RESPONSE TO MEDICINES INSPECTORS' REPORT
SOUTH EAST SCOTLAND BLOOD TRANSFUSION SERVICE

12 JANUARY 1983

CONTENTS

1. INTRODUCTION

The organisation of the report adds considerably to the difficulties of presenting this response. Some of the Inspectors' comments are classified according to the particular building inspected, while others are classified according to functions. In addition, we found it difficult in some cases to distinguish purely descriptive observations from comments which the inspector felt required a definitive response. We have therefore attempted in sections 3 - 6 to address briefly some general topics which are referred to at more than one point in the report. In Section 7 we have given our responses to each of the Inspector's comments in the order in which they appear in the report.

SCOPE OF THE REPORT

The Edinburgh Centre may have caused particular problems because of the large clinical blood banking element of our work and the presence of the clinical Cell Separator Unit. We were concerned that in looking at aspects such as crossmatching and clinical administration of blood, there was not time for sufficient consideration of the boundaries between the "production" and the "clinical" aspects of our work, and of the implications of extending concepts of GMP to the bedside.

We have some difficulty with many of the Inspector's comments in relation to cryoprecipitate as a clinical product: To respond adequately would involve detailed discussion of many aspects of Factor VIII therapy which are not, we feel, relevant to the Inspector's proper concern with the quality of our production of a standard and widely accepted blood product.

The SNBTS arrangements for Factor VIII distribution do not seem to us to be a topic for consideration in this report.

The Inspector's comments (23) on the clinical (in vivo) validation of products were appreciated. We were concerned however that these suggestions imply that regular quality control should involve parameters such as red cell and platelet survival, factor VIII recovery etc. It should be realised that the blood transfusion service may have difficulties in regularly obtaining clinical data of this type. We felt that the implications of this suggestion require further consideration.

The Inspector also commented (22) on the pursuit of "ever increasing" shelf lives for blood and blood products and questioned the desirability of this trend. It is our opinion that this comment touches on a trend of development which is being pursued by most if not all modern transfusion services, for very sound reasons of cost effectiveness. We feel it is not appropriate to include a response to this point in the document prepared by the S E Centre alone: A response on behalf of the SNBTS would, we feel, be more appropriate.

3. ACCOMMODATION AND FACILITIES

The Inspector's report comments at various points on the buildings and facilities of the S E Centre, and recognises that major changes were to follow shortly after the inspection.

In Summary, (i) moves completed to date

(a) Closure of the Archibald Place building

(b) Relocation in the new Royal Infirmary Phase I of the donor withdrawal suite, hepatitis testing laboratory, wash up and autoclaving facility, stores, and many of the other laboratories.

(c) Temporary relocation in Livingstone House of blood components processing.

(ii) building improvements now being planned and costed

(a) Enlargement and improvement of blood bank compatibility testing and issue areas.

(b) Construction of a new area for pooling clinical products.

(c) Construction of an improved environment for red cell washing and filtration.

(iii) further moves planned

The Inspector has stated (point 3) that blood components processing in Livingstone House must be considered an interim measure and must be transferred to Phase I Royal Infirmary "no later than June 85". He has also stated (point 38) that "the area (in Phase I RIE) presently being used as a temporary pharmacy should, when vacated, be converted for the use of the Blood Transfusion Centre into a processing and laboratory facility".

5. DOCUMENTATION

As mentioned in the National Medical Director's report, already referred to in (4) above, we are certain that the target of March 1983 for completion of full documentation of all procedures is not attainable. Priorities have been decided in the S E Centre for documentation of Standard Operating Procedures. These are given in Section 7 in the response to points 94 and 95.

Many of the requirements of documentation to improve the ability to 'trace' products through the BTS system will be met by introducing a comprehensive computer system. Funding has been sought for the phased introduction of such a system over the 3 years 1983/4 to 1986/7 and work in the Centre on planning the system has been in progress for 2 years.

6. TRAINING

The Inspector's report referred to the need for more formal training of staff in the blood components processing area.

This need is acknowledged, as is the need for improvements in training of other staff including donor team attendants: in the latter case, staff shortages have made it quite impossible to provide time for training.

There is a clear commitment on the part of the senior staff in the S E Centre to develop training programmes using training manuals which will be based on the SOP's for the relevant areas. It is envisaged that the introduction of these programmes will be phased over several years with priority being given to the areas mentioned above.

Where is page 4?

7. RESPONSES TO INDIVIDUAL COMMENTS AS PRESENTED IN THE REPORT. (The number in the left margin is the number of the relevant paragraph in the Inspector's report)

BLOOD DONATION

1.11.a "RESPONSIBILITY AND CONSISTENCY OF DECISION TAKEN OVER WHICH DONORS TO ACCEPT OR REJECT....WHETHER DONORS REALLY READ THE QUESTIONNAIRE. JUST HOW COMPREHENSIVE IS THE QUESTIONNAIRE?

We share the Inspector's concerns. The following actions have been taken: (i) a new comprehensive guide to donor selection has been prepared and is in routine use by donor selection staff (Appendix A). (ii) we have made a trial of a comprehensive donor health questionnaire administered by donor staff. This has been abandoned as we do not have enough staff to operate it and its use caused massive delays at donor sessions. (iii) we have introduced as a routine for all donors a detailed health check questionnaire which is self-administered (Appendix B). Positive responses are followed up by interviewing the donor before donation. Donor compliance is good and this system will continue. An evaluation of its efficacy will be undertaken if sufficient staff become available to conduct the necessary follow-up interviews of donors who have completed the questionnaire.

1.12.b. "THE LOCATION OF BLEEDING AND TYPE OF DONOR. FOR EXAMPLE , WHETHER PRISONS AND BORSTALS WERE REALLY APPROPRIATE OR NECESSARY AS A SOURCE MATERIAL. THE POSSIBLE ADVANTAGE OF A "MOBILE DONOR CENTRE" (CONSISTENCY OF ENVIRONMENT AND INCREASED PROCUREMENT CAPABILITY) WERE ALSO CONSIDERED"

(i) Prisons and Borstals. We do not visit these regularly. No such sessions have been held for two years. These donors will only be used in an emergency.
(ii) Advantages of a "mobile donor centre". This is the only solution to the problem of many of our most unsatisfactory session locations. Funds have been provided and the vehicle is under construction.

product. A study proposal to investigate this is being developed jointly by staff in S.E. and W Centres (Drs Gabra, Smith and Prowse). This study will also investigate the influence of donation time on quality of the product (see 15f).

15.(f) "LACK OF DEFINITION OF A SLOW BLEED"

(i) We have defined a slow bleed as one which takes more than 10 minutes to take the standard volume. (ii) Donor staff will be instructed to adhere to an SOP which requires that venesection is terminated if donation is not completed within 10 minutes.

(g) "THE SURPRISING PRACTICE OF RETAINING BLOOD AT AMBIENT TEMPERATURE FOR UP TO 18 HOURS"

With the commissioning of the Livingstone House facility this practice has been terminated. Donations with the exception of those destined for platelet production are transferred to 4 C storage at point of collection within 30 minutes and stored prior to processing at 4 C (excepting transit to and from vehicles). These requirements are being incorporated in the relevant SOP's. The only situation in which we cannot yet achieve this standard is when blood must be transported from a session in small vehicles (Ford Estate cars) which have no refrigeration. We are investigating the availability of cooled containers designed for the American Red Cross Transfusion Service which may prove suitable.

18.(h) "THE NON USE OF SEGMENTS ON THE DONOR TUBE FOR CROSSMATCHING PRUPOSES"

The use of donor line segments will be introduced by April 1983.

19.(i) "THE VOLUME OF BLOOD TAKEN. THIS IS PRESENTLY 420MLS BUT MAY BE INCREASED TO 450MLS."

The pack in current use is difficult to centrifuge containing a 450ml donation. Donation size will eventually be increased to 450ml when a new pack design is introduced, and/or modified centrifuge cups are obtained, and suitable balances for pack weighing during donation are obtained.

1.13.c. "PROBLEMS ASSOCIATED WITH BLOOD BAGS. (BLUNT NEEDLES, PIN HOLES, FUNGALLY CONTAMINATED OUTERS, SPLITS IN DONOR TUBE)"

It is not possible with our present staff to carry out detailed quality control of batches of packs or detailed inspection of individual packs before use and it is our view that the responsibility must rest with the pack manufacturer to supply a correct product. We are however, taking some steps to improve our control, (i) we now have relatively adequate store space making it possible to order larger stocks, to ensure that we have control over which batches are issued at any time, and to ensure proper stock rotation. (ii) consideration is being given to introducing a system whereby when a new batch of packs is brought into use a sample is inspected and used by a senior member of medical or nursing staff before the packs are released. (iii) guidance will be given to all donor staff (in the form of an SOP which will be used for training) on the inspection required of each pack before it is used (iv) consideration is being given to improving the system of documentation, reporting, and follow up with the supplier of pack defects identified at various points including withdrawal, components processing and blood bank. (v) a senior member of staff will be designated to be responsible for receiving and acting on all reports of pack defects.

14.(d) "THE PRACTICE OF PREFILLING SYRINGES FROM A VIAL"

No alternative is available. The Regional Director has actively pursued with several suppliers and the PFC the possibility of obtaining prefilled syringes: No suppliers have offered to produce these.

15.(e) "NON USE OF AUTOMATIC CUT OFF BALANCES DURING DONATION"

(i) Our discussions with Centres using automatic cut-offs suggest that accuracy and reliability are a problem, especially if floors are uneven. The present system has the advantage that donor staff must watch the balance (and so be close to the donor) during the donation. Our QA data on pack weights do not indicate that the present system is causing major problems. (ii) We know of no evidence that pack agitators lead to a better

20.(j) THAN SEEN ELSEWHERE. THIS HAS SAFETY AND TRAINING IMPLICATIONS AND SHOULD BE REDUCED"

We accept this and have been aware of it for some time. A bid was made in 1982 for a further 6 donor attendants and 1 nursing sister. This funding has not been received but we understand it will be given high priority during 1983-84. Since the inspections a new consultant has been appointed in charge of the blood donor service, and she is reviewing staffing levels requested for adequate donor care. It is anticipated that a further increase will be necessary. This need has been identified in financial forecasts for 1984-5. In the short term urgent steps are being taken to find temporary additional finance from within the Centre's existing resources to provide for extra staff. Training programmes have been designed but there is no possibility of implementing these until more staff are available.

21.(k) "THE USE OF A HAEMOGLOBINOMETER RATHER THAN THE COPPER SULPHATE TEST"

We are now using an OSM2 haemoglobinometer routinely in the donor centre to check all donors who fail the copper sulphate test. This has reduced the donor deferments for low haemoglobin from 5% to below 1%. Two further haemoglobinometers have been purchased and will be used in extended trials of their robustness, reliability and staff acceptability to staff on mobile sessions.

MISCELLANEOUS COMMENTS

22 "THE PURSUIT OF 'EVER INCREASING' SHELF LIVES OF VARIOUS PRODUCTS WAS BRIEFLY DISCUSSED. WHILST THE NEED FOR THIS CAN BE EXPLAINED THE DESIRABILITY OF SUCH A POLICY WAS QUESTIONED"

See section 2.

23 "DISCUSIONS WERE ALSO HELD ON THE CONCEPT OF CLINICAL VALIDATION OF PROCESSED MATERIAL. IN SOME RESPECTS THERE WOULD APPEAR TO BE ROOM FOR THE GENERATION OF MORE DATA"

See Section 2

24 "OUT OF HOURS SUPERVISION COULD WELL BE MISSING IN THE PROCESSING AREA. THIS SHOULD BE RECTIFIED WITHOUT DELAY."

From January 17, 1983 onwards we will provide for one trained MLSO to be responsible for out of hours supervision of laboratory assistants in the processing area. This MLSO will be present at all times during components processing.

"EDINBURGH IS A CENTRE WHICH APPEARS TO DO A NUMBER OF ACTIVITIES DIFFERENTLY FROM ELSEWHERE....."

We have difficulty in responding to the general comment but accept that where we are using practices which differ importantly from a universally accepted normal practice, the onus is on us to demonstrate validation of our practice. The specific points raised as examples were. (i) "STORAGE OF WASHED RED CELLS FOR FIVE DAYS" (this refers to recovered frozen red cells). The safety of this practice has been validated over many years by biochemical and bacteriological testing of all outdated units. The data, which show good red cell preservation and an exceedingly low rate of contamination, are given in appendix (c) . (ii) "THE TIME LAG BEFORE BLOOD IS COOLED". We have now adopted conventional practice as our facilities now allow us to do this. (iii) "DIFFERENCE IN CENTRIFUGE PRACTICE." We take it the reference is to centrifugation times and g- forces. With the purchase of new equipment our centrifugation protocols are now similar to those used by other centres. (iv) "REPEAT CHECKS IN GROUPING USING THE SAME REAGENTS AND EQUIPMENT." This practice has been modified. See reponse section 86ii. (v) "PIGTAIL PACKS." See response section. 61,62 (vi) "LACK OF AGITATION AND TEMPERATURE CONTROL OF PLATELETS." In preparation for the introduction of new plastic packs for prolonged platelet storage, rotators for platelet storage are now in routine use for all donations. Storage temperatures are monitored. Facilities for temperature controlled storage are provided for in planning of the new blood bank. Controlled temperature storage facilities are being installed in the components processing area to hold platelets (without

agitation) prior to transfer to the blood bank. Controlled (22C) storage of blood before platelet separation is not required as blood for platelet production is centrifuged within a very short period of receipt in the components processing area.

PHASE I RIE

34 "THE LACK OF SECURITY OF THE CENTRE 'OUT OF HOURS'. IT IS UNDERSTOOD THAT THE MAIN ENTRANCE MUST REMAIN UNLOCKED - A MOST UNSATISFACTORY SITUATION FROM THE SECURITY VIEWPOINT. PRIORITY MUST BE GIVEN TO RESOLVING THIS ITEM"

A computer controlled card access system has been purchased and will be operational in Phase 1 RIE in January 1983. This restricts access to holders of personalised identity cards. The system will operate in all 3 sites as soon as the suppliers overcome their problems in meeting the agreed performance specification for the system.

35 "SOME UNSUITABLE FURNISHINGS HAVE BEEN PROVIDED IN A FEW AREAS AND IT IS HOPED THESE WILL NOT DELAY THE USE OF THE DEPARTMENT"

We do not understand this comment.

36 "THE HEPATITIS LABORATORY HAS BEEN DESIGNED AS A 3-ROOMED SUITE BUT ACCESS TO THE CORRIDOR IS POSSIBLE FROM THE ROOM CONTAINING THE MICROBIOLOCICAL SAFETY CABBINET"

We accept this basic design fault in the building. A minor works proposal will be submitted to modify the access as shown on the sketch plan,(appendix D). This will allow access to all 3 hepatitis laboratories to be segregated from the main corridor; Access to this area will be restricted to designated staff.

37 "THE MICROBIOLOGY LABORATORY (DESIGNATED) IS NOT SATISFACTORILY EQUIPPED"

We have established a new microbiology laboratory which is equipped for the present level of bacteriological testing.

38 "IT IS STRONGLY RECOMMENDED THAT THE AREA PRESENTLY BEING USED AS A TEMPORARY PHARMACY SHOULD, WHEN VACATED, BE CONVERTED FOR THE USE OF THE BLOOD TRANSFUSION CENTRE INTO A PROCESSING AND LABORATORY FACILITY. THIS WOULD ALLOW THE MAIN FUNCTIONS OF THE CENTRE TO BE HOUSED TOGETHER ON ONE FLOOR."

See response section 3

39/467

LIVINGSTONE HOUSE CLEAN ROOM

41 "THE DESIGN OF THE DRAIN (NO AIR BREAK - WHICH SHOULD BE OUTSIDE THE CLEAN ROOM). WINDOWS INSTALLED WITH LEDGES AND RUBBER GASKET (ATTRACTS DUST)"

The responsible officer of the Building Division (Mr J. Stewart, Clerk of Works) does not accept the Inspector's criticism. The Building Division has been asked by the Regional Director to respond in writing to the point raised by the Inspector.

LIVINGSTONE HOUSE - CENTRIFUGE ROOM

42 "THE ARRANGEMENT FOR EXTRACTION HERE USING LARGE AND CUMBERSOME HOODS IS NOT THE MOST APPROPRIATE. IN PRACTICE LOCALISED POINT EXTRACTION IS USUALLY MORE EFFECTIVE"

We are of the opinion that the heat extraction system installed is appropriate for the heat outputs (3kw per centrifuge).

43 "IT MAY BE NECESSARY TO PROVIDE ADDITIONAL COOLING CAPACITY IN THESE TWO AREAS"

We have no evidence that additional cooling is needed. Temperature records in the centrifuge room are satisfactory.

44 "IT IS ALSO RECOMMENDED THAT THOROUGH SMOKE TESTS ARE CARRIED OUT UNDER VARYING WORKING CONDITIONS TO ESTABLISH THAT THE CONTRIFUGE EXTRACTS DO NOT CAUSE AN INFLUX OF UNFILTERED AIR INTO THE CLEAN ROOM ITSELF (EG BY WAY OF THE HATCH)"

The recommendation is accepted to carry out smoke tests to investigate this potential problem, and arrangements have been made with CSA Building Division to do this. Nevertheless, our discussions with the Building Division's Officers indicate that the risk referred to must be remote.

We take it that the main concern is that unfiltered air could be present in the downflow of the laminar airflow cabinets. For this to happen four faults would have to occur simultaneously.

(i) The air pressure in the large centrifuge room would have to be greater than that in the Guarded Systems Separation Area (G.S.S.A.).

(ii) Both hatches from the centrifuge room to the G.S.S.A. would have to be open at once.

(iii) The positive pressure filtered air system feeding the G.S.S.A. would have to fail.

(iv) The vertical downward flow of sterile air in the LAFCs would have to cease.

Faults (iii) and (iv) could happen in the event of a major power interruption but in the event of this occurring there is a firm instruction in the Standard Operating Procedure for the Operation of the G.S.S.A. that all processing will be abandoned until the power supply is fully restored.

"OLD" RIE SITES - CROSSMATCHING, ISSUE AND POOLING FACILITIES

47. "THE EXISTING CROSSMATCH LABORATORY IS DANGEROUSLY OVERCROWDED HANDLING ABOUT 6,000 UNITS A MONTH IN A VERY SMALL FACILITY"

48. "THE EXISTING ISSUE FACILITY IS MOST UNSATISFACTORY - IT IS OVERCROWDED AND BLOOD MAY BE LEFT FOR UP TO AN HOUR AT AMBIENT TEMPERATURE"

These criticisms are accepted in full. The attached sketch plan , appendix (E), shows the proposed enlargement of the Crossmatching Lab and issue room. Each crossmatching work station will have its own 4 C storage. These works are at present (December 1982) being costed by the CSA Building Division.

49 "THE EXISTING POOLING FACILITY IS MOST UNSATISFACTORY THERE ARE TOO MANY OTHER ACTIVITIES NEARBY AS WELL AS DRAUGHTS FROM OPENING WINDOWS. EVEN THE PROPOSED UPGRADING WILL NOT CONVERT THIS INTO A CLEAN ROOM ENVIRONMENT"

We acknowledge the inadequacies of the present pooling facility and have given serious consideration to the construction of a small clean room for pooling blood products (platelets and cryoprecipitate) immediately before issue from the

However, it must be noted that there are problems inherent in the operation of a clean room facility during out of hours periods in a busy blood bank which is manned for long periods by a single MLSO who must be instantly available to deal with emergencies.

If it was necessary to change completely, gown and glove to enter the clean room to pool platelets, the service could only be provided by having a second member of staff available during all out of hours periods. We consider that with the present commitment of our trained MLSO staff to various out of hours rosters it will be impossible to recruit staff for this new duty. In addition, there are financial implications in funding an additional person out of hours. We therefore propose the following solution:

Platelet and cryoprecipitate pooling to be carried out in a room within, but separated from, the Issue Area. (See Appendix E - Sketch Plan). The air suppy to this room will be supplied from the outside using a positive pressure filtered air system operating to the same specification as that used in the clean room in Livingstone House. The temperature of the air will be controlled at 22 C +-2 C by an incorporated air conditioning unit, to provide conditions for storage of platelets. Pooling will be carried out in a vertical laminar air flow hood. Personnel entry to the room will be by sliding door. Before entering the positive pressure ventilated room staff will remove their laboratory coats and put on disposable gown, hat and mask (the same procedure as adopted in clean room, Livingstone House).

STORAGE FACILITIES

"EXISTING STORAGE FACILITIES WERE SEEN TO BE INADEQUATE, WITH GOODS, EQUIPMENT AND RUBBISH CLUTTERING UP CORRIDORS"

Major inroads to this problem have been made with the availability of the new stores. Adequate storage, including expanded 4 C storage is provided for in the plans for the "old" Royal Infirmary site.

52 "INSUFFICIENT REFRIGERATOR SPACE WAS AVAILABLE SO THAT ONE REFRIGERATOR DESIGNATED FOR EXPIRED MATERIAL CONTAINED "IN-DATE" FVIII AND FREEZE DRIED CRYOP-RECIPITATE"

The storage of "in date" and expired material in a single refrigerator has ceased.

BLOOD PROCESSING

54 "ENTRY FOR STAFF AND MATERIALS IS VIA THE BACK DOOR WHERE ONE IS CONFRONTED WITH AN APPALLING MESS OF RUBBISH WHICH IS TOTALLY INADEQUATELY CONTROLLED AND REMOVED. WHIST IT MAY BE VERY DIFFICULT TO CONTROL THE COCKROACH AND RODENT INFESTATION IN OLD BUILDINGS OF THIS TYPE, THE UNACCEPTABLE HEALTH HAZARD POSED ATTENTION BY THE HOSPITAL AUTHORITIES"

The site referred to has been vacated.

55 "THE ONLY CONCESSION TO CLEAN ROOM WORKING CONDITIONS THAT HAS BEEN POSSIBLE IS TO SUPPLY HEPA FILTERED LAF CABINETS. THESE HAVE BEEN LOCATED IN STANDARD LABORATORIES OR WORSE, IN CORRIDORS. NO STAFF CHANGING FACILITIES ARE AVAILABLE. OUTER SURFACE OF BAGS ARE NOT SANITISED BEFORE ASEPTIC HANDLING"

Improved clean room conditions have been provided in Livingstone House - These are the subject of later comments and responses.

We do not accept the comment that the failure to sanitise the external surface of blood bags is a defect in our working practice. It is our understanding that the introduction of a system to sanitise blood packs in a large English RTC has not resulted in any documented improvement in the level of bacteriological contamination of separated plasma and we feel that further evidence is required before a case could be made for the cost-effectiveness of this change.

56 "UNDER SUCH CONDITIONS THE SKILL OF STAFF, A DISCIPLINED AND CONSCIENTIOUS APPROACH AND ADHERENCE TO GOOD HOUSE KEEPING PRACTICES ARE ALL OF IMPORTANCE"

We accept that these comments are valid regardless of working environment.

57 "WITHOUT WISHING TO DETRACT IN ANY WAY FROM THE EFFORTS OF STAFF SOME IMPROVEMENTS IN ASEPTIC MANIPULATION AND THE HOUSEKEEPING OF LAF CABINETS NEEDS TO BE CONSIDERED. EXAMPLES OF WORKING ON THE EDGE OF CABINETS AND WITH UNGLOVED HANDS IN A POSITION LIABLE TO CONTAMINATE CONNECTORS WERE SEEN"

We agree that there is a need to ensure that staff are trained to carry out manipulation aseptically, and to maintain those operational standards in practice. We disagree with the specific comment about ungloved hands as it is our opinion that gloves may become contaminated and are not "safer" than ungloved hands, and that gloves interfere significantly with manual dexterity to the detriment of the safety of the procedures. Staff are trained, and will continue to be trained, in how to avoid contaminating the opened sterile connectors. During early 1983, smoke tests on the LAF will be carried out during simulated operational procedures to highlight the parts of all manoeuvres which are accompanied by risks of contamination.

58 "THE WHOLE QUESTION OF TRAINING STAFF WOULD SEEM TO NEED SOME CONSIDERATION. BY ADOPTING A FORMALISED APPROACH IMPROVEMENTS SHOULD OCCUR"

(i) A standard operating procedure for the operation of the G.S.S.A. is now in use.

(ii) At present no formal training is given but in-service instruction is provided and as staff are under constant supervision assessment of their competence and continued adherence to good practice is continually taking place. The gradual production of Standard Operating Procedures will eventually build up to the detailed list of practices. Consideration is being given to providing regular periods in which formal training can be given on an uninterrupted basis to all the appropriate staff.

59 "IN TERMS OF SPEED OF PROCESSING IT IS UNDERSTOOD THAT DONATIONS TAKEN BY THE MOBILE TEAMS ARE NORMALLY PROCESSED THE SAME DAY (EXCEPT EVENING SESSIONS). BLOOD TAKEN IN THE CENTRE IS PROCESSED UP TO 7.00 P.M., THOUGH IT IS UNDERSTOOD THE CENTRE WOULD LIKE TO CONTINUE PROCESSING UP TO 11.00 P.M. THIS MUST, HOWEVER, BE DONE WITH ADEQUATE QUALIFIED SUPERVISION"

"Same day" processing now covers the majority of sessions and with new working arrangements starting in January 17, 1983, there will be a further increase in the proportion of donations processed on day of collection.

PIGTAIL PACK

61, "THE DEFINED USAGES FOR THE PIGTAIL PACKS ARE FOR THE PREPARATION OF PRECIPITATE BY THAW SYPHONING OR FOR PLASMA POOLING"

62. "THE INCREASE OF THIS PACK MAY DECLINE SHOULD THE MULTIPLE PACK WITH SAG OR SAGM INCREASE"

It is hoped to obtain funds to conduct a large scale trial of optimal additive packs which would remove the need for pigtails to be used in fresh plasma pooling. Development of the "tear bag" system may also remove the need for pigtails for this purpose. We consider however, that the present use of the pigtail connection system for fresh plasma pooling is a safe procedure which does not require to be altered on the grounds of microbiological safety. Data on the bacterial contamination of products prepared in the pigtail system are given in appendix F to support this statement.

Pigtail connections are also used for pooling of outdated plasma and also for pooling platelets and cryoprecipitate prior to issue from the blood bank. In the latter context we have made proposals (49) for improving the working environment. We would require further discussions with the Inspector to determine the standards to be attained for the pooling of outdated plasmas using pigtails.

64 "THERE IS A REDUCED RISK OF CONTRACTING HEPATITIS FROM A SMALL POOL DONOR SOURCE. IT IS ARGUED BY OTHERS THAT THE RISK OF CONTRACTING HEPATITIS IS SUBSTANTIALLY INCREASED WHEN A POOL EXCEEDS 10"

No comment. See Response Section 2

65 "EDINBURGH USE AN INITIAL POOL OF 3 BUT THIS IS LATER POOLED WITH 4 OTHER POOLS (MAKING A TOTAL OF 12 DONORS INVOLVED)"

In fact four or more pools may be issued at any one time to a particular patient. Hence, one treatment episode could involve a patient being exposed to 3, 6, 9, 12 or even more donors. We feel, however, that the inspector has missed the main point of the "donation-exposure" aspect of this system of providing cryoprecipitate. In fact, the factor VIII and fibrinogen yields are higher than with conventional cryoprecipitate so that for an equivalent dose of factor VIII (or fibrinogen) the patient is exposed to even less donors than would be the case with cryoprecipitate prepared conventionally. See also response to 74.

66 "THE INSPECTOR WOULD PREFER THE CENTRE TO INVESTIGATE THE POSSIBILITY OF USING ACCREDITED DONORS IN AN ATTEMPT TO REDUCE THIS RISK"

Because the triple pool is selected from donations of known group - ie from established donors - there is already an element of accreditation in the procedure. However, it is felt that the logistics of providing a panel of "fully accredited" donors for cryoprecipitate are not likely to make the procedure cost-effective. Nor are we clear how an "accredited" donor should be defined in terms of the risk of transmitting hepatitis, since all current evidence suggests that the great majority of cases of post transfusion hepatitis are clinically occult and can only be found by regular checking of the recipients liver function tests over long periods.

67 "CRYOPRECIPITATE PRODUCES A HIGHER YIELD OF FVIII FROM A GIVEN UNIT OF PLASMA COMPARED TO FREEZE DRIED INTERMEDIATE FVIII. IT IS ONLY BY PRODUCING 10.000 PACKS OF CRYOPRECIPITATE PER ANNUM THAT THE CENTRE CAN MEET ITS NEEDS"

It is true that, at the moment, self-sufficiency for factor VIII in the S E Scotland Region is dependent on the high-yielding cryoprecipitate production. However, developments are in hand which will increase the supply of high quality fresh plasma to PFC for factor VIII production: dependence in cryoprecipitate may be reduced in future.

68 "THE GAP BETWEEN NEEDS AND QUANTITIES OF FVIII AVAILABLE FROM THE PFC COULD BE SUBSTANTIALLY NARROWED IF A NATIONAL POLICY OF DISTRIBUTION WERE ADOPTED. THAT IS SUPPLY SHOULD GO TO THE CENTRES WITH THE GREATEST NEED"

No comment

69 "A SMALL QUANTITIY OF CRYOPRECIPITATE MIGHT STILL BE REQUIRED FOR ITS FIBRINOGEN CONTENT OR FOR THE TREATMENT OF VON WILLEBRAND'S DISEASE.

No comment

71 "THE CRYOPRECIPITATE IS PRODUCED FROM A TRIPLE POOL OF PLASMA FLASH FROZEN TO -30 TO -40 C. SIXTEEN SUCH POOLS ARE THAWED AT 2-3 C. THE CRYOPRECIPITATE DEPLETED PLASMA IS SYPHONED OFF AND THE CRYOPRECIPITATE IS FROZEN AND STORED FOR UP TO 6 MONTHS. (CONSISTS OF 4 BY 3 DONORS)"

The phrase in parenthesis is erroneous (see response to 65). The inspector appears to be under a misapprehension. Three donations are contained within each pack of frozen cryoprecipitate - not twelve. The volume of each pack is about 110 mls.

72 "THE TRIPLE POOLS OF CRYOPRECIPITATE ARE OF ONE ABO GROUP (NORMALLY 'O' OR 'A'). PATIENTS REQUIRING MORE THAN ONE TRIPLE POOL MAY BE GIVEN A MIXED POOL OF GROUP 'O' AND GROUP 'A' TO REDUCE THE AMOUNT OF 'ANTI A' PRESENT (ABSORBED BY 'SOLUBLE A SUBSTANCE')"

No comment

73 "INCREASED 'SIDE EFFECTS' ARE A CONSEQUENCE OF THE USE OF CRYOPRECIPITATE BUT AS USED IT DOES NOT APPEAR TO BE AMENABLE TO PURIFICATION"

No comment

74 "CONNECTION TO BAGS FOR POOLING AND THAW-SYPHONING ARE CARRIED OUT UNDER LAF PROTECTION. WHETHER BETTER FACILITIES ARE NEEDED WAS NOT RESOLVED - POOLED PRODUCT CAN BE STORED FOR UP TO SIX MONTHS, ALBEIT UNDER FROZEN CONDITIONS, SO A CASE COULD BE MADE FOR CLEAN ROOM FACILITY"

We agree that there is a case for the clean room facility to be made available for the connection procedures in thaw-siphon cryoprecipitate production. Investigations are planned to assess the feasibility of using the clean room for this.

We will also be investigating the effects of preparing the initial pool of plasma to be cryoprecipitated from two donors, rather than three, the donations to be collected in an "optimal additive system" with maximal plasma separation (300 mls) from each. As an extension of this, we will also be investigating the efficacy of the thaw-siphon process on the 300 mls of plasma from a single donation using a totally closed pack system. This is likely to result in about 50 mls of residual cryoprecipitate. These points are also relevant to paragraph 65.

"ALIQUOT SAMPLING MIGHT BE MORE REPRESENTATIVE THAN THE EXISTING SACRIFICE OF A SINGLE UNIT FOR TESTING PURPOSES"

It is our belief that aliquots which are frozen and thawed separately from the main bulk of cryoprecipitate are likely to give a less representative indication of the active contents of the whole pack than if the whole pack is thawed. Were aliquots to be collected from fully solublised cryoprecipitate prior to final freezing, we believe that this would cause a loss of activity. Hence, even though the current procedure involves the sacrifice of that pack, we believe that the standard of QA is thereby enhanced.

CELL WASHING

"THE MACHINE USED, AN IBM 2991, IS INAPPROPRIATELY LOCATED IN A CORRIDOR. BAGS ARE CONNECTED TO THE MACHINE WITHOUT THE PROTECTION OF HEPA FILTERED AIR"

Funds have been obtained for the purchase of a laminar flow canopy to protect the connections made in operating the IBM 2991 cell washer. This facility will be incorporated in the modifications to the "old" Royal Infirmary site, and should be operational early in 1983.

FROZEN CELL STORAGE

"RED CELLS IN THE CRYOPROTECTED STATE AND STORED IN THE VAPOUR PHASE OF LIQUID NITROGEN ARE GIVEN AN INDEFINITE SHELF-LIFE EVEN THOUGH TEMPERATURES ARE INADEQUATELY MONITORED"

We are investigating the availability of suitable temperature monitors but would note that there is an automatic and fully alarmed system to maintain the level of liquid nitrogen in the containers, and that the constant evaporation should maintain constant temperatures.

79 NO MICROBIAL DATA HAS BEEN GENERATED ON THIS PRODUCT. THIS WOULD SEEM WORTHWHILE AS NEONATES ARE PARTICULARLY 'AT RISK'."

We have introduced regular bacteriological QA on 4 samples of this product per week.

POOLING OF EXPIRED PLASMA

80 "POOLING IS CARRIED OUT IN AN LAF CABINET BUT THE ENVIRONMENT IS UNSATISFACTORY

This function has been transferred to Livingstone House.

QUALITY ASSURANCE

81 "THERE IS NO CENTRALISED QA FUNCTION AND SO FAR A DISTINCTION HAS NOT BEEN MADE BETWEEN A NOMINATED PERSON RESPONSIBLE FOR PRODUCTION AND ONE FOR QC"

As from March 1st 1983 a Chief MLSO with appropriate experience will be the person nominated to take responsibility for the coordination of quality assurance. The development of appropriate standard procedures for documentation, checking and reporting of QA data, and documentation of actions taken in response to QA reports, will be undertaken by this person working with appropriate senior members of staff.

83 "A QC PROCEDURES MANUAL IS AVAILABLE AND A SUMMARY OF THE 'TEST SUMMARY SHEET' WAS REQUESTED"

"Test Summary Sheet" was provided: copy at appendix G .

84. "MACHINE GROUPING IS CARRIED OUT ON A ~~TECHNICON~~ CONTINUOUS FLOW MACHINE BUT THIS HAS BEEN UNRELIABLE AND REQUIRES CONSTANT OPERATOR SUPERVISION"

85. "INVESTMENT IN MODERN EQUIPMENT LINKED TO A COMPUTER WHICH COULD 'SCAN' AND 'COMPREHEND' LABELS MUST BE A PRIORITY. THE SCOTTISH TRANSFUSION SERVICE AS A WHOLE IS STILL IN THE PROCESS OF EVALUATING THEIR REQUIREMENTS"

Funding was requested for a new automated grouping machine for 1982-83. This has not been funded but the request is continued for 1983-84. The SE Centre has prepared a detailed operational requirement for this equipment, received proposals from suppliers, and reached a decision on the instrument required.

Funding for a comprehensive integrated computing system has been sought for the financial year 1983-84. This matter is still under consideration by the Common Services Agency.

86 "TO PROCEED TO AN EVEN MORE AUTOMATED SYSTEM WOULD STILL REQUIRE STAFF IN THIS SECTION TO BE ABLE TO 'FALL BACK' TO LESS SOPHISTICATED TECHNIQUES SHOULD IT BE NECESSARY. IT IS ~~NOT~~ NOTICEABLE THAT HEAVY RELIANCE IS ALREADY PLACED ON THE CONTINUOUS FLOW ~~TECHNICON~~ MACHINE. REPEAT GROUPINGS ARE MERELY SENT THROUGH THE EQUIPMENT A SECOND TIME USING THE SAME REAGENTS AND PAPER. IN OTHER FIELDS THIS WOULD NOT BE CONSIDERED GOOD OR SAFE PRACTICE THOUGH IT IS TRUE IN THE CASE OF GROUPING ONE HAS A 'LONG STOP' IN THE SHAPE OF THE CROSSMATCHING LABORATORY. (IN A REAL EMERGENCY CROSSMATCHING MIGHT BE BY-PASSED AND THE 'LONG-STOP' NO LONGER EXISTS)"

(i) it is accepted that full back-up procedures are mandatory and the development of these, with ongoing arrangements for staff training etc. would be an integral part of the introduction of new grouping equipment.

(ii) the practice of repeat grouping with the same reagents has been abandoned. All new donors are regrouped with different reagents. Any grouping discrepancies are investigated by manual testing.

(iii) Blood is not issued without a confirmation of ABO group even in real emergencies. A small stock of manually re-checked group O is maintained for "instant" release.

SYPHILLIS TESTING

87 "THIS IS CARRIED OUT MANUALLY AND BY MACHINE. ANTIPATHY WAS EXPRESSED TOWARDS THE TEST BY THE CENTRE STAFF"

The cost-effectiveness of syphillis screening is challenged by many transfusion specialists and the practice of screening has been abandoned in at least one major Centre of high reputation. it is the view of the Regional Director that the benefits of screening should be formally revaluated by SNBTS. When a new grouping machine is obtained, syphillis testing will be automated.

HEPATITIS TESTING

90 "THE MAIN BIOHAZARD AREA ALTHOUGH SEGREGATED AND ENTERED VIA A CHANGE ROOM MUST BE CONSIDERED AS UNSATISFACTORY. IT HAS A VERY SLIGHT NEGATIVE PRESSURE AND HEPA FILTERS DO NOT APPEAR TO HAVE BEEN FITTED ON THE EXHAUST DUCTING"

This laboratory has been vacated. We do not however, accept the implication that a negative pressure ventilation room is needed for routine blood donation hepatitis screening since the materials handled are of low infectivity . Negative pressure rooms are not, we understand, used in many other transfusion centres. A hepafilter will be fitted at point of air extraction in the ventilation system of the laboratory to be used for hepatitis testing in Phase I RIE.

91 "THE AUTOCLAVE LOCATED HERE USED FOR INACTIVATING CONTAMINATED ITEMS STILL RUNS ON A PRESSURE GAUGE (20LBS FOR 45 MINUTES) AND HAS NOT BEEN CHECKED OR REGULARLY MAINTAINED."

A replacement autoclave has been commissioned in Phase I RIE

92 "A LEVEL OF MICROBIAL TESTING IS CARRIED OUT ON PRODUCT AND A LIMITED ENVIRONMENTAL TESTING SCHEME IS INCLUDED. THIS LATTER SYSTEM INCLUDES 'BIOTEST' CHECKS ON LAF CABINETS BUT THESE CANNOT BE CHECKED FOR PARTICLES OF FLOW (BY ANEMOMETER) NOR ARE SETTLE PLATES ROUTINELY USED. "BIOTEST" RESULTS ARE HIGHLY VARIABLE"

(i) We intend to maintain the present level of bacteriological testing products until there have been further SNBTS discussions about the appropriate levels of testing.

(ii) Environmental monitoring. From January 1983, air sampling and settle-plate checks will be made in the following areas:

(i) clean room air in LH
(ii) clean room LFC's in LH
(iii) cryo pooling LFC in LH
(iv) blood bank LFC
(v) cryobiology LFC

The frequency of sampling is as yet to be decided: details will be incorporated in the relevant SOP's. Results will be reported by Microbiology Section to the QA Officer.

93 "TEST METHODS APPLIED ARE NOT PHARMACOPOEIAL AND POSITIVE CONTROLS ON MEDIA ARE NOT DONE. SAMPLE SIZES ARE OFTEN SMALL".

Sample sizes are small by pharmacopoeial standards for pharmaceutical products, but there are obvious reasons for minimising the sacrifice of donated blood and its derivatives for QC purposes. We consider our sampling is not out of line with practices in other transfusion centres.

The bacteriological culture procedures in use are at present being reviewed with the intention of completing revised SOP's by mid 1983, which will be in line with accepted practices in other Centres. The matter of medium controls is particularly difficult in view of the range of organisms which we would require to detect: it is possible that this can be dealt with only by obtaining suitably tested supplies of media from an external source.

DOCUMENTATION AND SOP'S

94, "A WORKING PARTY AT THE CENTRE IS REVIEWING THE NEED FOR AND THE DETAILS TO BE INCLUDED. A USEFUL START HAS BEEN MADE."

95. "EXISTING DOCUMENTATION AND DATA GENERATION IS FAIRLY SUBSTANTIAL BUT IT IS NOT CLEAR WHETHER IT IS ALL 'USEABLE'"

Priority is being given to completion of comprehensive SOP's for donor selection, care and bleeding and for components processing. With our present staff resources we feel the completion of adequate SOP documents for all activities will take several years and unless clerical or word processing support is available this programme may have to be curtailed.

We accept that present QA documentation is not adequately accessible. It will be a priority of the person nominated to be responsible for QA to rationalise the presentation and distribution of QA information.

96 "WHEN IT COMES TO IDENTIFYING DONORS FROM A SPECIFIC BATCH OF PLASMA FULL TRACEABILITY IS MAINTAINED. HOWEVER, TRACING WHERE OTHER COMPONENTS MAY HAVE GONE FROM THE SAME DONATION (EG THE RED CELL CONCENTRATE) MAY NOT BE DONE WITH ABSOLUTE CERTAINTY"

We are not aware of the deficiencies referred to in documentation to trace components prepared from a donation. It is however accepted that the system is slow and cumbersome and that information tracing would be greatly improved by computerisation. See also 106.107.

PLASMAPHERESIS

97 "THE CENTRE HAS A SMALL (3 BED) MANUAL PHERESIS PROGRAMME GOING. ACCURATE IDENTIFICATION OF PATIENT AND RED CELLS FOR RE-INFUSION IS AIDED BY A COLOUR BAND AND SIGNATURE SYSTEM. THIS IS PROBABLY SAFE FOR ABOUT 7 OR 8 BEDS BUT CERTAINLY NO MORE."

We have no response to this observation

CELL SEPARATOR

98. "THIS CAN BE USED TO OBTAIN SINGLE DONOR COMPONENTS FOR A NAMED PATIENT (AS WELL AS FOR PATIENT TREATMENT)

99. "IT IS A COMPLEX PIECE OF EQUIPMENT WHICH REQUIRES THAT THE CORRECT CONNECTIONS SHOULD BE MADE USING ASEPTIC TECHNIQUE"

We feel there is a need for more discussion of the Inspector"s role and objectives in this area before a response can be made. We can respond to point 100.

100 "A FEW COMMENTS WERE PASSED OVER THE ABSENCE OF A 'USE BY' DATE ON AUTOCLAVED EQUIPMENT AND SOME CONFUSION WAS EXPERIENCED WITH THE USE OF AUTOCLAVE TAPE AS A SUBSTITUTE FOR ADHESIVE TAPE."

The need for autoclaving of reusable components of the patient circuit will be removed with the planned purchase of a new cell separator in 1983. All elements of the patient circuit will then be sterile disposables.

BLOOD BANK, ISSUE, WARD REFRIGERATION

104 "RETURNED BLOOD IS HELD AND PHYSICALLY EXAMINED BEFORE RETURNING TO STOCK. THIS DOES NOT PROVIDE TOO MUCH OF A GUARANTEE THAT HANDLING AWAY FROM THE CENTRE HAS BEEN ADEQUATE"

105. "IT IS UNDERSTOOD THAT NEW WARD REFRIGERATORS ARE TO BE PROVIDED IN THE NEAR FUTURE AND THESE WILL BE CHECKED DAILY BY CENTRE STAFF. (WOULD HAVE BEEN BETTER TO HAVE BEEN DOING THIS WITH EXISTING UNSATISFACTORY REFRIGERATORS"

We accept that this is an area where control is difficult.

It should be noted that unlike most RTC's, we issue a high proportion of our blood, crossmatched, to individual patients. It is

normal and correct clinical practice to order blood which is not, ultimately transfused and it is often essential that this blood is available close to the patient rather than held in the blood bank. There is no possibility of rejecting all blood which is returned untransfused, as wastage would be unacceptable. We have taken the following steps to improve the situation.

(i) Research and educational programmes including the introduction of blood ordering schedules to train clinicians to minimise the amount of crossmatched blood withdrawn from the blood bank: (see eg appendix H). (ii) Introduction, to relevant parts of the RIE, of a policy of issuing blood one unit at a time, for immediate transfusion. (iii) Introduction of monitored blood storage refrigerators to serve parts of the Royal Infirmary where policy (ii) above is not applicable. These have been in full operation since September 1982. A new staff post has been financed to carry out the surveillance of these refrigerators.

106 "DOCUMENTATION IN THIS AREA APPEARED SUFFICIENT FOR TRACING PURPOSES (THOUGH 'TRACEABILITY' MIGHT BE LOST AT WARD LEVEL)"

107 "'COMPATIBLE' LABELS ON EACH PACK SHOULD HELP ELIMINATE TRANSFUSION ERRORS PROVIDING THEY ARE READ AND UNDERSTOOD

These comments touch on points of fundamental importance to safe transfusion, since a high proportion of all serious transfusion mishaps occur as a result of documentation and identification errors occurring close to the point of transfusion.

(i) It is true that "traceability" of a unit of blood may be lost at ward or theatre level. The only safeguard is scrupulous attention to detail by clinical staff to ensure that all transfusions are fully documented and that all blood which is not transfused is promptly returned to the blood bank (the same applies to blood products).

(ii) There are important possibilities for the use of computers and machine readable identification systems to carry out pre-transfusion checks and to log transfusions, but implementation on anything other than a pilot trial scale must be considered to be several years distant.

(iii) Compatibility labels on packs are one important part of essential pre transfusion checks. Also essential is the scrupulous checking of the patients identity and the documentation accompanying the blood.

We have taken the following steps to improve safety in this area.

(i) Introduction of new blood and product request forms which elicit adequate identification information on patients.

(ii) Introduction, from September 1982 of a continuing programme of inservice training for all Royal Infirmary nursing staff of staff nurse or higher grade, which concentrates on informing staff of the biological basis of transfusion hazards and the practical aspects of safe transfusion (so far more than 200 nurses, including all senior grades, have received small group teaching).

(iii) A programme is being planned to extend this teaching during 1983 - 85 to staff of other hospitals served by our blood bank.