history.

Drs. Savidge and Kernoff asked regarding costing and the security of the research funding. Dr. Giannelli replied that patients travelling would be funded. He was unwilling to reveal the funding source but indicated that it was secured for the five year plan. On further questioning he stated that there was no involvement of the S E Thames Health Authority. His money is guaranteed for the five years. The pilot study of 30 patients should reach completion by this summer. He had no information when or if his techniques would be applicable to Factor VIII and indicated this was approximately 25 times the Factor IX problem!

Dr. Ludlam suggested that a copy of the data base should be kept in Oxford. Dr. Giannelli agreed. Dr. Kernoff asked if Dr. Giannelli would provide antenatal diagnosis. He agreed and stated that if previous data on the family were available, he could provide the information within two days, otherwise the results would take one week. Dr. Giannelli stated that there would be no cross charging. The discussion ended and the Chariman thanked Dr. Giannelli. Thereafter Professor Bloom said he was happy about the proposal but stated he would wish to continue his own work in the same field.
Dr. Giannelli had stated that members' approval and input were essential to the establishment of his data base. Members felt that they could not give blanket approval. Dr. Rizza agreed to write to Dr. Giannelli saying that the Referemce Centre Directors' were sympathetic to proposals but suggesting that he approach all Haemophilia Directors individually.

7. **Surveillance of possible viral transmission by coagulation factor concentrate**

The Minutes of a meeting held in Oxford on Monday 31st October 1988, were presented and discussed.

Dr. Rizza presented an adverse reaction card to the meeting. It was one used by the British Paediatric Surveillance Unit. It was agreed by the meeting to use a similar card for Haemophilia with appropriate amendments. It should be sent out monthly and non events recorded. Viral events would be investigated by CDSC and at Rockwell in Scotland. The card and proposals will be presented to the AGM in October.

8. **8Y Study Progress Report**

The report was presented. Dr. Rizza will send out updated report to all Directors to encourage participation.

9. **Hepatitis Working Party**

Dr. Craske felt that it was appropriate time to disband the

Working Party, at least temporarily. Professor Bloom suggested a compromise namely to change the emphasis from epidemiology to clinical and to rename the committee as the Chronic Hepatitis Working Party. Dr. Craske agreed and suggested that he stand down as chairman and a new Chairman be appointed. Dr. Kernoff proposed Professor Preston who was duly elected. Dr. Rizza thanked Dr. Craske for all his hard work in the past. During his reply Dr. Craske reminded members that intradermal vaccination for Hepatitis B was ineffective but that subcutaneous was satisfactory.

9b. **Von Willebrand's Disease Working Party**

Dr. Savidge reported only 30% return from his questionnaire on the diagnosis of von Willebrand's disease following the Dublin AGM. He indicated a further three months' grace before the results would be analysed. He stated that efficacy of factor VIII concentrates in treating von Willebrand's disease had not yet been taken up by the working party.

9c. **Inherited Platelet Disorders**

Professor Preston indicated that the guidelines for Platelet Function Testing had been published by the ACP in the Journal of Clincial Pathology. The project had been funded by the British Society for Haematology. Discussion followed, regarding the continuation of the working party. Professor Preston suggested that other than Haemophilia Centres should be approached for data. He had 230 patients registered, he felt that this was an underestimate. Dr. Kernoff suggested that there was little need for both the Directors' Working Party and the Haemostasis and Thrombosis Task Force to set up a register of inherited platelet disorders. It was agreed to take requests for registration of platelet problems back to the British Society for Haematology. It was suggested that they hold a one day meeting for those interested in platelet disorders.

9d. **Data Collection**

Dr. Rizza and members agreed to wind up the Working Party as from 13th February 1989.

9e. **Reorganisation of Haemophilia Care**

Dr. Savidge stated that a further meeting was due to take place on the 16th February 1989. He felt that several changes in the plans for reorganisation might be necessary in the light of the Government's NHS White Paper. Dr. Rizza and Professor Bloom suggested that the planned reorganisation should be pushed ahead as soon as possible regardless of the White Paper. During further discussion it was felt that changes in the numbers of representatives Reference/Regional Directors attending meetings would increase by September 1989. Dr. Kernoff was worried that several very active treaters of

haemophilia were excluded at present. He proposed a motion that several (Dr. Brian Colvin from London and Dr. Franklin from Birmingham) should be invited to become members. There was no seconder for the motion and no further discussion.

9f. **Adverse Reaction Working Party**

Dr. Kernoff agreed to draw up a document setting out the remit of the Working Party and giving a list of members. This would be presented at the next meeting of the Reference Centre Directors'.

10. **NEQUAS**

Dr. Kernoff reported that the current NEQUAS exercise included assays of Factor VIIIC and VW factor antigen.

11. **Any Other Business**

Dr. Craske reported that he had received a letter from Mr. Pettet (BPL) asking for further information regarding six cases of hepatitis from NHS VIII and IX. There was no absolute information available. Commercial products may also have been involved. Dr. Rizza, Dr. Craske and Dr. Kernoff agreed to get together to draft a response to Mr Pettet. Professor Bloom stated that all members should contact, in the first place, the manufacturer if they felt that any product was involved in an episode of hepatitis.

PROTEIN A separation

Dr. Savidge informed members that Travenol Ltd had installed a proteinase separator column "wash out" machine for the management of high titre inhibitor patients. He offered the facility to members at no cost.

Dr. Rizza read out a letter from Professor Shinton (Coventry) who was disturbed by the Reference Centre Director speaking directly to Haemophilia Nurses without first clearing the matter at the AGM. Dr. Rizza had written back asking for specific information and had received no reply. No one knew the background to Dr. Shinton's comments and no action was was taken.

Dr. Kernoff indicated that a payment of £10 was needed from all committee members to defray expenses of the meeting. Receipts were issued.

The meeting ended and the date and place of the next meeting was decided to be in St Thomas's Hospital, London at 10.30 am on Monday 11th September 1989.

GRO-C

14/9/89