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MEDICINES INSPECTORATE

INSPECTOR'S SUMMARY

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MB5B Report No. 1989 / 14-50

TITLE: Inspection of Northern Regional Blood Transfusion Centre, Holland Drive, Barrack Road, Newcastle upon Tyne NE2 4NQ

CO. TEL: 091 2611 711

DATE OF INSPECTION: 25-27 July 1989

INSPECTOR(S): M L Kavanagh

REGION/AREA (9.1) _ _
GMP ( ) _ _ HAZARD INTVL (12) _ _

CATEGORY (HP) _ _
NO. EMPLOYEES ( ) 220 COMPLEXITY add / delete _ _ _ _ _

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MISG	For routine distribution		Mr Green
	Dr H H Gunson ✓		Mrs Robinson
	Mr Barton		

DATE OF PREVIOUS INSPECTION: March 1987

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-inspection within 2 years.

COMPILED BY: GRO-C

M L KAVANAGH

DATE SIGNED: 6 November 1989

COUNTER SIGNATURE:
REGIONAL PMI

SMI GRO-C: Ayling 7/11/89

HEAD OF MEDICINES INSPECTORATE

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Northern Regional Blood Transfusion Centre
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1. INTRODUCTION

The Northern Regional Transfusion Centre is housed in a purpose-built building, opened in 1985, having previously been situated in the Institute of Pathology at Newcastle General Hospital.

The Centre serves a population of nearly 3.1 million over a wide geographical area, collecting around 120,000 donations annually and employing a staff of 220.

The Centre was last inspected in 1987.

2. SCOPE

The inspection covered the manufacture and control of the products listed in Section 5. Clinical matters, eg tissue typing and testing related to patients, were not included.

3. SENIOR STAFF LIST

Dr H Lloyd	:	Director/General Manager
Dr A Collins	:	Consultant Haenatologist
Mr S Smith	:	Donor Services Manager
Mrs A Dixon	:	Nursing Services Manager
Dr R Doughty	:	Laboratory Manager
Mr D Wightman	:	Assistant Laboratory Manager
Mr G Hedley	:	Head, Red Cell Testing Laboratory
Mr R Masterman	:	Head, Microbiology Testing
Mr G Davidson	:	Head, Reagent Production
Mr M Brittain	:	Head, Information Technology
Mr G Dinning	:	Head, Quality Assurance
Mrs C Mitchell	:	Head, Clerical Services
Mrs K Young	:	Head, Despatch Department
Mr E Hastie	:	Head, Components Production Section
Mrs A Hemsley	:	Head, Verification Section

4. CHANGES SINCE PREVIOUS INSPECTION

Dr H Lloyd has been appointed Director and General Manager, with effect from November 1988. (The previous Director was Dr A Collins.)

The functional organisation of the various laboratories and departments has been re-structured from 1 April 1989, the main changes being the co-ordination of all red cell testing (ante-natal and donor testing) into one department, making Component Production and Verification two sections of one department and the creation of three new departments, Quality Assurance, Information Technology and Clerical Services.

5. LIST OF MEDICINAL PRODUCTS

Product	Units Produced/Issued April 1988-March 1989
Whole blood	22600
Plasma-reduced blood	57776
SAG-M red cells	21361
Washed red cells	Figures not available
Platelet concentrates	28424
Fresh frozen plasma (FFP)(tonnes)	14.11
FFP for fractionation at BPL	64207
Single donor FFP	16852
Time-expired plasma (tonnes)	3.76
Cryoprecipitate	8601

6. INSPECTION

6.1 Blood Collection and Receipt

There is a plasmapheresis clinic in the Centre equipped with 8 Haemonetics machines, the donor panel currently numbering around 1000. However, apart from very occasional walk-ins, normal donations are not collected at the Centre and all normal donor sessions are mobile. A visit was made to a mobile session held in Whikham Community Association Hall.

Donor records are not computerised, the 101 Card System still being used. The cards for all called donors are brought to the session. At the clerking table, when a donor has completed the consent form, a set of 8 bar-code labels is issued, one label being stuck onto the Blood Donor Record Sheet (BDR) and another on the donor's record card. For known donors, pack group labels are also issued.

If a donor reports having had a recent illness or course of medication, brief notes of this are written onto a page of a duplicate notebook, alongside the donation number, and at the end of the session, this sheet, known as the "Illness Sheet", accompanies the blood to the Blood Components section, where it is used to identify unsuitable donations.

Haemoglobin testing is carried out using the copper sulphate method, the limits of acceptance being 125g/litre for females and 135g/litre for males. If a donor fails the test, no donation is taken and the MO takes a Venous sample for a full assay back at the Centre.

Accepted donors are led to a bleed-bed by a donor attendant. Meanwhile, packs and sample tubes are labelled up at a separate table before being taken over, together with the record card, to the donor where an identity check is carried out. At this stage, excess bar-code labels are clipped onto the donor's record card in case a spare is needed for a replacement sample tube; at the end of the donation, the spare unused labels are stuck onto a sheet of paper held on a central table.

Lignocaine is used routinely at donor sessions but the batch numbers are not recorded. The practice is to draw the lignocaine into a number of syringes held ready for use. At the time of inspection, on open vial of lignocaine was standing on the central table awaiting further use.

When a donation is completed and the bleed line has been sealed, the pack is taken to a separate table, where the driver strips and segments the line before placing the blood in a crate. (Sample tubes are racked at the central table). Blood is periodically removed to the van, usually when a crate is full, but at slow sessions this means that packs which should be refrigerated can stand in a warm room for a considerable time.

Blood (other than that to be used for platelet preparation) is transported in the refrigerated compartments of BTS vans. At present, the temperatures of these are not monitored with circular chart recorders but plans to fit them to all vehicles are well advanced. The current procedure involves the driver noting down the temperature from a dial readout on arrival back at the Centre. At the time of inspection, the van parked at the session did not have the refrigeration switched on, the practice being only to switch it on when blood was put into it.

6.2 Component Production

The Components Production area consists of three inter-connected rooms, one for blood reception and preparation for centrifugation, a middle centrifuge room and a room for processing. The area is equipped with 12 Hiraeus Christ Cryofuge 8000 pre-programmable centrifuges, 6 Beckmans (3 x J6B, 1 x J6-M and 2 x J6) and 1 sorvall RC3B.

Blood from sessions, unless it is to be used for platelets, is put into the reception fridge to await processing. The "Illness Sheet" accompanying the blood is used to identify any high risk donations, which are removed by components staff and put into cardboard boxes to await subsequent disposal. Packs that burst or are damaged are put into a bucket and lists of their numbers are kept on dog-eared sheets of paper in a clipboard. This information is later typed into the computer.

When products have been made, they are manually labelled with the appropriate product label on a small area of bench. Similar-looking products (concentrated red cells, SAG-M red cells and plasma-reduced blood) are often labelled together (with similar-looking labels). However, in addition to a visual check, the Components microcomputer has a checking function for the labels and so any mis-labelled packs are likely to be picked up.

All the products made from a session's donations are wanded into the components microcomputer which prints out a hard-copy Products List. This list is used to identify all products made from a donation should it be necessary to isolate them, for example if the donation has tested microbiologically positive. In such cases, Microbiology staff are responsible for collecting and removing all products.

Fresh frozen plasma is produced in 2 Cryoking Ultralow blast freezers. In the case of plasma for BPL, when it is frozen, the packs are wanded through the computer in boxes of 20, together with a batch number, and hard-copy print-outs are obtained. The boxes of plasma are then put into roller cages (each of which holds 24 boxes of 20 packs) and stored at - 40 ^{o}C until cleared for despatch.

If a donation tests microbiologically positive or equivocal, it used to be the practice for Microbiology to notify Components by means of a slip of paper of the numbers of the plasma packs concerned; components staff would wait until a roller cage was full before taking out the relevant packs (unless they had been cleared meantime). The procedure has now been changed so that such packs are now removed immediately, at the same time as the red cell components, and handed to Microbiology. (There was some confusion in the Components Production section about the implementation of this policy change).

The processing areas appeared generally clean and tidy but there are no written, scheduled cleaning procedures and any cleaning that is carried out is not recorded. Benches were said to be cleaned (with Protectos Bleach) "most days". No microbiological testing is performed to check the effectiveness (or otherwise) of the cleaning of benches and equipment. Although the windows to the outside were closed at the time of inspection, it was said to be necessary to open them sometimes when conditions in the area became too hot.

Open-processing, comprising the pooling of time-expired plasma and the washing of red cells, is carried out in what is known as the aseptic suite. No records were available for the preparation of washed red cells but the procedure was said to be performed about 4 times a year. The "aseptic suite" consists of an ante-room and a step-over changing room giving access to the processing room which contains 2 LAF cabinets. Flap-valves indicate the positive air pressure gradient going from the processing room through the change and ante-rooms to the corridor, but a bank of manometers in the ante-room is non-functional.

Conditions in the open-processing room were worse than in other areas of Components Production. Staff (and visitors) enter without any change of clothing or footwear. To carry out processing, staff wear their normal laboratory clothing with the addition of masks and non-sterile gloves. The floor of the clean room was dirty with dust and rubbish and the top of the Microflow LAF cabinet was covered with a layer of dust. The insides of the cabinets were dirty and there are no written, scheduled and recorded cleaning procedures.

6.3 Red Cell Testing

At present, donor grouping is performed on 2 Technicon Autogroupers. The donor samples are collected each morning from the fridge and the anticoagulated samples are centrifuged, put into numerical order and loaded onto the Autogrouper. The machine reads the bar-coded donation numbers on the tubes and groups the samples. If the machine laser fails to read any donation numbers, these are manually written onto the results print-out but the entries are not double-checked.

If the machine is unable to interpret a group, the sample is put through again. If the machine still cannot give a result then the sample is grouped manually. The Autogroupers provide results both as hard-copy, which is kept, and on disk. The results are compared against previous history (for known donors) by wanding the donation number and group labels put on the BDRs at the session.

The clotted samples from sessions are taken to the Manual Grouping laboratory, where 200 µl volumes are manually transferred into 3 Microtitre plates, 2 of which are for grouping and 1 is masterplate for Microbiology. There is no system of off-setting tubes as they have been sampled. Plates are identified by writing onto them the first and last donation numbers. "No sample" wells are marked with a ring.

Donor samples which are manually grouped are all those which do not have a group label on the BDR, ie mainly new donors but also "Walk-in" known donors. The tests are read in a Dynatech microplate reader; this does not give positive sample identification and much manual transcription is involved in linking donation numbers to a new set of consecutive numbers assigned by the Dynatech. If the plate-reader gives no result, then grouping is done manually in tubes and the result is written onto the results sheet. (New donors who cannot be grouped on the Autogrouper are manually grouped twice, once by microplate and once in tubes).

The manual grouping results sheets are taken to the Laboratory Office where one person from Red Cell Testing and one clerk go through the results and stick the appropriate bar-coded group labels on the BDR. Entries are double-checked using a call-back system. The manual grouping results are then entered into the disk by grouping staff and a person from the verification section. (Other information, eg discards, is also entered at this time). Access to the disk for editing data is checked against the BDRs.

Plans are well advanced to replace the system of manual pipetting of samples into Microlitre plates with a Kemble Kemtek 1000 and, in the longer term, to replace the Technicon Autogroupers with a Joyce-Loebal Image Analyser which will read microlitre plates. A new set of SOPs is being generated in the department but are not yet in use.

6.4 Microbiology

All samples are tested here for HBsAg (BPL R1A), HIV antibody (Wellozyme ELISA) and syphilis (VDRL). Microbiology staff takes a form (Laboratory Sheet) to the Laboratory Office and record the sessions, donation number sequences and total numbers of donors. The master Microlitre plates are collected from Red Cell Testing.

Subsampling from the master plate into plates for HBsAg and HIV antibody testing is done manually using a multichannel pipette. For HBsAg tests, the kit controls are included on every plate and the CPHL (Colindale) QC panel is put up daily.

In the case of HBsAg tests, equivocal results are first re-counted; if they are still over the cut-off, the plates are washed and again re-counted. If the result is still equivocal, the sample must be repeat-tested. However, as this cannot be done until the following day, the relevant products are put on hold. First, a duplicate copy of the Laboratory Sheet is marked with the repeat donation number and this is taken to the Laboratory Office, where a member of Microbiology staff marks the red record book to this effect. The BDRs are also marked as "Microbiology Repeats" against the relevant donation numbers.

Having obtained a list of the products made from the affected donation (from the Component Production product print-out) and written this onto the duplicate Laboratory Sheet, Microbiology staff collect the products and isolate them. Red cell products are put into a special "hold" crate. The Laboratory Sheet and the BDRs are marked to this effect.

If on repeat testing the donation is cleared, Microbiology staff go back and transfer the products from the microbiology hold crate to the ordinary hold (ie non-verified) crate, the BDRs being amended accordingly. In the case of repeat positives, all products are collected by Microbiology staff and removed to their department. The collection and disposal of products is badly recorded on the Laboratory Sheet, a tick indicating collection and "Destroyed" indicating disposal, but lacking dates and signatures. Similarly, the transcription of results onto the Laboratory Sheets is neither signed nor double-checked.

The system for holding and removing plasma is now similar to that for red cells in that Microbiology staff collect the packs immediately rather than waiting for a roller-cage to be filled (see Section 6.2). One problem with "holding" frozen plasma is that there is no quarantine freezer, only a fridge, with the result that the FFP is lost even if the donation is subsequently cleared. The records for plasma disposal are not satisfactory in that several entries record the collection of packs but not their disposal even though the packs could not be found.

The system for dealing with HIV antibody and VDRL equivocal results is slightly different in that a repeat test can be done on the same day as the initial test. Repeat positives are sent to the local PHLS for confirmatory testing.

The release of products is not on an assumed negative system, each individual donation number being stamped as microbiologically negative in the BDRs (although no-one signs as having done so). The remains of samples in the master Microtitre plates are being kept as retained samples, initially for 2 years. There is a set of SOPs available in the Microbiology Laboratory.

6.5 Verification

The Verification Section is responsible for checking that all blood and derived components have been correctly labelled and tested and are suitable for issue by the Despatch department. The first part of the process is to edit the data disk containing the raw data from the Autogroupers using the up-dated BDRs. (This includes the entry of Microbiology positives). Following this, the labelling is verified by wanding the donation numbers into the microcomputer and checking on the VDU that the information is correct; the labelling is then cleared by wanding the donation number together with a menu card of labels (eg 'Not for Transfusions', 'Hold', or the Group label). If there is an error it is highlighted on the screen and the process ceases. A note of each such event is made on a piece of scrap paper which is given to a senior member of staff to instigate on investigation.

Clearance of products for issue again makes use of the BDRs. All the products from a session are brought out of the fridge into the verification area and, from each pack, the donation number is wanded into the computer. The group is displayed and is checked against the BDR. At

the same time, a visual check is made to see that the product label conforms to the product that has been ticked on the BDR and that the donation has been cleared by Microbiology. Finally, wanding right across the pack donation number and group label clears the product for issue.

This system of verification is exceedingly manual; the computer checks only the group label on the pack, all other checks being visual. At the end of the process, the computer will list any packs which have not been verified and an investigation is made. (Common reasons include the accidental passing of a pack to the "cleared" side of the bench before it has been verified, or the pack being put into the wrong session crate in Reception fridge or the pack having burst in Components Production). Finally, when everything is resolved, the cleared packs are transferred to the Issue coldroom.

6.6 Despatch

Orders for blood and products are generally telephoned in to the Despatch department but there is also a "milk run" of set journies to a number of hospitals. Telephoned orders are first noted onto a piece of scrap paper and then transcribed onto an official order form. If the blood is available, the packs are collected from the Issue cold room and the order is put together. The donation numbers, destination, date, time and mode of delivery (eg collection) are all recorded manually, together with the signature of the entrant, in the Blood Issues Request/Despatch Book. There is a system of using different coloured ink for each type of product but this is not always adhered to.

Platelets, which are stored in a shaker/incubator, are issued in a similar way, using a Platelet Issue Request/Despatch Book. In addition, a separate list of platelet issues is maintained which gives a running stock figure.

When each Request/Despatch book is full, it is sent up to the Laboratory Records Office, where the despatch information is supposedly transferred to the BDRs, which form the main record of traceability of the fate of individual donations. However, the work of transferring information from the Despatch books to the BDRs is one month behind. In addition, insufficient information is put onto the BDRs; the only entry is the hospital initials scribbled beside each donation number. Dates of despatch are not entered and neither are Returns, nor discards. On some records which had been completed, there was no information at all against many packs, just blank spaces.

Returned packs (of which there are many) are logged into a Returns book, being entered manually, there being one sheet for each hospital. The sheets are sent to the Laboratory Records Office but the information is not transferred to the BDRs. As the entries in the Returns Book (and the Despatch books) are not in numerical order, the task of tracing the fate of an individual pack would be extremely laborious and, in some cases, impossible.

Within the next 2-3 months, it is hoped to introduce a measure of computerisation into the Despatch department. Basically, this will give a computer generated despatch note by wanding in the donation number, product code, group code and destination (from a menu card). By using passwords, the note will record who made the entry, together with the

date and time. It will not, however, form a computerised record of the fate of all packs. Returns will not be included and FFP for BPL will still be on its own separate system. While it will eliminate one possible source of transcription error (manually filling out the Despatch books), the main record will remain the manually completed BDRs.

6.7 Quality Assurance

The Quality Assurance department was established on 1 April 1989, headed by a MLSO3 who reports directly to Director/General Manager on QA matters. The other staff in the department are 2 x MLSO2, 3 x MLSO1 and 1 part-time clerical assistant. Prior to the establishment of the department there was no QA work done other than a small amount in Reagents Production.

A comprehensive programme of QA has now been drawn up and is in the process of implementation. The programme covers process monitoring, quality monitoring of products and documentation production and review and when fully implemented will cover all stages from blood collection through to Despatch and Returns.

QA of donor sessions at present is restricted to checking the specific gravity of the copper sulphate solutions used for haemoglobin estimations. There are plans to check all the session balances with standard weights on a regular basis but this is not yet being done. A study of the effectiveness of disinfecting donors' arms prior to venepuncture by using before and after swabs has been carried out in the plasmapheresis clinic. (The results indicate that disinfection is effective). A similar study has not been performed at mobile sessions.

The refrigerated compartments of transport vehicles are checked on a monthly basis using thermocouples. All vehicles are to be fitted with circular temperature recording charts which will be examined and signed by QA. Fridges and freezers in the Centre are also checked with thermocouples on a monthly basis but there is no system of regular checking and logging of temperatures of the equipment. Some are fitted with circular chart recorders, the records of which are inspected and retained but not by QA. Balances and centrifuges are checked monthly and records are maintained.

The only environmental monitoring at present carried out is in the "aseptic suite". The suite is checked for air velocity and particle counts three times a year by the Sub-Regional Pharmaceutical Quality Control Laboratory, who send a report to the Head of QA. The most recent report, dated April 1989, concluded that conditions in the LAF cabinets, with the room unmanned, conformed to Class I specifications. A fourth yearly check is performed by Micro Filtration systems who perform DOP tests and report to the Head of QA via the Sub-Regional Pharmaceutical QC laboratory.

In-house monitoring of the clean-room suite is limited to the twice-weekly laying of Tryptic Soya agar plates, one inside the LAF cabinet and one on the bench in the clean room. The plates are usually exposed when time-expired plasma pooling is in progress, the exposure time being 60 minutes. The exposed plates are sent back to the suppliers,

the Sub-Regional QC laboratory, for incubation and reporting. No action limits for contamination have been set. There is no other environmental monitoring of "aseptic suite" and none at all in other areas of Component Production.

A limited programme of product quality monitoring has been introduced using the specification contained in the draft document, "Guidelines For Regional Transfusion Centres Derived Blood Components", drawn up by the UKBTS/NIBSC Liaison Group.

Whole blood donations are check-weighed and pressure-tested on approximately 10 packs per session per day (roughly 10% of the total). Plasma weights and volumes are checked (FFP) and platelet counts and platelet viability tests are performed on out-dated platelet concentrates, in addition to checks of the pH, volume, leucocyte and erythrocyte counts.

FVIII:C assays are performed on all types of FFP using a Coagamate coagulometer and FVII, FIX and Fibrinogen levels are assayed in cryoprecipitate. The 16th British Standard (NIBSC) is used for FVIII:C assays and a "standard plasma" supplied by NIBSC is used to control FIX assays.

At present, there is no sterility testing of products but a programme is being drawn up which will cover sterility testing of FFP, (expired) whole blood, platelets and cryoprecipitate.

A monthly report of the quality monitoring results is drawn up and submitted to the Director/General Manager; copies may be circulated to the Laboratory Manager and the Head of Component Production and Verification. (This latter position is currently vacant). Selected parts of the report also go to other appropriate members of staff.

Documentation within the Centre is being reviewed. In particular, SOP production is being undertaken at present. The style of SOP is based on that developed at Glasgow and West of Scotland BTC and the target for full completion is December 1989. There is an SOP Review Committee comprising the Head of QA, the Laboratory Manager and the Health and Safety representative.

7. FUTURE PLANNED CHANGES/DEVELOPMENTS

Sample handling for donor grouping and microbiology testing is to be automated using Kemble Kemtech machines which give positive sample identification. In the longer term, the Technicon Autogroupers will be replaced by an image analysis machine for interpreting microplate grouping tests.

The manually produced despatch notes for red cell products are to be replaced by computer-generated records. The management of the Centre has expressed an interest in becoming a Self-Governing Trust.

8. MATTERS OF CONCERN

a. At donor sessions, the batch numbers of lignocaine used are not recorded; at the session visited, a vial of lignocaine intended for further use was left standing open on a table.

b. The procedure for holding blood at sessions and for delivery back to the Centre is in need of review; at the session visited, blood was being held in a warm room for long periods and the transport refrigerator was not switched on.

c. There are no written, scheduled cleaning procedures for the Components Production area and no records of cleaning are maintained.

d. Similar products (concentrated red cells, SAG-M red cells and plasma-reduced blood) are manually labelled together, using similar-looking labels, on a confined area of bench.

e. Procedures and conditions in the "aseptic suite" in general are unacceptable. In particular:

i. There is no defined entry/change procedure, with staff and visitors entering in normal clothing.

ii. There are no defined, scheduled and recorded cleaning procedures.

iii. The floor of the "clean room" is covered in dust and dirt, the insides of the LAF cabinets are dirty and there is a layer of dust on top of the cabinet.

iv. Staff performing open-processing only don masks and non-sterile gloves in addition to their normal laboratory clothing.

f. When an Autogrouper machine fails to automatically read a sample bar-code number, these numbers are manually written onto the results print-out but the transcription is not double-checked.

g. When samples are manually pipetted from tubes to Microtitre plates, there is no system of off-setting sampled tubes to minimise the risk of double-sampling the same tube.

h. Microbiology records are in need of revision. In particular, results entries onto Laboratory Sheets should be signed and checked and the system of recording the fate of removed packs is inadequate; a number of plasma packs, recorded as having been collected by Microbiology, were not recorded as having been discarded but could not be found.

i. There is no quarantine freezer for "held" plasma, with the result that subsequently cleared plasma packs must still be destroyed.

j. Records of product issue are of an unacceptable standard. The main records for tracing issued products, the BDRs, are one month out of date

and the fate of many packs is not recorded on the sheets. The dates of issue of products are not recorded and Returns are not entered. The system of record-keeping involves double and triple manual transcriptions.

k. There are no records of the preparation of washed red cells (an open process) or their issue.

9. POST-INSPECTION SUMMARY

After the inspection, a discussion took place, attended by Dr Lloyd, Dr Doughty, Mr Smith and Mrs Dixon. The inspector welcomed the much-needed establishment of a Quality Assurance department and commented favourably on both the size of the QA department and the planned programme of QA, which demonstrated a good understanding of what was required. However, the Inspector also expressed surprise at the lack of computerisation in the Centre and the high reliance on manual procedures.

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

10. CONCLUSIONS

1. The full effects of the recent reorganisation in the Centre have still to work through but the establishment of a well-staffed Quality Assurance department is a major improvement.

2. Correct clean-room procedures must be adopted if open-processing is to continue.

3. The Centre has very little in the way of computerised systems and is heavily dependent on manual record-keeping. Many of the records are inadequate.