DHSS — MEDICINES INSPECTORATE

Site: Protein Fractionation Centre
21 Ellens Glen Road, Edinburgh, EH17 7QT

COMMERCIAL IN CONFIDENCE

INSPECTOR'S SUMMARY

DRAFT

FILE REF: 285/IN/S/656/H	MB5B Report No. 1988 /
TITLE: Inspection of Protein Fractionation Centre, Edinburgh	CO. TEL: 031 - 664 2317
DATE OF INSPECTION: 31 May, 1,2 June 1988	INSPECTOR(S): M L Kavanagh K J Ayling (part-time)

REGION/AREA ( ) 9.2 CATEGORY ( ) HP add
GMP ( ) _ _ HAZARD INTVL ( )12 _ NO. EMPLOYEES (170) _130 COMPLEXITY delete _ _ _ _ _

COPIES TO:

MISG	For routine distribution		

DATE OF PREVIOUS INSPECTION: 6 April 1988

PURPOSE OF VISIT:

First formal inspection

LICENCES HELD OR APPLIED FOR:

See Section 1

LICENSING CHANGES: ACTUAL:

IMMINENT:

RECOMMENDATIONS/ACTION:

Copies of this report to be sent to PFC and SHHD for comment and proposed action.

COMPILED BY: M L Kavanagh	COUNTER SIGNATURE: REGIONAL PMI
	SMI
DATE SIGNED:	HEAD OF MEDICINES INSPECTORATE

147/MC

DRAFT

CONTENTS

DRAFT

Protein Fractionation Centre,
Ellen's Glen Road,
Edinburgh,
EH17 7QT

031-664 2317

1. INTRODUCTION

The Protein Fractionation Centre (PFC) is the manufacturing facility of the Scottish National Blood Transfusion Service (SNBTS) and shares a site on the Southern side of Edinburgh with the SNBTS headquarters. A range of human blood products (albumin solutions, clotting factors, immunoglobulins) is manufactured from plasma derived from voluntary blood donations collected by Regional Transfusion Centres. A small range of Crystalloid products (saline, water-for-injections, anticoagulant solutions) and laboratory reagents are also produced.

The existing building opened in 1975 and is currently fractionating around 80 tonnes of plasma per year, serving a population of about 7 million (Scotland and N. Ireland) and employing approximately 170 staff. Microbiology/Virology laboratories and a pilot plant were added in 1983.

The site does not have a manufacturing licence although PLs are held for all the aqueous crystalloid products and for intravenous Normal Immunoglobulin. Factor VIII Concentrate and Factor II, IX and X Concentrate were licensed but their PLs have expired. Albumin solutions have never been licensed. It is planned to submit PL applications for the clotting factor concentrates and albumin products within the next 12 months.

PFC has never previously been formally inspected although a number of informal visits have been made by the Inspectorate, the most recent being a one-day visit by K J Ayling and M L Kavanagh on 6 April 1988.

2. SCOPE

The inspection was concerned with the facilities and procedures for the manufacturing and control of human blood products. The manufacture of crystalloid products was not subjected to an in-depth inspection on this occasion.

3. PERSONNEL MET

Dr R J Perry	:	Director
Dr B Cuthbertson	:	Quality Assurance Manager
Mr A Dickson	:	Process Section Manager
Mr J Sinclair	:	Sterile Filling and Freeze-drying Section Manager
Mr R Howieson	:	Preparation and Finishing Section Manager
Mr R Robson	:	Chief Analyst (Microbiology)
Mr W McBay	:	Chief Analyst (Biochemistry)

All the above attend the Summary Session.

4. PRODUCTION, PROCEDURES, PREMISES AND EQUIPMENT

4.1 Plasma Receipt

Plasma receipt/indenting is currently being computerised but at the time of inspection a manual system was in operation. Plasma is collected from all the Regional Transfusion Centres except Edinburgh and Belfast in the PFC van. Edinburgh and Belfast Centres deliver in their own vans. Deliveries are from one Centre at a time, accompanied by a consignment note.

Plasma is delivered to the loading bay. The specification for Fresh Frozen Plasma (FFP) states that it should be transported at -40$^{+}_{-}$ 5°C. It is known that the PFC van does not achieve this so the circular temperature recording chart is not checked. (A new van is on order with a programmable recorder). The Edinburgh van has no recording of temperature and the Belfast van is not checked.

From the loading bay, plasma is transferred to the Plasma Reception Area, a 4°C cold room (Room G88). Plasma is weighed here and the numbers are checked off against the consignment note. The balance is not routinely checked. The information from the consignment note is then transcribed to a Plasma Traffic Sheet, which forms a stock record, groups of 4 Transfusion Centre boxes being assigned a PFC number.

In addition to serving as the Plasma Receipt Area, room G88 is also used for storing buffers and reagents for use in processing. Although these items were released for use, they did not carry "Released" QC stickers.

When it has been checked-in, plasma is put into a -40°C storage area. This room is totally inadequate, being far too small for the volume of plasma being stored. Reject/recall plasma is stored on an open shelf, which is not clearly marked, next to plasma for use, some of which is on the floor. The room is covered with "snow" and is so full that it is almost impossible to enter. Plasma is quarantined here for 3 weeks.

The temperature of the -40°C cold store is monitored on a screen in the control room and is also checked and logged daily by a member of the engineering staff. There is no SOP covering plasma receipt procedures.

4.2 Primary Processing

When plasma is requisitioned for a pool, it is removed from the -40°C store, deboxed and transferred to the Plasma Conditioning Unit, where its temperature is slowly raised to -16°C, prior to being transported into the Plasma Preparation Room in the Fractionation Area.

DRAFT

Personnel enter the Fractionation Area via a changing-room, where they don boiler suits and Wellington boots. There is no step-over and at the time of inspection the floor was very dirty. Although a Wallgate hand-washer is installed, there is no requirement for staff to wash their hands and the wearing of gloves is optional.

Plasma packs are opened using a band-saw, the single donor packs being sliced diagonally in two. They are then stripped and the plasma plugs are collected in a plastic bin for transfer to the crusher, from which it emerges as "snow" into the thawing vessel.

The plasma is thawed at the rate of 220-250 litres/hr and passes over a wier into a break tank where the ice is separated from the cryo-suspension, which is pumped directly into a Westfalia BKA25 centrifuge via autoclaved silicone tubing through a hole in the wall.

Cryoprecipitate supernatant (CPS) is collected in a mobile vessel. Masks and beard-covers are not worn by staff working over open vessels or handling pastes. Headcovers were not always being worn correctly, leaving much of the hair exposed.

During fractionation, paste is unloaded into unlabelled polythene bags and transferred to another room where it is weighed before being put into a second bag and a hand-written label is inserted between the two. Occasionally, two or more unlabelled bags of paste may be handled together in this area.

The weight of paste is marked on a bit of cardboard and handed into the control room, so that the Batch Record is filled in by someone else. The Batch Records do not record who does what, eg who weighs the paste.

CPS may be kept at 4°C for a maximum of 5 days, although it is usually processed the following day. After 5 days storage it has to be filtered through a 10" 3 um filter, a sample for bacteriology being taken before and after.

At the time of inspection, buffers with an expiry date of the previous day were in use in the process area, as the fresh buffers were too cold, having been stored in the fridge.

Pastes to be discarded are listed in a diary. When they have been disposed of, they are crossed off the list but such entries are not dated or signed and no record of such discards are entered into the Batch Records.

4.3 Intermediate and Final Processing

4.3.1 Albumin

This stage of the process starts with frozen Fraction IV_4 + V paste, which is stored at -40°C in the Product Cold Room. This cold room also holds Factor IX eluates and other intermediate pastes. Because of the shortage of space it is also being used to store some in-coming plasma. A crate of blood-bags containing haemolysed cells was lying on the floor and could not be identified.

The frozen paste is emptied into a mobile vessel and pyrogen-free water is added. The Batch Record for this step calls for 10 litres to be added per kg paste; in fact, the amount to be added is 2.2 litres per kg paste. Batch Records do not record calculations of the caprylic acid volume to be added or the pH titrations. Calculations are not checked.

The albumin solution is de-ethanolised and concentrated in 2 Alfa-Laval thin-layer vacuum distillation devices (Centritherms). These are maintained at ambient temperature but the solutions are maintained in the adjoining 4°C fractionation room and are piped through the wall. The Centritherm process takes approximately 4½ hours to complete.

The albumin solution is adjusted for concentration and Nacl is added, the batch number not being recorded in the Batch Records, prior to filtration through EKS filters and a Millipore 0.5 um CW03 depth filter. The solution is then held overnight at +4°C in a closed (but not sealed tank) before being finally sterile-filtered and filled.

4.3.2 Immunoglobulins

Fraction II is received in this Section as a solution, with a protein concentration of 50g/litre. For intra-muscular immunoglobulin, this is freeze-dried and the resultant powder is stored until required for final product manufacture. It is stored both in a dedicated fridge in a corridor and in the cold-room where albumin is filtered and stored.

For iv immunoglobulin, 3 batches of Fraction II solution (each batch consisting of 14 litres of 50g/litre solution) are combined for processing through to 1 batch of iv Ig.

During processing, a pH probe is used to measure the pH of the bulk iv Ig solution prior to the pH4/pepsin incubation step, which is virucidal. Subsequently, the same probe is re-introduced into the bulk for titrating it back up to pH 7.

The batch numbers of chemicals used are not recorded on Batch Records and at the time of inspection the Records were not being fully completed.

Anti-HBs immunoglobulin, prepared from accredited donors, is added to all other immunoglobulin preparations (at the rate of 1000iu per 8 litres of product for ivIg).

4.3.3 Factor IX

Factor IX is prepared from 300 litre volumes of CPS prepared the previous day. After filtration through a 3 um membrane filter, the solution is diluted with 100 litres of PFW and adjusted to pH 6.9. DEAE - cellulose (DE-52, Whatman) is added and mixed before being collected by centrifugation in a Rousselet Rapide basket centrifuge.

The DE-52 is then packed into a column and the absorbed Factor IX (and II and X) is eluted and collected into sterile bottles. (The bottles are autoclaved but only 4 in a crate of 10 carry autoclave tape). Between runs, the column is sanitised and stored in 1% NaOH. The DE-52 is recycled using the centrifuge but there is no SOP for this procedure.

When the Factor IX solution has been collected, the bottles are spun-frozen and stored at -40°C in the Product Cold Room pending QC results, when bottles are then selected for processing to final product.

4.3.4 Freeze-Drying

The Freeze-Drying area is equipped with 5 driers: 2 are steam-sterilizable (1 Edwards EK4 and 1 Usifroid SM600) and 1 Usifroid SM200 which can be sanitized with free steam. There are also 2 smaller Edwards machines which are not used for vial drying (one is used exclusively for drying bovine serum control reagent and the other for drying intermediate Fraction II for im Ig production).

ivIg is dried only in the steam-sterilizable driers, while FVIII and FIX preparations are also dried in the Usifroid SM200.

The freeze-drying area is situated a considerable distance from the sterile filling area, which necessitates transporting the filled vials through 'black' areas to the driers. This is done by placing the filled vials in lidded freeze-drying trays, heat-sealing them into sterile hazard bags and trolleying them round to the freeze-driers where staff in clean-room clothing open the bags and load the vials into the driers under a localised HEPA-filtered air supply. At the end of the cycle, the vials are removed, again heat-sealed into sterile bags and transferred to the nearby Dico oversealing machine which operates under a curtained HEPA - air supply.

ivIg bottles are oversealed manually and this is normally done in the curtained area in front of the freeze-driers under HEPA - air flow. At the time of inspection, ivIg bottles were being oversealed outside this area in the dirty general laboratory area.

4.3.5 Sterile Suite

The sterile suite is excessively large, consisting of an inspection area for crystalloids, a "sterile store" with a bank of autoclaves and a "high security" sterile filling area, all supplied with HEPA - filtered air.

Entry to the suite is via a changing-room and stepover wearing full clean-room clothing and washing hands with "Hibiscrub". Clothing is hired, cleaned and sterilised under contract with Micron-Clean.

Particle counting in the area is currently carried out using a portable Royco air sampler but a permanent system with 10 sampling points has been fitted and is under test. In the high-security unit near the filling area there is a blanked-off window to the outside which is flaking paint and which has a triple-stepped ledge at its base which is trapping dirt.

4.4 Preparation and Finishing

The work of this Section comprises (a) Inspection, Packaging and Despatch and (b) Technical Services. The latter includes the heat-treatment of clotting factor preparations, the pasteurisation of albumin solutions, the supply of sterile equipment and in-process solutions, the preparation of crystalloid products and validation. This span of work is unusual and is only practicable if there are nominated under-managers that are in practice supervised by the Section Manager.

4.4.1 Services/Preparation Area

There is a Services/Preparation area providing input of sterilised bottles, plugs, metal seals and clean equipment. Equipment utilised in this preparation area includes a Gilowy tunnel steriliser, two Pickstone Ovens, a smaller vial washing machine and other ancillary equipment.

In an adjacent room there are four Southrim autoclaves, ie two 30 cu.ft. porous load autoclaves and two 40 cu.ft. fluid sterilisers. There are in the same room two 60°C pasteurisatiron cabinets for stable Plasma Protein Solution (SPPS).

The preparation area itself which houses the Gilowy sterilising tunnel and other equipment is extremely congested but was reasonably tidy in view of this congestion. Part of the mechanics of the Gilowy tunnel requires a bottle to be placed off line. This is part of a "baffle" system requiring comparison of an outside bottle to the bottles being sterilised. A variety of bottles to be used in this comparison are kept outside the tunnel and these should be labelled.

The Pickstone ovens are used for the heat treatment ie viral inactivation, of blood factors in their final containers. At present, Factor VIII is treated at 75°C for 72 hours and Factor IX at 80°C for 72 hours. The ovens have two control sensors and a third recording sensor.

The preparation area for assembling clean components is of a good standard and operators were noticeably well dressed.

In the autoclave/pasteurisation area, packs of sterile test pieces are kept near to the autoclaves. These should be stored securely in a locked cabinet.

The two 60°C pasteurisers were designed locally. Deionised pyrogen free water is sprayed onto the SPPS and each of six shelves has a bottle probe to record temperature. Product leaving the pasteuriser is not stamped or labelled to indicate this stage.

4.4.2 Storage Areas

Stored bottles of SPPS do not have any marking such as ink jet labels to identify them.

After pasteurisation SPPS enters a bonded cage which goes into a 30°C hot room. This store also has various other items congesting it.

A stage has been introduced into the process with SPPS whereby bottles are inverted. This was said to ensure that any contamination residing in bungs would be washed into the solution.

Material was also stored in an adjacent corridor.

There is an engineering-come general store ie "General Store G64". Plasma Protein Solution is stored here which gives further incubation time. The room is totally congested and not suitable for product to be stored.

Boxes of stoppers were crammed under the metal stairs.

Further product is stored in the basement. At the entry to the basement, a bottle of sterile distilled water was on a ledge.

In the basement store reject material, some of which is for reworking, was not securely locked away. One unlabelled reject was on top of a cage.

These so called holding areas for product are interspaced wherever space allows. Water for Injections and Plasma Protein Solution are stored here.

4.4.3 Distilled Water Production

There are two Schott glass stills producing 50L per hour each. These are fed with pyrogen-free deionised water and there is an 80°C recirculation loop for the distilled water. The temperature of the water as it re-enters the storage tank is not known. Production if DI water encompasses the following -

softening
40 micron filter
Reverse Osmosis
Deioniser (mixed bed)

Microbiological and chemical checks are performed daily. Regeneration is decided by conductivity and, surprisingly, can last for five months.

4.4.4 Crystalloid Filling

This area was not functioning at the time of the visit.

There appears to be sufficient space and acceptable conditions for the operations carried out. The sterile areas were in acceptable condition.

A detailed review of this area should be carried out at the next visit, but major problems are not anticipated.

4.4.5 Validation

In-depth validation studies have been performed for autoclaves, ovens and pasteurisation equipment but a defined agreed schedule for such work is necessary. The high priority for ensuring that any equipment used for sterilising and pasteurising/heat treating is obvious, particularly with possible viral problems associated with blood products.

Viral inactivation of Factor VIII at 80°C is being investigated. The validation of the cycle presently used was conducted using a 12 probe recorder, with thermocouples inserted in reject product.

Virucidal efficacy trials of the process using spiked samples are being conducted by QC.

The modern autoclaves have a 'Duplex' control system and incorporate microprocessor "Dataclave" controls.

Simple tests such as Bowie-Dick and a manual leak test are performed as necessary.

Standard CSA log sheets are used to record daily and weekly autoclave steriliser tests but there is no SOP defining what should be routinely done. There is also no SOP defining what routine maintenance should be done but it does appear that HTM 10 is complied with.

Validation of the 60°C pasteurisers should be performed at three monthly intervals, using a 12 point recorder for each pasteuriser, and a second check with 6 points per pasteuriser.

This target is not in practice achieved.

4.4.6 Inspection

When the QC tests of finished product are satisfactorily completed, the Quality Assurance Manager authorizes inspection by signing an authorization sheet in the Batch Record.

The Inspection Room is equipped with Seidenader semi-automatic inspection machines which provide illumination both from behind and below (Tyndall effect). Even freeze-dried products are run through the machine as foreign bodies can often be detected using the Tyndall effect.

DRAFT

Bottles of SPPS cannot yet be ink-jet coded on the overseals so inspection staff are handling un-labelled bottles. Rejects are labelled "Not for Clinical Use".

Training of inspection staff is "on the job" and there is no SOP. A "suggested method" was stuck on the wall.

4.4.7 Packing

Packaging materials are stored off-site in the Dry Goods Store, operated by ANC (Scotland) Ltd in Newbridge, about 12 miles away. (Reject material is also stored there pending re-processing). Small consignments (eg vials) are received at PFC and held on the loading bay until QC have sampled and approved them, when they are sent to ANC. Large consignments go direct to ANC and are sampled there by QC. "Approved for Use" stickers are applied to approved materials.

All labels are held-on-site in a locked store, with 3 people normally authorized to draw labels. QC staff are not involved in the approval of labels, this being done by Inspection and Packing staff.

Although there is 100% reconciliation of bottles and vials after labelling and packing, label reconciliation is not performed. There is no record kept of the numbers of labels drawn, used or left over and no record of line-clearance, even though some products (eg im immunoglobulins) have very similar labels.

All final products are stored on-site, either in the 4°C store in the Labelling/Packing area or in the ambient warehouse. This is a pre-fabricated building, erected about $2^{1}/2$ years ago and in addition to finished goods it also holds a working stock of dry goods (vials etc). At the time of inspection a stock of 46.7% tri-sodium citrate anticoagulent was found to have passed its expiry date.

5. QUALITY ASSURANCE

The QA department consists of coagulation, chemistry, biochemistry, bacteriology and virology laboratories. No animal testing is done on site, samples being sent to either Law Hospital, Carluke (pyrogen testing) on the Institute of Occupational Medicine at Edinburgh University (toxicity testing).

The QA manager is responsible for finally vetting and authorizing SOPs after they have been prepared and circulated by an internal committee. He also reviews all Batch Records and authorizes the release of product to inspection and packing.

5.1 Chemistry and Biochemistry

The chemistry laboratory performs non-protein chemistry on, eg, water, crystalloids and in-process buffers and performs the QC of in-coming raw materials. The biochemistry laboratory performs protein chemistry (total protein assays, GLC, atomic absorption, gels, columns, HPLC).

DRAFT

Samples are left by production staff on the top of a cupboard, usually but not always accompanied by a request sheet. There is no sample-signing in procedure and no receipt given. A member of the laboratory staff picks up the samples and enters them into a loose-leaf sample record book. Samples are recorded as "date in" and "date completed" but entries are not signed or initialled.

Test results are entered on a work sheet and are checked by the Section Controller. At the time of inspection a set of results was noted which had been reported but not signed as having been checked.

Protein assays on albumin solutions are currently performed by the Biuret technique but it is planned to switch to the micro-Kjeldahl method to conform to Pharmacopoeial requirements.

5.2 Coagulation

The coagulation laboratory is equipped with 4 Organon Teknika Coag-a-Mate machines which are calibrated every 2 weeks. 2-stage assays are performed on final products but 1-stage assays are used on in-process samples. The substrate is monoclonal antibody-depleted plasma.

At the time of inspection, the results sheet for coagulation assays was not being correctly entered, lacking dates, headings and signatures. Standard concentrations were hand-written on pieces of card, pinned to the shelf.

5.3 Virology

The virology laboratory performs HBsAg and HIV antibody assays on all plasma pools and final products, using Abbot RIA kits. All batches of finished product are also tested for HBsAg at Edinburgh Royal Infirmary. If the results are discrepant, samples are sent to Dr R S Tedder at the Middlesex Hospital Medical School.

At present, plasma pool samples are not retained but it is planned to do so.

5.4 Bacteriology

The bacteriology laboratory is responsible for environmental monitoring, in-process bacteriological monitoring, sterility testing, LAL testing, DOP testing and broth fills.

Clotting Factor products (FVIII and FIX) are sterility-tested by direct innoculation, all other products by membrane filtration. Testing is performed under LAF in a protected area. The number of sterility test repeats was approximately 2% in 1987 and is currently 1.1% (1988).

The broth used is made from Gibco powder and is given a PFC batch number; this, however, is not related to the Gibco batch number. The broth is tested for sterility and for growth with C.albicans, S.aureus, B.subtilis and C.Sporogenes. No SOP was available for this procedure.

Not true

6. FUTURE PLANNED CHANGES/DEVELOPMENTS

A production Manager, reporting to the Director, is to be appointed. The Quality Assurance staff structure is also under review, with proposals to appoint a Quality Surveillance Manager and a Product Registration Officer, both reporting to the Quality Assurance Manager.

A computerised system of plasma despatch and receipt, involving both the Regional Transfusion Centres and PFC, is being set up.

In the albumin production process, Fraction IV_4 + V solution is to be ultrafiltered in place of the current procedure of thin-layer vacuum distillation ("Centritherming").

In phase III/IV of the development plan, the premises are to be extended, enabling the freeze-drying area to be moved such that there will be direct access to the re-located sterile suite. At the same time, it is planned to replace the existing Usifroid SM200 drier with a steam-sterilizable model.

7. MATTERS OF CONCERN

a. There is a need to re-evaluate the staff structure and workload. In particular, the position of Production Manager should be filled and the Workload of the Preparation and Finishing Section seems excessive.

b. Storage areas in general are patently insufficient. In particular (i) the -40°C storage capacity for plasma is totally inadequate, leading to overcrowding and to the practice of storing some in-coming plasma in the Product Cold Room; (ii) Storage of albumin products following the 30°C incubation is in random areas which are totally unacceptable and not controllable, eg in the engineering store G64 and the basement area; (iii) packaging materials, "dry goods" and reject material awaiting re-processing are stored off-site in a contract store some 12 miles away.

c. SOPs do not exist for much of the work to be performed. Also, Batch Records need revising as they often lack records of all that is needed (eg batch numbers of chemicals) and at least one also contains incorrect instructional information.

d. Batch Records are frequently filled in restrospectively from notes written in a diary or notebook.

e. In the -40°C plasma cold room, reject and recall plasma is stored on open shelves, not clearly marked, next to plasma for use, some of which is stored on the floor.

f. In the -40°C Product Cold Room, a crate of unidentified blood bags containing haemolysed cells was on the floor.

g. Although the specification for the transport of FFP is $-40° \pm 5°C$, this is not checked and not complied with.

h. In-process buffers and reagents do not carry "Authorized for Use" stickers.

i. Balances are not regularly and routinely checked.

j. The changing area for entry into the Fractionation Area is inadequate, lacking a step-over and defined procedures. Although a Wallgate hand-washing unit is provided, its use is optional, as is the wearing of gloves.

k. Masks and beard-covers are not worn in the Fractionation Area, even when working over open vessels or paste. Some staff wear their headcovers incorrectly.

l. Paste is unloaded into unlabelled bags and transported and weighed, giving the possibility of a mix-up.

m. Out-of-date buffers were in use in the Fractionation Area.

n. Pastes for discard are listed in a diary. There is no system of signing and dating to confirm they have been discarded, nor is there an entry in the Batch Records.

o. ivIg was being over-sealed in a dirty, open area, not under LAF.

p. The same pH probe is inserted into bulk ivIg solution both before and after the virucidal pH4/pepsin incubation, giving rise to the possibility of re-contamination.

q. In the high-security sterile filling area there is a triple-level ledge which is a dirt trap in the vicinity of the filling machine.

r. Bottles of SPPS do not carry in-house labels or ink-jet codes when they are inspected.

s. Label reconciliation does not occur, no record being kept of the numbers of labels drawn, used and left-over. Line clearance is not recorded.

t. Validation is not carried out against a planned, agreed programme. In some cases, proposed re-validation of autoclaves, pasteurisation and dry heat treatment of Factor VIII is not performed to schedule.

u. Work-in-process should be more fully labelled. In particular, cage labels should indicate when pasteurisation or heat-treatment has been performed.

v. Test pieces used in the autoclave area should be locked away when not being used.

w. A pack of sterile, distilled water was found at the entrance to the basement.

x. Not all reject material is securely stored.

y. The sample receipt procedure in the QA department needs review and completed reports should be signed and dated.

8. POST-INSPECTION SUMMARY

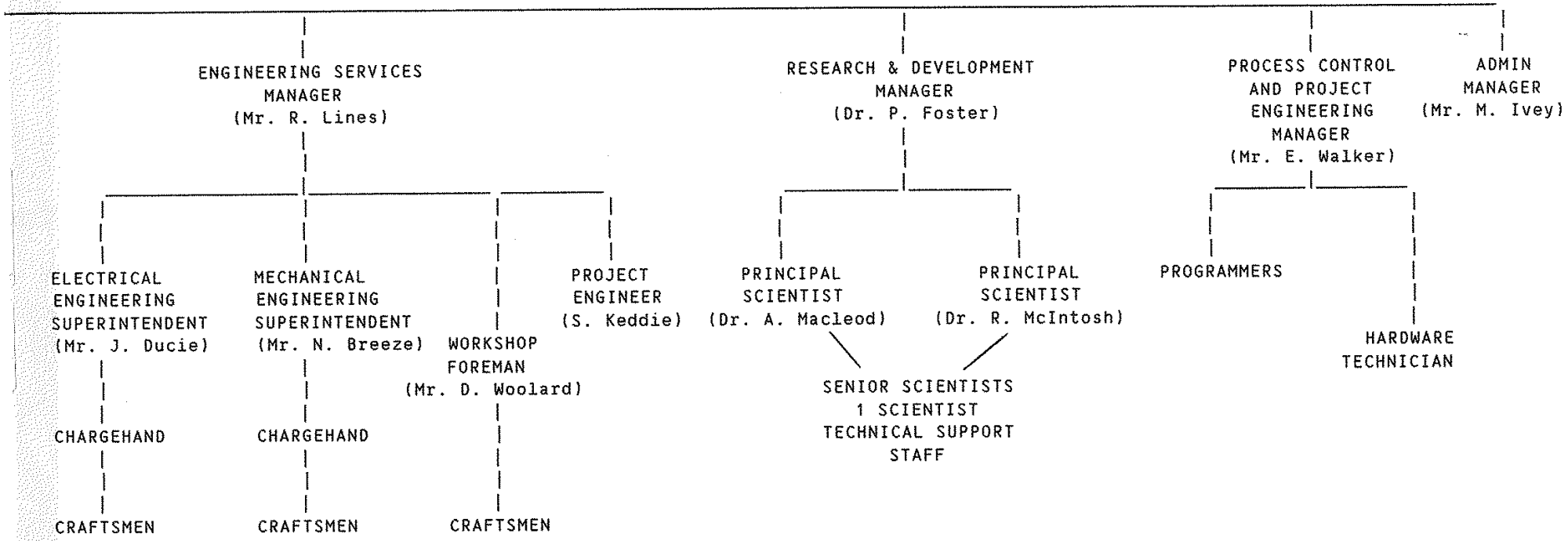
After the inspection, a discussion took place with the staff listed in section 3, above, and the deficiencies noted above (section 8) were listed. The possibility of a future application for a Manufacturer's Licence was discussed and the inspectors indicated that such an application could not be supported on the basis of the present situation.

9. CONCLUSIONS

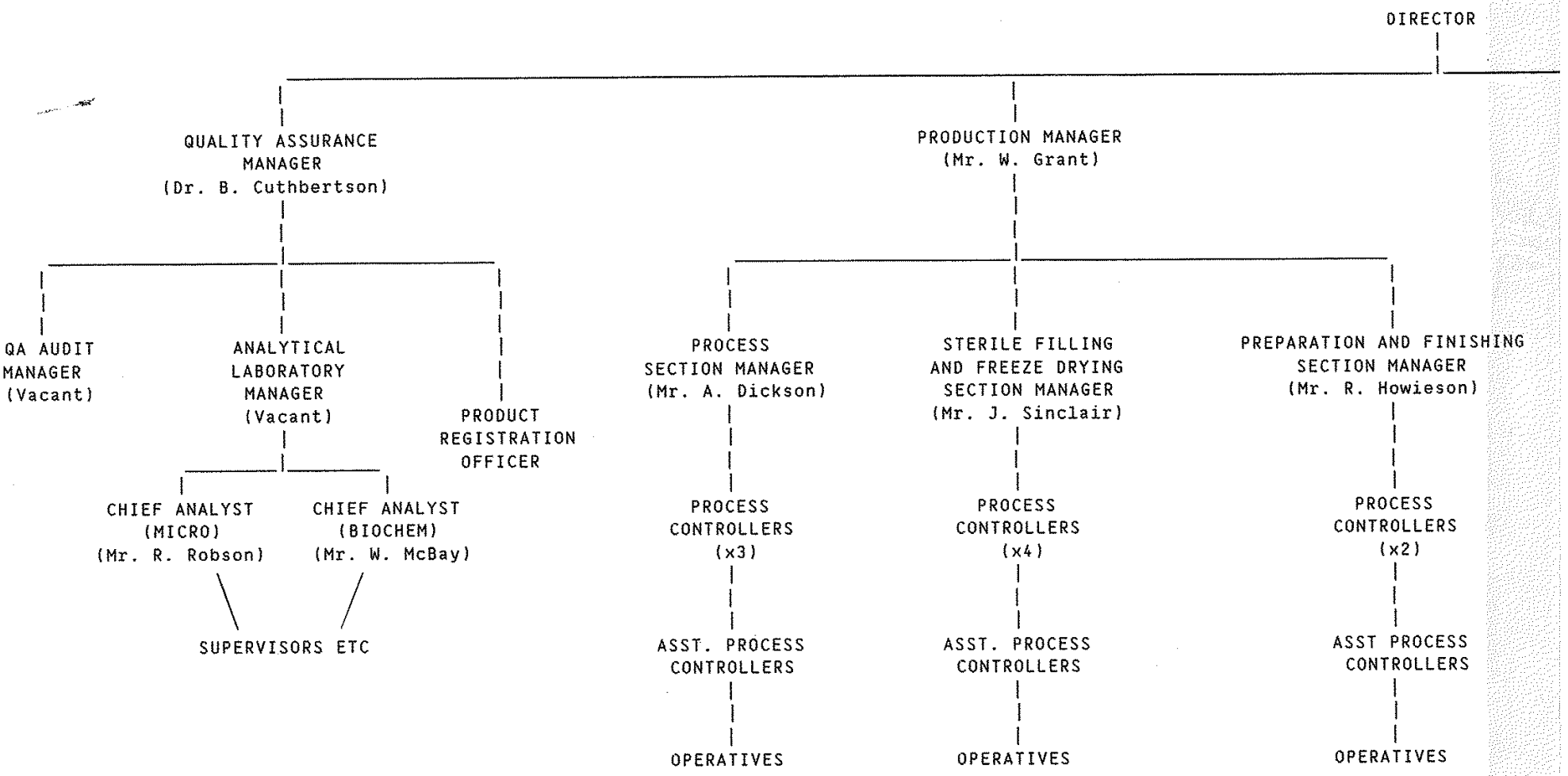
(i) Although the general standards of the staff seen were high, the staff structure and organisation needs to be re-evaluated. In particular, the position of Production Manager, which it is hoped to fill shortly, is an extremely important post for the management of PFC. Also, the work-load of the Preparation and Finishing Section Manager requires re-assessment. If he is to continue with this wide range of responsibilities, he will require adequate supporting staff for the separate aspects of production and validation.

(ii) Documentation in general is in need of review. In particular, a full set of SOPs needs to be provided and Batch Records need to be revised and up-dated.

(iii) Plans to expand the factory premises should be expedited as the present situation is unacceptable. In particular, storage areas are totally inadequate, both at -40°C and for incubating and quarantined albumin solutions. Until these problems have been addressed, an application for a Manufacturer's Licence could not be supported.


ENGINEERING SERVICES MANAGER (Mr. R. Lines)
RESEARCH & DEVELOPMENT MANAGER (Dr. P. Foster)
PROCESS CONTROL AND PROJECT ENGINEERING MANAGER (Mr. E. Walker)
ADMIN MANAGER (Mr. M. Ivey)
ELECTRICAL ENGINEERING SUPERINTENDENT (Mr. J. Ducie)
MECHANICAL ENGINEERING SUPERINTENDENT (Mr. N. Breeze)
WORKSHOP FOREMAN (Mr. D. Woolard)
PROJECT ENGINEER (S. Keddie)
PRINCIPAL SCIENTIST (Dr. A. Macleod)
PRINCIPAL SCIENTIST (Dr. R. McIntosh)
PROGRAMMERS
HARDWARE TECHNICIAN
CHARGEHAND
CHARGEHAND
CRAFTSMEN
CRAFTSMEN
CRAFTSMEN
SENIOR SCIENTISTS
1 SCIENTIST
TECHNICAL SUPPORT STAFF

SNB.008.8807


DIRECTOR
QUALITY ASSURANCE MANAGER (Dr. B. Cuthbertson)
PRODUCTION MANAGER (Mr. W. Grant)
QA AUDIT MANAGER (Vacant)
ANALYTICAL LABORATORY MANAGER (Vacant)
PRODUCT REGISTRATION OFFICER
CHIEF ANALYST (MICRO) (Mr. R. Robson)
CHIEF ANALYST (BIOCHEM) (Mr. W. McBay)
SUPERVISORS ETC
PROCESS SECTION MANAGER (Mr. A. Dickson)
STERILE FILLING AND FREEZE DRYING SECTION MANAGER (Mr. J. Sinclair)
PREPARATION AND FINISHING SECTION MANAGER (Mr. R. Howieson)
PROCESS CONTROLLERS (x3)
PROCESS CONTROLLERS (x4)
PROCESS CONTROLLERS (x2)
ASST. PROCESS CONTROLLERS
ASST. PROCESS CONTROLLERS
ASST PROCESS CONTROLLERS
OPERATIVES
OPERATIVES
OPERATIVES

SNB.008.8808