DEPT. OF HEALTH - MEDICINES INSPECTORATE

INSPECTOR'S SUMMARY

SITE: NHS BLOOD TRANSFUSION CENTRE **COMMERCIAL IN CONFIDENCE**

FILE REF: 285/380/595/H	MB5B Report No. 1990 / 1469
TITLE: Inspection of East Anglia Regional Blood Transfusion Centre, Cambridge	CO. TELE: 0223 245921
DATE OF INSPECTION: 25-27 July 1990	INSPECTOR(S): Dr M L Kavanagh

REGION/AREA (9.1) _ _ CATEGORY (HP) GMP ( ) _ _ add
HAZARD INTERVAL (12) _ _ NO. EMPLOYEES (180) _ _ COMPLEXITY delete _ _ _ _ _

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MISG	For routine distribution		MR P.E Green
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	MRS Robinson		

DATE OF PREVIOUS INSPECTION: February, 1988

PURPOSE OF VISIT: Routine re-inspection

LICENCES HELD OR APPLIED FOR:

LICENSING CHANGES: ACTUAL:

IMMINENT:

RECOMMENDATIONS/ACTION:

1. A copy of this report to be sent to the Regional Health Authority for comment and proposed action.
2. Re-inspect within 2 years

COMPILED BY: M. L. KAVANAGH	COUNTER SIGNATURE: REGIONAL PMI
GRO-C	SMI / HMI GRO-C
DATE SIGNED: 2 October 1990	3.10.90

The factual matter contained in this report relates only to those things that the Inspector(s) saw and heard on the occasion of the visit. This report is not to be taken as implying a satisfactory state of affairs in premises, equipment, personnel or procedures not examined on this occasion.

FSH.

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East Anglia Regional Blood Transfusion Centre
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1. INTRODUCTION

East Anglia RTC, situated in the grounds of Addenbrookes Hospital, Cambridge, serves a population of 1.9 million, employs 180 staff and collects over 90,000 donations annually. In addition, the plasmapheresis suite handles 100-120 donors per week.

The Centre was last inspected in February 1988.

2. SCOPE

The inspection covered the manufacture and control of the products listed in Section 5. Clinical matters, e.g. clinical apheresis, tissue typing and testing relating to patients, were not included.

3. SENIOR STAFF LIST

Dr M McDougall	:	Acting Director
Dr J Blagdon	:	Consultant
Dr W Ouwehand	:	Consultant
Dr A Rankin	:	Associate Specialist
Dr D Voak	:	Top Grade Scientific Officer
Mr M Fletton	:	Principal MLSO
Mr A Slopecki	:	Quality Assurance Manager
Mr N Clark	:	Chief MLSO, Special Investigations Laboratory
Mr D Wenham	:	Chief MLSO, Donor Laboratory
Mr P Eldridge	:	Chief MLSO, Virology Laboratory
Mr R Fagence	:	Chief MLSO, Blood Components/ Biochemistry Laboratory
Mr M Toone	:	Chief MLSO, Antenatal Laboratory
Mr R Pepper	:	Chief MLSO, Reagents Laboratory

4. CHANGES

Dr Darnborough (Director) and Dr Gibson (Deputy Director) have both retired and Dr McDougall has been appointed Acting Director until the appointment of a permanent Director. The position is being advertised as a University appointment (Professor of Transfusion Medicine and Director of the Transfusion Centre). Dr Ouwehand has been appointed as Consultant/Lecturer and Mr Slopecki has been appointed Quality Assurance Manager.

Phase II of the redevelopment programme has been completed and the plasmapheresis suite has been transferred to the newly-refurbished area and enlarged.

The procedures in the Centre are now computerised using the system developed at Cardiff RTC.

5. LIST OF MEDICINAL PRODUCTS

Product	No of Units Issued April 1989-March 1990
Whole blood	34,528
Concentrated red cells/plasma-reduced blood/SAG-M red cells	47,917
Leucocyte - poor red cells	16
Platelet concentrates/platelet-rich plasma	25,524
Fresh frozen plasma (FFP)	6,878
Stored plasma	250
Cryoprecipitate	1,961
FFP for fractionation at BPL (single units)	41,610
FFP for fractionation at BPL (apheresis) (Kg)	2,256
Time-expired plasma for fractionation at BPL	3,900
Hyperimmune plasma for fractionation at BPL	833

6. INSPECTION

6.1 Blood Collection and Receipt

A visit was made to a mobile donor session held in St Neots. The main change since the previous inspection is that donor records are now computerised and pre-printed session slips for called donors are taken to sessions. New donors are still required to fill out a buff-coloured 101 card.

Haemoglobin checking of donors is by the copper sulphate method, blood being taken from a finger prick. The copper sulphate solutions are checked for specific gravity at the Centre and dispensed into smaller containers for use at sessions. Each container is given a fill-date and a life of 7 days. The solutions are changed at the end of each session or, if the session is considered to be busy, half-way through. If a donor fails the copper sulphate test, a repeat test is not performed and a donation is not taken; a venous sample is taken into EDTA for a full blood count (Coulter) back at the Transfusion Centre.

A set of eight bar-code labels is issued for each donor (new donors having pink-edged labels) and the sample tubes, packs and session slip are labelled. Three sample tubes are used, including an extra clotted sample as a spare for any extra tests that may be required. Excess bar-code labels are rendered unusable by scoring across the code and are discarded. The labelled packs, tubes and session slip are put into a polythene bag and placed in a box for collection by a DA, who takes the donor to a bleed bed.

Donors' arms are swabbed with a hibitane/70% industrial methyl alcohol solution prior to venepuncture. This solution is made up in the Centre from bought-in materials which are not QC-checked or filtered prior to use. The made-up solutions are not given batch numbers or expiry dates and no microbiological validation of the effectiveness of the solution has been performed.

Lignocaine is used routinely, the batch number being recorded on the Team Leader's Record, along with the syringe batch numbers and the blood bag batch numbers. The balances used to monitor donation volumes are regularly checked with standard weights.

At the end of a donation, the bleed line is clipped and cut-off, samples being taken from the arm-line stub. Packs are taken to the stripping station where they are stripped and clipped. Tubes are not segmented and are not heat-sealed. The donations are sorted into racks (new donors and old donors) and are removed to a refrigerated vehicle. The temperature of the refrigerated compartment is recorded hourly by the driver but the read-out has not been calibrated. At the time of inspection, milk and orange juice for the session were being stored in the van alongside crates of blood.

6.2 Blood Components

Since the previous inspection, the adoption of the Cardiff computer system has brought about changes in the recording and handling of blood components manufacture. In addition, all open-processing has been discontinued except for the pooling of time-expired plasma which is sent to BPL, Elstree. This pooling takes place 3-4 times per week and is performed in the LAF cabinet in the Class 2 room in the clean room suite.

The Blood Components processing area consists of a centrifuge room, the processing laboratory and the clean room suite. The centrifuge room is equipped with 7 x IEC 6000B centrifuges and 4 x MSE Coolspin 2 machines. At the time of inspection, the windows to the outside were wide open in an attempt to reduce the temperature in the room. The processing laboratory is fitted with effective air-conditioning and outside windows are kept closed.

There is a hand-written cleaning procedure for the benches and equipment in the Components area and cleaning is recorded, with signatures, in a book. The cleaning schedule, however, does not cover other parts of the room and at the time of inspection thick layers of dust were evident on window shelves and the services spur at the rear of the processing bench. Platelets are left to disaggregate in a tray on a bench in front of a dust-covered shelf.

Blood from sessions is received into the Components area together with the session slips. From the session slips, a list is compiled of those packs which are not suitable for platelet preparation (e.g. slow or part bleeds, tropical areas etc.) and these packs are isolated. The remaining packs are processed.

Quarantined platelets are left on an open bench in the processing laboratory overnight. Although the recommended storage temperature for platelet preparations is 22 ± 2°C, the temperature recorded here ranged from 19°C - 28°C. In-process platelets are kept in an orbital shaker in a cabinet which is not temperature-controlled; the lid is permanently open and a fan is directed into it. At the time of inspection, the temperature in the cabinet was 25°C. In addition, the platelet incubator in the Issues department was said to be broken and so platelets for issue were being held on a shaker on an open bench in the processing laboratory. Quarantined, "Held" and for-issue platelets were all being kept in the same room and all had inadequate temperature control.

Both platelets and red-cell products are product-labelled in the Components laboratory. SAG-M is drained back onto the red cells from a rack, the cell-pack lying on the bench. Packs which burst during processing are put into bins in autoclave bags and entered as "discard" in the computer. The final discard of the packs is recorded and signed for but not dated. Prepared red cell products are transferred to the cold room. The cold room temperature is monitored with a circular chart recorder, charts being changed daily, checked and signed. There is also a thermometer inside the room but this is not read. A high-low alarm is fitted but there is no programme for testing or challenging it.

The system for passing platelet preparations into stock is a complicated procedure involving manual checking and physical transfers. Initially, the donation numbers are wanded into the computer and the groups are displayed on the VDU; a small bar-coded group label is then put on each pack, along with a "platelet concentrate" label, and these are wanded through again for verification. This process, however, does not clear the platelets for issue. The morning after the products are prepared, the computer prints out a "cross-check platelet list" which lists all those packs which are suitable for issue, i.e. those with satisfactory microbiology and grouping results; packs not suitable for issue are omitted from the list. Components staff then have to manually go through the list, ticking it if the pack corresponding to a listed number is present. By a process of elimination, unlisted packs (not suitable for issue) are identified and transferred to the "hold" platelet rotator.

Platelet issues are handled by Blood Components staff. A request form is delivered by Issues to Blood Components, listing the name of the patient (usually), the group and the date required. Components staff select packs from the "for issue" shaker and send them off to Issues, at

the same time altering the appropriate ticks on the cross-check list to crosses. The cross-check list seen during the inspection contained a mixture of ticks, crossed ticks and double crossed ticks. No explanation was forthcoming as to the significance of the differences. Platelets can be issued on the basis of HIV antibody and HBsAg clearance and a single grouping result. Occasionally, platelets prepared from new donors are issued on the basis of a single grouping result and before all the computer reconciliation procedures are complete.

FFP both for clinical use and for fractionation at BPL is prepared in 2 blast freezers in the freezer room. When frozen, the packs are boxed. For BPL, 20 packs are put into each box. The sequential box numbers are keyed into the computer and the individual packs are then wanded in as they are boxed. The boxes are sealed and stored in the -20°C freezer.

The following day, the computer lists the individual clinical-use FFP packs which are not cleared and these are removed, the remainder being logged-in to confirm that the correct packs have been taken out. For plasma destined for BPL, the computer lists the whole boxes which are suitable for use. The computer does not allow boxes with fewer than 20 packs to be despatched so implicated packs have to be substituted rather than simply removed. The manual record of the despatch of boxes to BPL contains a mix of ticks, double crosses, half-ticks and other inexplicable ticks.

6.3 Grouping Laboratory

The main change since the previous inspection has been the introduction of the computerised system. The grouping equipment remains the same as do most procedures; however, new donors are now grouped twice on the machine (previously once on the machine and once manually).

Whilst the Grouping Laboratory sets up the tests, the Donor Records Office wand-in details from the session slips into the mainframe computer (i.e. session, donor numbers, donation numbers etc).

All donor samples are put through the Autogroupers. If the machine is unable to read a bar-code, the sample is manually grouped and the donation number is wanded into the computer; there is no manual keying-in of bar-code numbers. If the Autogrouper fails to interpret a result, the sample is re-run and if it still fails it is manually grouped. However, new donors are not manually grouped twice so if they do not have a machine result, the donations are used for plasma only.

The Autogroupers print out a hard-copy of the results and also directly transfer the results to the main-frame where known donors' records are held. Manual results are entered by wanding the donation numbers from the tube label and the results from a menu card. When the transfer for each session is complete and all the information is in, the mainframe computer cross-checks the results with previous history. The computer then lists mismatches, new donors with only one group result and any results expected but not produced (e.g. missing tubes). Work sheets are then produced automatically listing repeats needed etc.

6.4 Virology

Since the previous inspection, a Tecan liquid handling system has been acquired which gives positive sample identification. Virology now have their own sample tubes (previously they were subsamples of Grouping Laboratory samples) and testing has been extended, since 2/7/90, to include antibodies to HIV 1 + 2. Around 450 samples per day are handled here.

Microplates for use on the Tecan and for testing are labelled with in-house printed bar-code labels identifying the plate number, test type and day of the year (numbered sequentially from 1 January). The Tecan reads the bar-code labels on the sample tubes and dispenses sera into the microplates. If the Tecan is unable to read a bar-code number on a sample-tube, the number is not entered manually. The total number of samples is entered manually but if this entry is incorrect (e.g. 80 instead of 82) then the Tecan will ignore the last two samples. However, as the Tecan computer is not linked to the main computer, individual sample tubes are wanded into the main-frame prior to the results transfer. If the two "extra" tubes are wanded-in, they would, under the existing procedure, be assumed negative.

The Tecan dispenses samples and controls. Reagents are added manually with multipoint pipettes. These pipettes are not routinely calibrated to check the accuracy of the dispensed volumes. The completed test-plates are read on a "Multiscan" reader which is linked to the Tecan computer. The plate numbers are wanded-in and the Multiscan reads the absorbances of each well, printing out an absorbance block, highlighting those testing positive. Results are identified with their donation numbers, not merely by rack position, and a histogram is also produced with a list of all the sample numbers annotated as positive or negative.

In all cases of positive test results, the tubes are identified by fitting them with yellow caps. Two people are responsible for checking that the correct sample tubes have been capped. For HBsAg initial screen positives, the policy is to "hold" all products and repeat the test. To this end, a quarantine form is filled out and taken to Blood Components and Donor Grouping. This form is in need of revision as it carries

redundant details. The form lists the donations to be held and the accuracy of the listed donation numbers is double-checked before the form is signed by the Department Head. However, no follow-up action is taken to ensure that components have, in fact, been held. When products (e.g. plasma) are subsequently cleared and taken off "hold", this is only done on the computer and written notification is not given.

For HIV antibody initial screen positives, all products are immediately withdrawn and the test is repeated. Withdrawal of products is investigated by the Virology Department using a form known as Viro 1 (sample held on file). One form is used for each implicated donation and contains spaces for recording the list of products made from the donation and the withdrawal of all such products and samples. The Grouping Laboratory is responsible for collecting all the products and delivering them to Virology. To this end, the Viro 1 form is delivered to the Grouping Laboratory for action. If no one is available in Grouping, however, the form is left on the bench.

When the Viro 1 form has been actioned, it is photocopied and returned to Virology. The Virology Department checks-in all withdrawn products and keeps records of their autoclaving and disposal, using a diary to maintain a progress record. However, no record is kept of the contents of the Virology quarantine freezer where held or withdrawn plasma may be kept. At the time of inspection, a plasma pack in the freezer was recorded on the computer as "issued to missing bags" but no other record of its existence was available.

There is no firm policy on dealing with equivocal results, nor with initial HBsAg screen positives which repeat negative. In both cases, the current policy is for the results to be reviewed by the consultant, Dr Blagdon, who decides on repeats or clearances. When the results form has been signed (by Dr Blagdon), the results are entered into the main computer. Entry is controlled by the use of individual passwords but these are not routinely changed. Results are entered using a hand-written "Tecan Rack Allocation Log" which identifies rack numbers with sample tubes. Each rack number is keyed in manually and then the sample tubes are wanded-in to locate their positions. The computer then prints out a list of donation numbers linked to rack position.

At this point, the computer asks which samples have not been cleared and the appropriate numbers are manually keyed-in. All the others are then automatically cleared. The accuracy of the entry of the non-cleared numbers is normally double-checked by a second person but out-of-hours (usually a Friday evening), a single person takes responsibility.

Library samples are dispensed into 1 ml glass tubes identified by their positions in bar-code labelled,lidded, sealed cardboard boxes. The computer prints out an inventory listing donation numbers, position in box and box number. The current plan is to retain such samples for 2 years.

6.5 Blood Bank and Issue

Blood and red cell products are transferred into stock using the computer. When the computer reports that all the testing is completed for a session, the blood is brought out into a cooled (15°C) area and each donation number is wanded. The VDU then instructs the operator to apply a specific grouping label after which the group, donation number and product labels are rewanded. If these details are not in agreement, the computer prevents further action until it is acknowledged and corrected; if the details are correct, the computer accepts the pack into stock for issue.

Whole blood and red cell products for issue are kept in separate cold rooms which are maintained in a clean and orderly condition. FFP for clinical use and cryoprecipitate preparations are held in two chest freezers. The high-low alarms on the equipment are checked every morning. (The platelet incubator in the Bank was out of action at the time of inspection - see Section 6.1, above.)

The system of "milk round" deliveries described in the previous report is no longer used. All hospitals are now visited every day except Wednesday and orders are 'phoned in the previous evening. Orders are put together and issued via the computer which generates a triplicate delivery note. As the computer lists all products in stock but not necessarily available for issue (e.g. held cross-matched blood), stock control is still handled manually using a Magiboard.

The issuing of all products through the computer should give 100% traceability of all donations. However, staff from the Reagents Laboratory were said to occasionally remove blood for laboratory use without wanding it through the computer. This results in the apparent disappearance of donations with no records as to their fate. Examples were seen of untraceable donations.

Blood returned from hospitals is wanded in as 'Returned' and is sent for discard. However, there are no records kept of the actual disposal of the returned packs. BPL products are issued through the computer, which also maintains stock control for these products.

Although many Departments at the Centre are progressing the production of SOPs, none at all are available in the Bank and Issue section.

6.6 Quality Assurance

Since the previous inspection, a Quality Assurance Manager has been appointed, the appointment dating from June 1989. As yet, no other QA staff have been appointed although steps are being taken to appoint both a Deputy QA Manager and a QC Officer. The former post is to be re-advertised following an initial disappointing response, while the QC Officer post is currently being advertised.

Following a self-audit of all Departments, the need for improved documentation was highlighted as a priority, with particular attention being given to SOPs. A common format for SOPs within the Centre has been agreed and most Departments (with the exception of Blood Bank and Issue) have produced at least a set of draft SOPs. there is a controlled system of issue and review of SOPs in place.

Quality monitoring of products is minimal. As information for BPL, all FFP packs for fractionation are weighed to determine whether they are above or below 300g. Some checking of platelet counts in platelet concentrates was started but has since been discontinued. (Indications were that the NIBSC/UKBTS Guidelines specification on platelet counts was not being met.) In addition, when platelet concentrates are being cleared to issue, packs which look obviously too light or too heavy are weighed against a target of 30-38g. Action limits, outside which packs are discarded, are 20g and 100g; however, no recording of data or action on packs in the ranges 20-30g and 38-100g are taken.

There is no check-weighing of whole blood and no FVIII:C assays on FFP or cryoprecipitate. When the QA Department is expanded, it is intended to encompass quality monitoring of all products and apply the specifications of the NIBSC/UKBTS Guidelines. The QC laboratory is very sparsely equipped, containing an incubator, a pH meter and a platelet aggregometer. In addition, a Coulter ZF Counter is available in Dr Blagdon's laboratory.

Some environmental monitoring of the clean room suite is performed. Nutrient agar settle plates are produced in-house, batch records being maintained. Plates are pre-incubated for 24 hours at 37°C and 48 hours at room temperature before being exposed in the changing room, pooling room, LAF cabinets and "sterile room". Exposure is for 1 hour followed by incubation at 37°C (24 hours) and room temperature (48 hours). Incubation times are not accurately recorded with "on" and "off" times. Batches of plates are not fertility tested by challenge with control cultures but an unexposed control plate is exposed at the end of the incubation period. There is no continuous temperature monitoring of the incubator.

Action limits are defined as >1 cfu/hr/plate in a LAF cabinet and >5 cfu/hr/plate in a clean room. There is no defined action if these limits are exceeded and, to date, they have not been.

In addition to the settle plate monitoring, a Ryan Static Air Particle Counter and a Biotest Centrifugal sampler are borrowed from the Regional Pharmaceutical Quality Controller and used in the clean room suite, supposedly at 3 monthly intervals but in practice at approximately 5 monthly intervals. At 6 monthly intervals, the manufacturers check the LAF cabinets, including DOP testing.

There is no environmental monitoring of the closed-processing areas other than the monitoring of centrifuge buckets by Components staff, as described in the previous Inspection Report; there is no QA Department involvement in this procedure. The role of the QA Department has not yet expanded sufficiently to encompass temperature monitoring equipment (including transport) or autoclave control and validation.

The QA Manager checks the weekly virology results report sheets, identifies initial screen positive donations and fills out a proforma which is used to check that such samples have, in fact, been repeat tested and a conclusion reached. The Virology records are checked to ensure that all potentially infective material has in fact been removed to the Virology laboratory. The QA Manager also signs the Despatch Sheets for plasma going to BPL.

7. FUTURE PLANNED CHANGES/DEVELOPMENTS

A permanent Director is to be appointed. This is to be a University appointment as Professor of Transfusion Medicine in addition to being Director of the Transfusion Centre.

The Quality Assurance Department is to be expanded with the appointment of a Deputy Quality Assurance Manager and a Quality Control Officer.

8. MATTERS OF CONCERN

a) The role of the Quality Assurance Department needs rapid expansion to implement a full programme of QA, including quality monitoring of products.

b) The solution used for swabbing donors' arms at sessions is made up from bought-in materials (hibitane and 70% industrial methyl alcohol) which are not QC-checked or filtered prior to use; the made-up solutions are not allotted batch numbers or expiry dates and there is no microbiological validation of their effectiveness.

c) The high-low alarm on the Blood Components cold-room is not regularly checked and tested.

d) In the centrifuge room, windows to the outside are opened, allowing the ingress of dust and insects.

e) In the main processing laboratory, layers of dust were present on ledges, shelving and at the back of processing benches close to disaggregating platelet preparations.

f) Quarantine platelets are left overnight on the open bench of the processing laboratory. At the time of inspection, the temperature there had ranged from 19-28°C, against a recommended storage temperature of 22±2°C.

g) In the Blood Components area, Quarantine, Held and For Issue platelets are all held together in the same room.

h) The procedure for transferring platelet concentrates to stock for issue involves cumbersome manual checking and gives rise to the possibility of error. The sheet used in this procedure (the 'cross check sheet') is completed with a mixture of ticks, crosses and double ticks which are meaningless as a record.

i) The "Viro 1" form, listing potentially-infective donations which are to be withdrawn is occasionally left on the bench of the Grouping Laboratory, if no-one is available to receive it; this form should be personally handed-over and signed for.

j) The Quarantine Form used by Virology is in need of revision to remove redundant details.

k) There is no double-checking procedure to ensure that the correct total number of sample tubes is manually entered into the Tecan computer.

l) There is no inventory of the contents of the Virology quarantine freezer.

m) There is no procedure for informing other Departments when Virology lift the "hold" condition of products, other than a change of the computer status.

n) Occasionally, blood is removed from the Blood Bank (e.g. for laboratory use) without following the correct issuing procedure and without being issued through the computer, rendering the donation untraceable. All issues should be made through Blood Bank staff, using the computer.

o) There are no SOPs, even in draft form, available in the Blood Bank.

9. POST-INSPECTION SUMMARY

After the inspection, a discussion took place with Dr Blagdon, Dr Ouwehand, Dr Rankin, Mr Slopecki and Mr Fitton.

The Inspector acknowledged the greatly increased security brought about by the implementation of the computerisation programme and expressed the hope that the remaining small problems with the system would gradually be overcome.

The appointment of a Quality Assurance Manager was welcomed but the need to expand the Quality Assurance Department in order to achieve standards required for licensing was stressed.

The deficiencies noted above (Section 8) were listed and discussed.

10. CONCLUSIONS

1. Conditions and procedures have improved since the previous inspection, largely as a result of the introduction of a fully computerised system.

2. The lack of a full Quality Assurance and Quality Control programme means that the operation of the Centre is not yet of a standard that would be expected to meet a future licensing requirement.