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NB Since the next meeting will not take place for over a year, Directors are asked to address any comments or queries to the Chairman immediately.

MINUTES OF THE MEETING OF THE DIRECTORS OF THE SCOTTISH NATIONAL BLOOD TRANSFUSION SERVICE AND HAEMOPHILIA DIRECTORS HELD AT THE SNBTS HEADQUARTERS UNIT ON THURSDAY 5 MAY 1988

Present: Chairman: Dr J Forrester, SHHD

SNBTS Directors: Professor J Cash, National Director
Dr R Perry, PFC
Dr P Foster, PFC
Dr D B McClelland, Edinburgh and South East
Dr R Mitchell, Glasgow & West (items 1-3 only)
Dr S Urbaniak, Aberdeen & North East
Dr F Boulton, Edinburgh and South East
Dr E Brookes, East
Dr T Taylor, North
Dr M McClelland, North Ireland

Haemophilia Directors: Dr C Ludlam, Edinburgh
Dr G Lowe, Glasgow
Dr A Dawson, Aberdeen
Dr B Gibson, Glasgow

In Attendance: Mr T R Macdonald, Senior Executive Officer, SHHD

Secretary: Mr R Angus, Executive Officer, SHHD

Introductions

The Chairman introduced new members to the Meeting.

1. Apologies for Absence

Apologies for absence were received from Dr McDonald, Dr Heppleston, Dr Mayne, Dr Wilson, Dr Bennett, Professor Girdwood and Dr Whitrow.

The Chairman expressed the Committee's thanks to Professor Cash, Dr Perry and members of their staff for their help in arranging the accommodation for the meeting and the tour of the Protein Fractionation Centre to be held after the meeting.

2. Minutes of Meeting on 9 February 1987

The Chairman apologised to Dr Brookes whose name had been recorded wrongly in the minutes.

For the record it was stated that Mr D Macniven was and is an Assistant Secretary in the Scottish Home and Health Department. In item 4 paragraph 3, "Four Factor Concentrate" is the same as PPSB.

Dr Ludlam maintained his recollection that Mr Macniven had stated that the compensation scheme extended up to the grant of a product licence, and Dr Dawson stated that Dr Bennett had the same recollection. The

Chairman confirmed that the minute corresponded precisely to what Mr Macniven believed he had said, to what the Chairman believed had been said, and to the Department's position at the time. Professor Cash requested that the minutes of the present meeting should record the disagreement. Mr Macdonald pointed out that minutes of meetings were not the sole record of the position on particular issues as relevant correspondence backed up discussion. The Chairman requested that any question about the minutes of the present meeting should be raised promptly with him, by letter. [Members may wish to know that no criticism of Dr Ludlam is implied, since he had raised his question in writing after last year's meeting and had been answered in writing.] The Chairman undertook to advise those present if any significant disagreement occurred about the minutes.

It was agreed that item 3(c) of the minutes was incomplete and should read: "No one under the age of consent should take part in trails to determine recovery and half life."

3. Current Position of Scottish Blood Products for use by Haemophilia Directors

Professor Cash introduced the pre-circulated report from himself and Dr Perry, and drew particular attention to the following points:-

* The input of plasma to PFC has fallen for the first time since 1974. Professor Cash discussed possible reasons, and pointed out that since the recent campaign in the media, an increase in the number of donations had begun.

* A very recent surge in use of Factor VII concentrates had raised use beyond 10 million units in 1987-88 and beyond current production, so that stocks were being depleted; and if the surge continued, Scotland would have to resort to commercial products for part of its supplies.

* Intake of plasma cannot be further raised without increased expenditure on blood collection and plasmapheresis.

* Increased processing capacity at PFC requires capital investment on developments already planned. Professor Cash was asked whether enough extra capacity would be released if fractionation of plasma from Northern Ireland were to stop. He replied that the Medicines Inspectorate would still require the planned developments to take place, to achieve compliance with the standards of good manufacturing practice.

* Comments on PFC's Factor IX product would be welcome.

* From July, Dr R Stewart would take up the new post of Manager of Clinical Trials and Product Surveillance. His responsibilities will include coordination of all SNBTS clinical trials, and the continuous surveillance of existing products.

Dr Perry then introduced his contribution to the Report, and emphasised the following points:

* The yield of the new Z8 product had not come up to initial expectations, partly because of losses inevitably incurred during

heat treatment for virus inactivation. Thus greater production, especially in face of the surge in demand, entailed greater throughput than before, and strained the design features built into PFC. Production of more than 9 million units of Factor VIII per year for Scottish use might be hard to achieve.

* The new Z8 product now being developed is expected to give a yield of 250-300 units from each litre of plasma, and an activity of 2-3 units per milligram. It should be available for trial by the end of 1988. A product of very much higher purity (50-100 units per milligram) is being developed in collaboration with the New York Blood Centre.

* Use of Factor IX (DEFIX) has multiplied 2.5 times since 1983. Production may encounter a limit at 3 million units per year, which may prove technically hard to exceed.

* Laboratory studies of HIV inactivation will now proceed wholly within PFC, and not require University involvement any longer. It is hoped that progress will now be speedier, since DHSS will not recommend licences for Factor VIII and IX until the data is available.

* Factor VII and Anti-thrombin III will probably undergo animal studies late in 1988 and become available in 1989.

* Substrates depleted of Factor VIII and Factor IX are now available for trial.

During discussion of the Report, the following points were made:

* There was general disappointment that the 58% increase in yield of Z8 and the adequate supplies held out to last year's meeting had not materialised. Technical difficulties have led to inconsistent yield, and the expected 300 units per litre is now unlikely to be achieved, 210-220 units being more likely now. In the future, highly purity is likely further to impair yield, and world-wide, Factor VIII becomes scarcer and more costly.

* A number of reasons for the current surge in demand for Factor VIII were proposed. Increasing confidence in its safety has let to a foreseeable change from use of cryoprecipitate to use of Factor VIII, especially in the West. (Data on use of cryoprecipitate should however continue to be examined annually.) Dr Lowe said that some of his patients lacked confidence in the efficacy of the current heat treated factor VIII concentrate, which induced them to use higher doses than previously to achieve the same therapeutic effect and that patients already infected with HIV were feeling progressively miserable, and were thus determined to at least treat all bleeds with high dosage. Elective operations previously postponed were now being performed. Further, the current increases may in part reflect transient non-recurring heavy consumption by a very small number of patients.

* The initial testing of a new product for haemophiliacs requires to be done in a number of untreated patients, as many as 60 being required. This number is hard to find in England and impossible in

Scotland. Dr Ludlam was invited to convene a small group to address this problem.

* The new Z8 Scottish product is comparable to the English 8Y product. To mimic the 8Y product in Scotland would entail substantial changes in equipment, and acceptance of a lower yield.

* Dr Lowe doubted whether the activity of PFC's Factor IX in patients with inhibitors of Factor VIII approached that of its commercial competitors, and pointed out that Glasgow had only 5 recipients for it, so that the development programme was directed towards a small market. Dr Ludlam stated that his patients with inhibitors found heat-treated Factor IX from PFC ineffective, and he therefore used commercial FEIBA instead. Professor Cash pointed out that commercial purchases equivalent to PFC's production of Factor IX would prove costly.

4. Current Target for Factor VIII Production

It was noted that the current target of 2.75 million units per million population was originally an aim for the year 2001, and it was agreed not to revise it on this occasion.

5. Compensation for Donors of Hyperimmune Plasma and Participants in Clinical Trials

Mr Macdonald reiterated that the previous year's minutes correctly described the position at that time. He reported that the compensation scheme now extended to all clinical trails of Factor VIII, therapeutic as well as non-therapeutic. During considerable discussion the meeting noted with disappointment that, in any period intervening between the end of clinical trials and the issue of a product licence, the ABPI guidelines cannot apply, since they relate only to clinical trials; and the "three wise men" scheme would not apply either. Mr Macdonald agreed that the Department would give further consideration to this issue. Haemophilia Directors and SNBTS Directors present agreed that the Z8 product was still currently under trail, so that the ABPI guidelines and the "three wise men" scheme continue to be applicable.

Dr Ludlam said that he had been issuing an explanatory leaflet to patients, on the advice of the Medical Defence Union, although Dr McIntyre (on behalf of the Department) had requested him not to do so. The Chairman suggested that he should write again to Dr McIntyre.

Dr Ludlam expressed concern that the "three wise men" included 2 who were linked to SNBTS, the produced of the product. Further, no Haemophilia Director was among them so that appropriate expertise was lacking. the Chairman pointed out that the "three wise men" were not a court of law but a group providing advice to the Treasury, and no doubt in any specific instance the membership would be modified appropriately. The meeting agreed to note the points made.

6. Non-A Non-B Hepatitis Screening

The Chairman said that a research project was being mounted in England and that a decision whether to introduce screening would probably wait upon its outcome. Dr McClelland and Professor Cash considered the delay

unjustifiable. Haemophilia Directors had not identified any case of non-A non-B hepatitis transmitted by heat-treated PFC products for haemophiliacs.

7. Legal Proceedings by Haemophiliacs

The impending legal proceedings were discussed.

8. Date of Next Meeting

It was agreed to arrange this for 11.00am on Thursday 4 May 1989, at SNBTS HQ Unit.