Freedom of Information request: AIDS Meeting Minutes - ref UKRI – 2018/0141 M

Thank you for your Freedom of Information request submitted on the 5th September 2018 in which you requested the following:

Your Request:

Please could you provide me with copies of the following minutes:

1. The first meeting of the MRC ‘ad hoc’ Working Party on Acquired Immune Deficiency Syndrome convened on 29th July 1983.

2. The second meeting, held on 10th October 1983.

Our response:

I can confirm that UKRI does hold the information that you have requested. Our response is detailed below:

1. The meeting held on 29th July 1983 was an informal meeting involving senior members of staff from the MRC, DHSS and PHLS. The note of the informal meeting was never finalised but the attached document, UKRIFOI2018-0141 File S819/1 Informal meeting on AIDS 29th July 1983, is the last draft copy we hold. The draft note was not recirculated but reflects comments made by participants on an initial draft. The note includes an Annex and the name of the author has been redacted under Section 40(2), the exemption for personal information.

2. The minutes of the first meeting of the MRC Working Party on AIDS held on 10th October 1983 are also attached as, UKRIFOI2018-0141 File S819/3 WORKING PARTY 1ST MEETING.

If you have any queries about this response please contact me, or if you are unhappy with the service you have received in relation to your request and wish to request a review of our decision, please write to:
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Yours sincerely,

Information Manager  
UK Research and Innovation, Information Governance Team  
Email: foi@ukri.org
Circulation

Participants

MRC WORKING PARTY ON AIDS

Minutes of the meeting held at 20 Park Crescent, London W1N 4AL on Monday 10 October 1983

Present:

Members

Dr D A J Tyrrell (Chairman)
Dr A J Pinching (Secretary)
Professor M W Adler
Professor A L Bloom
Dr J R W Harris
Professor P J Lachmann
Dr D Taylor-Robinson
Dr A D B Webster
Dr R A Weiss

Departmental Observers:

Dr W M Prentice (SHHD)
Dr Diana M Walford (DHSS)

By Invitation:

Dr S R Palmer
Dr R S Tedder
Dr J E M Whitehead

MRC Office Staff:

Dr M P W Godfrey
Dr Katherine Levy
Dr M J Fisher
Dr Jane E Cope

Apologies for absence:

Dr N S Galbraith
Professor H P Lambert
Professor K Murray

1. Chairman's Introductions

The Chairman welcomed the members of the Working Party and introduced Dr Whitehead of the PHLS, Colindale, Dr Palmer of the PHLS, Cardiff who was standing in for Dr Galbraith and Dr Tedder of The Middlesex Hospital. He outlined the background to the setting up of the Working Party and indicated the need to ensure that the best use be made of the special combination of suitable patients for study and the clinical, immunological, virological and other expertise available in the United Kingdom. The Working Party would review the current position and seek out areas in which a UK contribution might be most effective. He invited the Working Party to make comments, both judicious and outrageous, and to generate ideas that might stimulate new research objectives. The importance of high quality work was stressed, along with the need for the Working Party to ensure that truly original scientific objectives are encouraged subject to the normal peer review mechanisms. The Working Party would advise the Systems Board on the whole area of AIDS and review specific grant proposals prior to their consideration by that Board.
2. **Terms of Reference of the Working Party**

The Chairman reminded the members of the Working Party's remit:

1. To review scientific knowledge and research on AIDS in the UK and abroad.
2. To encourage contact and co-operation between research workers in this field.
3. To advise the Council on the current state of knowledge in the field and on topics for research.

Concern was expressed by several members that the Working Party was to act in part as a grants committee. As many of the members of the Working Party were closely involved in the projects coming before it, there was a potential problem of impartiality. It was explained that the Working Party had no delegated authority, it would act as a panel of referees and further expert opinion might also be sought. Applicants would, of course, be excluded from discussion of their own proposals. The Working Party would make recommendations to the Systems Board (which was represented on the Working Party) which would consider the applications for Special Project Grants.

3. **AIDS: The current position**

The Working Party reviewed the present position on AIDS, assuming that most of the major literature was known to members in advance. Members of the Working Party with particular expertise spoke on individual sections of the discussion.

(a) **Clinical**

It was noted that AIDS provided a good example of a problem arising in clinical medicine which was posing many new and unexpected questions of basic science. The overall clinical picture of AIDS was of a specific and severe form of immunodeficiency with a range of presenting disorders extending from Kaposi's sarcoma to multiple opportunist infections. The broad resemblance to the congenital immunodeficiency SCID was noted. The manifestations were noted to vary according to both host and environmental factors. The pattern emerging in early UK cases seemed different in some respects from the American experience, and the gastrointestinal problems were noted as a particularly important area for research. The laboratory markers for disease were well established for AIDS itself but their relevance in screening and in a possible precursor state was not established. The problems of definition and interpretation of these so called precursor syndromes were outlined by several members. The special features arising in relation to haemophilia were discussed and the possibility of identifying the role of imported Factor VIII concentrate used for UK patients was outlined. There followed discussion on the varying and considerable period of incubation (1 to 4 years) and the possible relationship between the size of inoculum of the proposed agent and the length of latency. The possibility that AIDS as currently defined was the tip of an iceberg in terms of a range of clinical or subclinical responses to infection with a putative AIDS agent was mentioned; it was recognised that the existence of milder forms would be hard to establish without a marker for such an agent.
(b) **Epidemiology**

The epidemiology of the disease in the United States was reviewed and also the rather limited information which had emerged from the national case control study - a study which had been widely criticised. The six months doubling time of cases appeared to be continuing and a suggestion that there was a plateau in cases had not been substantiated. There was no apparent change in the geographical or risk groupings. The UK figure of 24 cases indicated that there had been a recent increase almost conforming to a six month doubling time. Possible effects of changing behaviour/life style were indicated. It was argued that AIDS was new to the western world in 1978/9 although the disorder may have been present in Africa for much longer.

(c) **Aetiology**

The aetiological background to AIDS was considered with passing allusion to the antigen overload hypothesis. An increased microbiological load with multiple infections associated with active virus replication in the host was thought a possible mechanism for immunodeficiency. The more widely held view that AIDS was due to a novel "AIDS agent" was also discussed. It was noted that attempts to detect such an agent in the United States were being made in only a few centres, and it might be better to look for an agent early rather than in the later stages of severe disease. For this reason reliable identification of the early phases of disease/infection was crucial. It was possible that the agent was a zoonosis and the importance of looking to veterinary virology for models as well as for possible agents was emphasised. The analogy, in terms of transmissibility, with hepatitis B virus was noted and it was suggested that a hepatitis B mutant or an agent analogous to the delta agent should be high on the list of candidates. It was certainly possible that instead of being a totally new virus, the agent for AIDS could be a familiar one that had developed new properties.

Retroviruses were considered and it was noted that HTLV was a possible candidate on the basis of its known tropism for T helper cells. However a critical evaluation of the data led to the view that it was more probably an opportunist was unlikely to be the aetiological agent. The assumption that the agent was necessarily a virus was challenged and the need to keep an open mind on organisms such as protozoa was stressed. Systematic antimicrobial therapy might provide leads on such agents. It was noted that blood product associated cases could enable some of these alternative hypotheses to be tested.

(d) **Pathogenesis**

The T helper cell depletion seemed to provide the best current clue as to pathogenesis. However, polyclonal B cell activation and abnormal macrophage function had also been shown. Whether a single pathogenetic mechanism could be the cause of all these features or whether there were varying cellular responses to the same agent was not clear. The need to define mechanisms was particularly important for the logical planning of therapeutic immunoreconstitution. The limitations of studies on blood were noted and several members stressed the need to examine lymphoid tissue - the site of immune response events. It was however agreed that data available from blood studies appeared to be broadly representative of events in lymphoid tissue.
The importance of virus-like particles found on electron microscopy was considered doubtful but the need to look at such material was agreed. Rectal lymphoid tissue was thought to be a potentially important site for study in homosexuals. Release of factors into the host by organisms colonising the gut could provide an alternative pathogenetic mechanism. Another possibility, that the disease or some of its manifestations were transmitted directly by transplanting malignant or virus infected cells, was suggested on the basis of an animal model.

4. Opportunities special to the UK

The Working Party sought to identify particular opportunities for research unique or special to the United Kingdom. The fact that the epidemic was lagging some three years behind that in the USA was considered an important factor in enabling the background against which AIDS develops to be delineated. This could enhance our ability to detect the emergence of AIDS and AIDS-related conditions in high risk groups. The underlying immunological and virological status of the high risk groups before they encountered the "AIDS agent" could thus be defined.

(a) Clinical

The pattern of disease in the UK seemed somewhat different from that elsewhere and this needed careful documentation. The environmental and host factors determining the particular pattern of opportunistic infections were clearly relevant to the prevention and treatment of the secondary disease. The ability to detect an increase in cases of unexplained persistent lymphadenopathy in prospective studies would be useful in establishing the background causes for this rather nonspecific syndrome before the rise in truly unexplained cases probably relevant to AIDS emerged. There were opportunities for research programmes in respiratory medicine, gastroenterology and other organ-based specialities, and for carefully monitored therapeutic trials, and such studies could readily be made in the UK. The structure of venereology in the UK allowed the highest risk group to be studied in a small number of well equipped centres with good contact in the community and experience relevant to this type of problem. Clinical immunologists in the UK had greater experience of adult immunodeficiency than their counterparts in the US, and their clinical and laboratory base was thought to be a particular advantage. Gastroenterology in the UK was thought to be in a good position to exploit the opportunities available in AIDS research. The UK system for haemophilia treatment and for blood product organisation would allow detailed study of haemophilia associated cases which has not been possible in the USA due to their system of record keeping and organisation.

(b) Epidemiology

Some of the epidemiology in the American studies was thought to be insubstantial and not of the highest quality. The erasure of patients' names from the records held at the Centres for Disease Control in Atlanta as a result of political pressure would limit the ability of CDC to conduct proper epidemiological studies. The organisation of epidemiology in the United Kingdom was well suited to studying this problem. The importance of establishing such studies early in the emergence of disease was again stressed. Further emphasis was given to the concept of identifying early phases of the disease for testing aetiological hypotheses. It was emphasised that at this stage national collaboration was possible and indeed essential on
items such as an AIDS case-control study and active surveillance. This would need to be backed up by individual centres conducting cohort studies of patients in high risk groups etc. The close liaison between clinical and laboratory medicine in the UK was again stressed as an important background for such work. Blood transfusion policy was discussed in relation to the possibility of using "clean" donor panels for blood products.

(c) Immunology

The importance of the established close links between clinical and laboratory workers in this field in the UK was again mentioned. It was noted that in addition the UK offered particular opportunities to pursue carefully controlled and monitored therapeutic trials.

(d) Virology

It was noted that there were no unique facilities in the UK but that it was important to use the available clinical material to best advantage. The importance of detailed microbiological documentation was stressed as was the need to ensure appropriate facilities for detailed virological studies in animals and in tissue culture. It was noted that, in the search for particular recherche viruses, collaborative research with units having special expertise in these areas was essential. In the course of discussion it was emphasised that research would need to be focused on particular scientific objectives rather than seeking a broad all-inclusive sweep.

(e) Genetic Engineering

A telex from Professor Murray was tabled and this made clear that there was no special expertise that was not available in other countries. Professor Murray indicated possible areas for work including the analysis of serum for AIDS-specific nucleic acids. This was thought to be rather laborious but worth exploration. Alternatively, genetic engineering could facilitate the search for proposed etiological agents. This would involve the development of specific probes, of value in both diagnosis and possible vaccine development. The time scale for such work was thought to be relatively long. In discussion, the limitations of the first approach where it had been applied to other agents such as non-A, non-B hepatitis were mentioned. It was thought that suspect blood products could provide valuable raw materials for work of this type. Indeed, the possibility of fractionating blood from patients with "pre-AIDS" in order to concentrate the agent was a notable suggestion. Pooled material by contrast caused substantial problems as judged by previous experience in other settings. The potential difficulty of finding large numbers of different agents in such patients might pose problems of interpretation.

5. Opportunities for communication about AIDS in the UK

The clinically and epidemiologically based AIDS information group was mentioned, and it was noted that other avenues in specific areas of interest were also available.

6. NIH memorandum

The attention of the Working Party was drawn to the NIH memorandum as a useful means for rapid and confidential publication of AIDS work among active researchers. It would enable positive and negative results to be rapidly
disseminated among such teams. The memorandum system was strongly supported from its success in other settings and individuals were encouraged to contribute.

7. **Role of the DHSS and relationship between MRC and DHSS activities on AIDS**

The role of the DHSS in liaison with national and international groups was sketched out. The importance of cooperation between DHSS and MRC in health services research products was indicated. Avenues for communication were agreed to ensure that projects that were inappropriate for MRC funding could be taken on by the DHSS if it was considered appropriate on the advice of the Working Party. The repercussions of AIDS in respect of blood products received particular comment.

8. **Safety standards in projected AIDS work**

The safety aspects of AIDS work were briefly discussed in order to ensure that the Working Party was aware of the necessary standards applicable to AIDS projects coming before it. The Chairman, also chairman of the HSE Advisory Committee on Dangerous Pathogens, noted that this latter body was drawing up guidelines based on those produced by the Centres for Disease Control in response to a request from the DHSS and the HSE. It was suggested that the guidelines had to be practicable. In the meantime it was agreed that precautions similar to those used for hepatitis B should be taken.

9. **Specific grant applications**

Applicants were asked about aspects of their projects before being requested to leave the meeting while their applications were discussed. Further disquiet was expressed about the Working Party's ability to assess projects in this way, especially in view of the fact that a number of members not involved in any of the projects had been obliged to leave by this stage.

(a) **Adler, Tedder, Crawford (Middlesex)**

This large epidemiological study with extensive laboratory support was considered to be very much of the type that had been regarded as necessary by members of the Working Party earlier in the proceedings. The scope of the study and its approach seemed correct, asking good questions with an outline of high technical quality. The considerable expense of the project was noted and it was felt that while much of it could be justified there was room for judicious reductions on the laboratory side perhaps by employing Research Assistants on the 1B rather than the 1A scale and pruning out 1 MLSO. The clinical staffing was regarded as mandatory and should not be cut as this would jeopardise the whole project. Similarly the duration of the project was discussed and it was recognised that a 3-year project was essential to allow completion. The Working Party recommended that the project should be passed on to the Systems Board with approval subject to careful cost review.

(b) **Jeffries and Taylor-Robinson (St Mary's)**

This project was considered together with the supplementary application for technical support. The proposal represents an extension of current work on AIDS at St Mary's Hospital with a view to studying virology as well as epidemiology and immunology. The major aim is to test the hypothesis that a mutant form of cytomegalovirus (CMV) is responsible for, or contributes to, the establishment of AIDS. Although the Working Party were unsure of the
likelihood of this, it was felt that no particular viral candidate stood out and that CMV was one which should be investigated. In view of local expertise it was thought that St Mary's would be the best place for such work. The methods were thought to be appropriate although the control group of patients should perhaps be chosen differently. It was felt that it was not clear what the individual duties of the 2 proposed staff would be, and that the applicants should be asked to recast their proposal in order to incorporate the request for an MLSO in the body of the application. It was hoped that this would be possible in time for the next Systems Board meeting.

(c) Weiss (ICR)

A proposal for a single technician was submitted which would enable Dr Weiss to collaborate with several groups in research on HTLV and other retroviruses. He explained that the tentative nature of his application resulted from his existing CRC/MRC joint funding status and was reassured that there was no procedural barrier to his receiving SPG support in the present circumstances. The application was then discussed in his absence and was warmly commended in its own right as an example of specialist expertise being made available to several different collaborating groups in the best possible way. Existing work on HTLV had left a number of questions unanswered and there were methodological problems which Dr Weiss was in the best position to overcome. It was thought likely that other retroviruses would be isolated in the course of the work and that these would need to be investigated in addition to HTLV. The request was seen as very modest and it was agreed that it would give very good value for money if granted.

10. **Date of the next meeting**

It was agreed that this should be a half day meeting in mid December. Specific dates were to be arranged by the MRC office.

11. **Any other business**

There was no other business. The Chairman closed the meeting with thanks to the members and invited participants for their valuable contributions.

A J Pinching
Scientific Secretary.
Informal meeting on AIDS

A meeting took place at 10.30 am on 29 July 1983 at 20 Park Crescent. Those present were Sir James Gowans, Dr M P W Godfrey, Dr D A J Tyrrell, Dr E L Harris (DHSS) and Dr J E M Whitehead (PHLS). Dr Dickens was in attendance.

Sir James welcomed the visitors and said that the purpose of the meeting was to advise him as Council Secretary on what steps MRC could usefully take concerning AIDS. He drew attention to the papers circulated before the meeting and referred to his own visit to the US National Institutes of Health in March 1983. He had continued to receive papers from NIH as they were issued. He invited Dr Harris and Dr Whitehead to comment on the AIDS problem.

Dr Harris stated that DHSS maintained close contacts with the NIH in America and with the Ministries of Health of the important Western Countries. He described recent discussions with Regional Blood Transfusion Directors, including a European group who were planning to issue a Code of Practice for donors. A DHSS Code was also in preparation, for distribution to all potential blood donors - copies would be sent to the MRC when available. The object of the Code was to stress the delicate point that homosexuals or drug addicts should not volunteer donations until further notice. Dr Harris circulated a short paper by [Redacted] referring to heat treatment of blood products (see Annex). He hoped that in the UK it would be possible to avoid problems encountered in the USA where many donors were homosexuals and drug addicts - groups with a high rate of chronic infection with multiple pathogens, especially viruses such as hepatitis B. There was, of course, no scientific evidence that the use of heat treatment in the preparation of blood products achieved the specific aim of preventing AIDS transmission (by inactivtion of a causative virus) and there was concern about the possible effect of heat on the subsequent activity of blood products. It was likely, however, that such a step would be added to the manufacturing process in the UK. 50% of the UK requirement for Factor VIII was manufactured at the Blood Products Laboratory at Elstree and a new building, costing £18M, should open in 18 months' time and provide for total UK needs. Dr Harris also mentioned that there was much interest on the part of the Trade Unions on
vaccination of personnel against hepatitis B who might be exposed to infections. It could cost up to £30M to vaccinate all NHS personnel who might run any risk of infection with hepatitis B; the latest demand from ASTMS had been for a categoric assurance by Ministers that such vaccination would not in itself constitute any form of enhanced risk of contracting AIDS. Close collaboration with MRC would be welcomed by DHSS concerning any forthcoming research activities and it was agreed that both parties should keep the other informed.

Dr Whitehead, for PHLS, described the AIDS national surveillance scheme organised by the Communicable Diseases Surveillance Centre at Colindale, and also a proposed new scheme of 'sentinel' STD clinics which would make weekly reports about possible causes of AIDS. Recognition of early cases was particularly important in the UK context, and protocols were currently being drafted to ensure that the epidemiological work was as soundly based as possible and carried out consistently throughout the UK; the aims of this work were to help recognition of early cases of AIDS (and thus facilitate the obtaining of specimens), to maintain surveillance of registered haemophiliac patients, to obtain data from the hospital sector to compare with those from the 'sentinel' clinics, and to survey areas where no case of AIDS had as yet been reported (eg Manchester). Copies of the protocols would be sent to the Council when they were available. It was also agreed that attention should be paid to possible early forms of AIDS, eg Extended Lymphadenopathy Syndrome (ELS).

In further discussions about blood products, the DHSS Advisory Committee on the National Blood Transfusion Service had a Working Party on Plasma Supply chaired by Dr H H Gunson of Manchester and maintained a watch over blood product manufacture. There was also a Central Committee for Research and Development in Blood Transfusion under the aegis of the Central Laboratories (a Special Health Authority) - which was considering sponsoring research in AIDS. In Scotland the National Blood Transfusion Service was keeping a close watch on hepatitis B and AIDS.

Dr Tyrrell commented that AIDS was indeed a mysterious disease. Further virological work was needed; current work in the USA was of great interest. He did not think that it would be possible for the MRC to undertake studies on all possible facets of the disease, but it would be worthwhile to concentrate on the early stages of the epidemiology and cases of early, and possibly unrecognised, infection. The aetiology could be studied, and also the disturbances to immunological function which were present; cultured cells could be looked at by various methods, including electron microscopy, and animal inoculation could be carried out; another possibility was that there might be more than one
aetiological agent and they might interact to produce the disease picture. He suggested that the disease would spread in the UK, but not on the scale of the USA.

It was thought that some central point of reference was needed for research studies and it was agreed that the Clinical Research Centre should have a definite 'presence' in this context - it was known that Sir Christopher Booth would welcome such a development. A working party was the best way for the Council to assist the exchange of information, to maintain enthusiasm, to facilitate co-operation, and possibly to plan and promote large scale projects; it would also advise on applications to the MRC for grant support. Links with NIH should also be maintained, through Sir James. Animal studies were worth considering, although it had not yet been possible to transmit the infection in an animal population. As well as cases from Haiti, a worrying number had arisen in Zaire - eg 16 cases had been reported in Belgium, 14 having come directly from Zaire; it was possible that there were areas in Central or West Africa where the condition was endemic but as yet unrecognised because the infections or tumours from which the patient died were not investigated in sufficient depth. The Working Party could also be kept informed of the progress of a DHSS study of the 2,100 haemophiliacs in England and Wales, with particular reference to those exposed to a possible risk of AIDS from imported American Factor VIII.

Dr Harris and Dr Whitehead then left, it having been agreed that the Council would have ready a statement in reply to press enquiries, although it would not be formally issued as a press statement. The guidelines compiled for the press were as follows:

"i) On 29 July 1983, representatives of the Medical Research Council, the Department of Health and Social Security and the Public Health Laboratory Service met to discuss the problems of AIDS and to advise the MRC Secretary on any action which should be taken in regard to research.

ii) The MRC has kept in close touch with the highly expert work being undertaken by the National Institutes of Health in the USA, and the position of the United Kingdom was reviewed against that background.

iii) The representatives of the three organisations agreed to keep in close touch in order to exchange information.

iv) The Medical Research Council is setting up a working party which will act as a forum for discussion about research on AIDS and will advise the Council in this field."
Progress with heat treatment of human plasma products

Heat treatment or pasteurisation of blood products is directed towards inactivation of a group of transmissible viruses which result in sub-clinical or clinical hepatitis in a proportion of treated patients. Currently, albumin fractions are pasteurised at 60°C for ten hours to inactivate hepatitis B virus and there is the assumption that this heat process also inactivates the group of viruses responsible for non-A non-B hepatitis. Long-standing use of pasteurised albumin products without the complication of hepatitis suggests that the pasteurisation process is effective.

Pasteurisation of other blood products has not been developed to this extent because these products are not amenable to the heat treatment process:-- examples are fibrinogen, factor VIII, factor IX, which are all known to transmit hepatitis B and non-A non-B viruses.

Immunoglobulin produced by ethanol precipitation in Cohn Fraction II is not pasteurised but in long-standing wide use has acquired only a marginal anecdotal association with transmission of hepatitis virus. The earlier assumption that virus in immunoglobulin would be immune-complexed and therefore inactivated is more likely to account for the lack of transmission of infection rather than the view that the virus is not fractionated in with Cohn Fraction II immunoglobulin intermediates.

Virus transmission in haemophiliacs

Hepatitis B transmission in large-pool factor VIII and factor IX concentrates is recognised in haemophilia patients but the incidence has been effectively reduced by screening of plasma to exclude source material from hepatitis B antigen carriers. The absence of markers for non-A non-B hepatitis virus does not allow for this screening of source material and epidemiological evidence suggests that large-pool concentrates are universally associated with effective transmission of non-A non-B hepatitis virus.

The severity of non-A non-B hepatitis in haemophiliacs probably associated with the co-existent impaired immune responsiveness of these patients has motivated plasma fractionation organisations to re-examine means whereby hepatitis virus can be inactivated in large-pool concentrates. Heat treatment of blood products is still primarily directed at the inactivation of transmissible viruses causing hepatitis in recipients.
AIDS

The syndrome of acquired immune deficiency currently under investigation is likely to include in its aetiology transmission of an infective virus and the possible phenomenon of reactivation of an existing virus in individuals concerned. In limited numbers, AIDS sufferers have included individuals receiving human blood-based fractions. This aetiological observation has promoted more activity in the area of blood products pasteurisation with the empirical view that a virus is involved and, as with hepatitis virus, is likely to be partially or completely inactivated by heat.

Means of heat treatment of blood products

Heat treatment represents only one pathway by which viruses may be inactivated. Nonetheless, it is the most favoured route at present. Heat treatment may take place during the process of blood product purification, i.e. during a wet process step or heating a finished freeze dried product can be attempted. Heat transfer in the wet state is more homogeneous and efficient and to satisfy reliability in manufacture is to be preferred; however, wet treatment is associated with more molecular damage of heat unstable proteins than occurs by the dry-heat route.

Wet-heat pasteurisation of blood products at BPL is now available with albumin fractions, anti-thrombin III, factor XIII, and is likely to be successful during this calendar year with factor IX. The loss of yield of factor IX incurred may be tolerated within the considerable excess of source material available to the fractionation facility.

Wet-heat of factor VIII intermediate concentrate is likely to require a longer programme of work if a satisfactory reliable method is to be developed which does not carry unacceptable penalties related to loss of yield of factor VIII activity. Progress with this procedure will be reported to the Authority.

Dry-heat: the majority of commercial manufacturers are currently depending upon dry-heat of the finished factor VIII concentrate to reduce the infectivity of the product relative to transmission of hepatitis. The associated claims (which are entirely unfounded in scientific and quality control terms) are that the heat process will inactivate the putative virus transmission causing AIDS.
Appreciating pressure under which users are currently operating in the management of haemophilia, BPL has undertaken preliminary studies to assess yield of factor VIII intermediate concentrate after dry-heat. It has been shown possible to maintain greater than 95% of factor VIII activity in the finished product after heating at 75°C for ten hours or heating at 60°C for 24 hours. Both these presentations of heat exceed the requirements established for virus inactivation by wet-heat with albumin products (60°C for ten hours).

Since this form of product treatment will allow BPL to present to clinical managers of haemophilia a product carrying equivalent weight of claims for safety as those of rival commercial organisations, this product is being advanced with high priority to enable manufacture to become routine by the late summer 1983.

To introduce the product, the full co-operation of the haemophilia directors will be required since a non-human primate testing facility is not available to BPL accepting that this system of testing may not be appropriate with regard to hepatitis or AIDS transmitting viruses.

Introduction of an extra stage in the process of purification of factor VIII may impose costly intermediate reorganisation of manufacturing and equipment for which there is no budgeted sum. It is assumed that this contingency will be met recognising the political sensitivity of AIDS transmission in the UK caused by treatment with blood products.

26th July 1983.