Fibrin Sealant Clinical Trials Strategy Group Meeting

Monday 21 April 1997, 2pm, PFC Seminar Room

M I N U T E S

Present:	*Fraser Leslie* *Jane Pelly* *Bob Perry* *Sarah Reading* *Marc Turner*	**Copy to:**	*Bruce Cuthbertson* *Ian MacGregor* *Ron McIntosh*

ACTION

1. *Apologies*

Apologies were received from BC, IMacG and RMcI

2. *Minutes of 6 March meeting*

These were accepted without changes.

3. *Matters Arising*

3.1. Role of the medical adviser.

MT reported that the National Medical & Scientific Director, Prof Franklin has confirmed him as the Medical Adviser to PSD for clinical trials of Fibrin Sealant, Human Thrombin Concentrate and Human Fibrinogen Concentrate. His responsibilities are:

- To advise this group on the design and implementation of clinical trials for these products;
- To liaise with Clinical Investigators as and when necessary;
- To monitor Serious Adverse Events in real time.

In this role MT is accountable to Prof Franklin. Prof Franklin will continue to sign off forms for new trials (ie to approve formally new clinical trial protocols) and Adverse Event Reports. Prof Franklin has written to MT (cc JP) confirming this arrangement.

3.2. Discussion on any implications for trials and Named Patient Basis issue of Fibrin Sealant, Human Thrombin Concentrate and Human Fibrinogen Concentrate of Paul Brown's presentation to the WHO on v-CJD.

SR asked whether this should be discussed with the PFC CJD Working Group. RJP replied that the PFC group's remit was to address how PFC as a *manufacturer* could reduce the risks of possible CJD transmission and that it would not have a position on clinical trial and Named Patient Basis use of these products.

Following discussions with Prof Franklin, MT reported that they were "uneasy" about conducting a clinical trial of Fibrin Sealant in acoustic neuromas due to the proximity to neural tissue of the use of the product. MT will write to Prof Ramsden and Simon Hargreaves to let them know that in view of Paul Brown's recent comments the SNBTS do not wish to proceed with a clinical trial in this indication. He may advise them that they can use our product on a Named Patient Basis.

MT

Neurologists at the Southern General Hospital, Glasgow have been using Fibrin Sealant on a Named Patient Basis since 1994 and Western General Hospital has recently expressed a preference for using our product instead of Tisseel (which they have been using for several years). As with the acoustic neuromas above, Prof Franklin and MT are concerned at the proximity to neural tissue of Fibrin Sealant application in such indications. MT will discuss further with Prof Franklin and decide whether it is considered necessary to write to these Neurologists to highlight to them the possibility that intercerebellar inoculation of plasma products might transmit CJD. Such a letter would need to come from the National Medical & Scientific Director.

MT

There are no relevant trial indications or anticipated Named Patient Basis uses of Human Thrombin Concentrate and Human Fibrinogen Concentrate.

3.3. Studies on spraying Fibrin Sealant with the use of the Tissomat.

SR reported on RMcl's behalf that the equipment had been passed to John Hardy. RMcl is waiting for a protocol for the spray studies.

These studies are required before the planned possible clinical trial with the liver unit at Queen Elizabeth Hospital (Mr Buckels) can be progressed. MT confirmed that this was a good trial indication for Fibrin Sealant since there is very heavy blood product use and the potential benefits outweigh the risks.

It was agreed that as a matter of some urgency these studies should be progressed.

RJP

3.4. Discussion on strategy for supplying Fibrin Sealant outwith Scotland & NI and on Named Patient Basis issue from non-BTS blood banks.

MT will discuss with Audrey Todd the SOP for Named Patient Basis issue of SNBTS products (SOP no: 95 110 0012 01) and will come back with comments.

MT

It was agreed the Regional Transfusion Centres should be audited to see the extent to which they are complying with the SOP. Since it is a PFC SOP it was thought appropriate for the audit to be arranged through PFC. FL to discuss with BC for the next meeting.

FL/BC

3.5. Error in thrombin paper

RJP has written to Kel Palmer about this (see minute of 21/11/96) and will pass a copy to SR and MT for their files.

RJP

3.6. Maternity leave cover for SR

SR is planning to go on maternity leave in early August and return mid-January 1998. JP confirmed that there would definitely be maternity leave cover of some kind for this period, preferably a secondment from elsewhere in the organisation. She will be submitting to Meg Tunstall an application for a secondment and, if approved, the post will then be advertised.

JP

4. *A Surveillance Study of Patients Treated with SNBTS Fibrin Sealant (FS003)*

Nineteen patients at GRI have been recruited onto this trial (4 have dropped out including two cardiac transplant patients who have died). MT asked to receive details on the 2 deaths (patients G-3-004 and G-3-018).

SR

MT asked to see receive a copy of the clinical trial protocol for the trial so he can decide whether he thinks a protocol amendment should be made specifying that anticoagulated and haemophilic patients must previously have been exposed to a blood product to be eligible for the trial. JP pointed out that he will receive (in the very neqr future) a PSD master set of documents which contains all current trial protocols.

MT

5. *Hip Replacement Study (FS006)*

MT will review Robin Prescott's report on this trial and the clinical trial protocol before deciding whether he thinks a full scale trial is worthwhile?

MT

The clinical trial protocol is in the master set of documents and SR will send MT a revised copy of Robin Prescott's report (to include the power of the study) once she has received it.

SR

6. *A prospective, randomised, controlled clinical trial of SNBTS Fibrin Sealant versus nasal packing in patients undergoing nasal surgery (FS007)*

The trial is progressing well: 35/40 patients have been recruited.

SR

7. *Development of Percutaneous Endoscopic External Ring (PEER) Hernioplasty using Mesh Plug Technique with SNBTS Fibrin Sealant Kit (FS009)*

The trial is progressing well: 7/20 patients have been recruited.

SR

8. *Pilot study to evaluate the use of autologous cultured keratinocytes and SNBTS Fibrin Sealant Kit in the treatment of chronic leg ulcers (FS010)*

8.1. Current status of clinical trial protocol

MT pointed out to SR some minor errors in the draft 2 of the clinical trial protocol. Once these have been corrected and MT has had the opportunity to discuss some other points with the Clinical Investigator at Ninewells (Dr Sue Morley) the third and hopefully final draft can be prepared.

MT/SR

8.2. Written clarification on the suitability of Fibrin Sealant used as described in the DDX

MT agreed to provide RJP with a letter to this effect.

MT

9. *Other possible trials for the double virus inactivated Fibrin Sealant product*

9.1. Progress on possible ENT/neurology trial at Manchester Royal Infirmary

See item 3.2

MT

10. *Prospective, randomised, double-blind, multi-centre, placebo controlled clinical trial of SNBTS thrombin in gastrointestinal haemorrhage (HT001)*

10.1. Update of current status (including coagulation activation results).

SR reported that 36 patients had been recruited. Pre-treatment samples for all of these have been tested for HAV and B19. Not unexpectedly in a patient group of this age, there are not very many patients susceptible to these viruses: 83% B19 POS; 89% HAV POS.

The coagulation activation results were not discussed in detail. SR to seek advice from Robin Prescott on whether absolute figures will be required for analysis (ie rather than >600 and <20 etc) and, based on the results to date, the number of patients he estimates would be required to show a statistical difference between the groups with any power.

SR

There have been a number of Serious Adverse Events reported for trial patients (8 in total: 5 patients injected with placebo and 3 patients injected with thrombin; deaths in each - 3 and 1 respectively) but the trial clinicians do not consider this number to be significant. However due to the advanced age of these patients (all except 1 over 75 years old) MT and Prof Franklin think it would be advisable to discuss with the trial investigators at the Investigator meeting on 22/4/97 whether they think there should be an upper age limit for trial recruits.

MT

10.2. Named Patient Basis issue of Human Thrombin Concentrate.

Issue on a Named Patient Basis of Human Thrombin Concentrate will be from PFC. All requests for the product should be referred to MT for medical approval.

RJP

11. *Human Fibrinogen Concentrate*

It is likely that the SNBTS Safety Committee will need to review the clinical trial protocol for the fibrinogen clinical trials. RJP is responsible for getting this off the ground.

RJP

JP agreed to send MT a copy of the draft remit for the group. Proposed Committee members are: Brian Colvin, Frank Hill, Dan Reid, Ernest Briet, Martin Vessey and Adrian Grant.

JP

12. *Any Other Business*

There was none.

13. *Date of Next Meeting*

Tuesday 3 June 1997, 9.30am, PFC Seminar Room

(We arranged 27/5/97 at the meeting but BC can't make this)

Sarah Reading
30 April 1997