

CENTRAL BLOOD LABORATORIES AUTHORITY  
CENTRAL COMMITTEE FOR RESEARCH AND DEVELOPMENT  
IN BLOOD TRANSFUSION

Minutes of the third meeting of the Central Committee for Research and Development in Blood Transfusion, held on 28 February, 1984 in the Board Room, The Crest.

Present: Dr H H Gunson (Chairman)  
Professor A L Bloom  
Dr I A Fraser  
Dr K I Gibson  
Dr R S Lane  
Dr C Rizza  
Dr D P Thomas

In Attendance: Mr W P N Armour (CBLA)  
Dr A E Bell (SHHD)  
Dr A Smithies (DHSS)

By Invitation: Professor G G Brownlie  
Dr T Wallington

The Chairman welcomed to her first meeting Dr A Smithies, who had replaced Dr D Walford and welcomed also Professor Brownlie and Dr Wallington, who were attending by invitation.

1/84 Apologies for Absence

Apologies for absence were received from Dr A M Holburn, Professor L Luzzato, Dr D B L McClelland, Dr G A Stewart and Dr R Tedder.

2/84 Minutes

The minutes of the meeting held on 7 December, 1983 were approved as a correct record.

3/84 Matters Arising from the Minutes

3.1 Status of Central Committee for R&D in Blood Transfusion

Following questions raised at the last meeting about the status and functions of the Committee, the Secretary confirmed that the CBLA had been asked by the DHSS to set up such a committee and look after its administrative needs, and he reiterated upon its terms of reference. He said that the Authority had not established sub-committees because of the size and nature of the activities of the Authority. By organising the Central Committee in this way advantage could be taken of widening the expertise available on blood transfusion. In answer to a question raised by Dr Thomas, Mr Armour said that the Committee was considered to be a UK committee rather than an England and Wales committee only. Dr Bell however stressed that it was not his understanding that the Committee was a UK committee and questioned the authority of the DHSS to deem it so. The Secretary said there was clearly a need to clarify the situation but it did not conflict with the terms of reference.

It was subsequently agreed that the CBLA should seek clarification from the DHSS on this matter, Dr Gunson in the meantime confirmed the advantage of the Central Committee being a UK Committee.

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3.2 Applications of Genetic Engineering to the  
Preparation of Blood Products

Professor Brownlie had been invited to the meeting to outline progress he had made in regard to the preparation of Factor VIII and Factor IX through genetic engineering.

Professor Brownlie informed the Committee that he had made some progress with Factor IX and he referred to the six stages of investigation needed to be passed through for the preparation of genetically engineered blood products which were:

- (1) Obtaining a clone
- (2) Development of the clone
- (3) Fermentation of clone material
- (4) Purification of protein
- (5) Toxicity trials
- (6) Clinical trials

It was noted that three groups from the USA had already completed the second stage of developing a clone for Factor IX. Professor Brownlie reported however that no significant progress had been made on Factor VIII and he outlined the difficulties for its cloning. He expressed the view that it would be possible to reach stage (2) for Factor VIII in the future, although a lot of research work, possibly over a two year period, would be required. It was noted however that the Genetics Institute, Boston, USA, had reached the stage of obtaining a clone for Factor VIII. In answer to a question raised by Dr Thomas, Professor Brownlie expressed the opinion that the scientific stages could be completed in approximately five years.

The Chairman questioned the future role of BPL in regard to genetically engineered products and Dr Lane expressed the view that in the long term the Laboratory would not purely be involved in human products and in the late 1980's or early 1990's it would have the potential for downstream purification of cloned material.

The purification of protein was discussed further and Dr Lane said that when the new BPL was opened the old facility might be used for pilot processing and a product started from bacteria could be developed for purification.

Professor Bloom asked about DNA contamination and Professor Brownlie confirmed that the protein would have to be as pure as possible.

After summing up the current position the Chairman felt that the Authority could not ignore the work which was currently taking place in genetic engineering and it was agreed to recommend to the CBLA that investigations should be made into possible collaboration for the preparation of Factor VIII through genetic engineering with the appropriate USA companies, although it was noted that this may require negotiations with respect to processes which had been patented. There was no UK company involved in this work at present.

The Chairman thanked Professor Brownlie for his interesting and helpful comments on this subject.

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### 3.3 Possible Areas of Collaboration with CAM-R, Porton Down

Consideration was given to a report of the Director, BPL and it was noted that a visit had been made to CAM-R on 21 February 1984, and tabled a report which is appended to these minutes.

Dr Lane confirmed that a production building was now under construction at Porton and would be augmented by a pilot fermentation process for development in genetic engineering. Facilities for fermentation at CAM-R up to 3,000 litres capacity, were incorporated in the design for the new buildings.

The potential collaboration aspects were highlighted and it was agreed that with proper management and liaison, the resources of CAM-R, BPL and the Transfusion Service were complementary. It was noted that the Director of CAM-R had been invited to visit BPL and that an appropriate occasion for a visit would include meeting members of the Central Committee for R&D in Blood Transfusion.

### 3.4 Trials of BPL Heat Treated Factor VIII Concentrate

The Chairman reported that an approach had been made to Dr Delamare, Director, Manchester Haemophilia Centre, for a collaborative study using heat treated Factor VIII. It was noted that Newcastle and Liverpool Haemophilia Centres had now agreed to join Manchester in this study. Birmingham would be approached as the final centre owing to the fact that Sheffield was already involved in commercial trials. The Chairman said that hopefully a meeting would be arranged in the near future to draw up a protocol outlining proposals for the trial.

The question of funding for the trial was raised and members agreed that it would be appropriate for the CBLA, bearing in mind that it was their product, to take this matter up with the DHSS rather than an approach being made to the MRC for funds.

## 4/84 Working Group on AIDS

### 4.1 Minutes of Second Meeting of the Working Group on AIDS

The Chairman enlarged upon the minutes of the second meeting of the Working Group.

At the second meeting of the AIDS Working Group it had been agreed that Drs. Wallington, Tedder and McClelland would consult Dr Contreras and Dr Fraser (Directors of N. London and Bristol RTC's respectively), to consider putting forward proposals for a study, involving blood donors, to investigate the practicality and usefulness of performing non-specific tests which have given a significant number of positive results in the majority of patients suffering from AIDS. Dr Wallington presented proposals which were discussed by the Committee.

The plan of investigation was based on the screening of 50,000 blood donor samples for anti-HBc at the N. London and Bristol RTC's. Recent experience has shown that this will produce 500 positive results; both the positive donors and an equal number of controls will be traced and interviewed by medical staff. On the samples from both positives and controls further laboratory investigations will be carried out, viz; TPHA, Alpha interferon, circulating immune complexes, beta-2 microglobulin, immunoglobulin and HTLV antibody.

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Following questions by the Chairman, Dr Wallington confirmed that plasma from positive donations would be separated and stored frozen to use in the investigations but the red cells would be transfused since there was no indication yet that they were not safe. The problem with respect to supplies of plasma for anti-HBs immunoglobulin which was also anti-HBc positive had not been considered and it was thought that the acceptability of this material was a matter for the fractionaters.

Dr Thomas pointed out that the proposed study, although initiated by a consideration of the AIDS problem in blood donors did not in itself constitute a study into AIDS. Nevertheless, he considered that it was an important investigation in its own right. Members of the Committee agreed that the proposals should be written in the form of a grant application to the MRC. Dr Gibson commented that the MRC was in the position of having to turn down acceptable projects on AIDS because funds were over-stretched; however, a study such as the one proposed may be appropriate for funding under health services research.

Dr Wallington undertook, in collaboration with his colleagues, to put forward a formal grant application and the Committee request that these proposals receive support from the CBLA and DHSS which could be communicated to the MRC.

- 4.2 Dr Lane commented on the study which was being undertaken with Dr Rizza on the use of Factor VIII which had been prepared from pools of plasma which had been obtained from the panel of plasmapheresis donors at Leeds. Encouraging initial results had been obtained with 18 patients where the short-incubation non-A, non-B hepatitis appears to be absent whereas with Factor VIII obtained from plasma from randomly collected donations the attack rate was 100 per cent.

The implications for the plasma supply if these results were confirmed was noted, and the need for Factor VIII derived from similar plasma obtained from other parts of the country was recognised. In the latter regard Dr Lane was hoping to obtain plasma from the Mersey region in the near future.

4.3 Report on Activities of MRC Working Party on AIDS

Professor Bloom confirmed that the MRC Working Party on AIDS had last met in December 1983 and concern had been expressed that in spite of the quality of research projects put forward, the Systems Board had not been able to support all of them. He emphasised therefore the need for research project applications to be well written.

Professor Bloom said that the importance of blood transfusion in regard to AIDS had been emphasised at the meeting. It was noted that the MRC Working Party had been particularly interested in patients who had contacted the disease, whether or not they were blood donors, and the follow-up of recipients who had received blood products.

4.4 Report on Meeting with Commercial Manufacturers

Dr Thomas reported upon discussion held with commercial manufacturers about the implications of AIDS.

It was generally agreed that an effective scheme was required in the UK indicating awareness if an AIDS patient had contributed to a plasma pool. It was noted that the PHLS had recently informed Dr Lane of one such case, although the Chairman pointed out that the system was purely informal.

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Dr Smithies referred to a weekly report from CDC and agreed to follow up the question of arrangements for reporting cases of this nature.

5/84 Date of Next Meeting

The next meeting would be held at Elstree on Tuesday, 9 October, 1984 at 11.30 a.m.

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