MEDICINES INSPECTORATE REPORT ON THE CURRENT STATUS AT THE PROTEIN FRACTIONATION CENTRE, EDINBURGH AS OF OCTOBER 1 1981

D HAYTHORNTHWAITE

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1. Introduction and Background

Following the response of The Protein Fractionation Centre (PFC) to the inspection of Messrs Flint and Purves a series of visits for discussions at PFC has taken place to progress matters. These were held on the following dates:-

11th and 15 June 1981 - D Haythornthwaite
30th September-1st October - K J Ayling and D Haythornthwaite

The discussions were principally with

Mr J Watt - Scientific Director
Dr R Perry - Quality Controller

During the visit of 11th June the DRG Flexpack process was examined, since a product licence for this has been issued recently. A separate draft report on this was issued to SNHD.

Detailed comments have been received upon the draft, and the Medicines Inspectorate response to this is therefore included in this report.

2. General Comments

With the appointment of Dr Perry as Quality Controller, progress towards a fully integrated Quality Assurance system as would be expected of an equivalent industrial company has been progressed rapidly bearing in mind the resources available.

Detailed comments are therefore not offered at this stage regarding Quality Control, general documentation, and standard operating procedures, with the exception of sections 3.7 and 3.8 of this report.

Routine visits in the future will review progress of these aspects and an in-depth inspection in approximately three months will be scheduled to cover these aspects and offer any necessary advise and recommendations as is normal M.I practice.

Areas where progress towards acceptable levels of GMP are still not adequate are as follows.

1. Inadequate space in some production and storage areas

2. Unsatisfactory processing conditions

3. Poor surface finishes

4. Unsatisfactory work flow patterns, which could lead to product mix-up

5. Unacceptable staff movements through production areas, which could lead to contamination of components and product

It is stressed that the comments in this report are made regarding the present level of output, and the present facilities.

Where alterations of the facilities have been positively scheduled then account of these is taken.

For ease of reference the section numbers used in the PFC "Response To Medicines Inspectors' Report 1980" are used where necessary. The specific references are found in book I, pages 19-69.

3. Specific Comments on Premises and Facilities

3.1. Storage Areas (ref 3.16.4; 3.29.9 of PFC Response). There is insufficient cold storage on site and plasma is stored in contract cold storage facilities. It is understood that locked tamper proof cages are being purchased to store plasma.

Such contract facilities are difficult to control and should not be longterm.

On site stores are generally unacceptably overcrowded and congested.

The cold rooms suffer badly from a surfeit of "snow" produced by the refrigeration system which covers shelves and products. This problem is worst in cold stores G87 and G86.

3.2 Processing Areas

Processing areas should in general conform to the WHO Guidelines (1978) or where appropriate to the Guide to Good Pharmaceutical Manufacturing Practice (1978).

Air filters should normally be terminal, ie immediately prior to the air entry to the room. Where design restrictions make this impractical then the filters should be as near to the room inlet as possible.

3.2.1 Plasma Processing Areas (G89/G92) (ref 3.1 of PFC response)

A great deal of traffic proceeds through these areas, but with present work patterns this is inevitable. Plans to alleviate this were discussed. Some rebuilding is necessary

Greater assurance would be obtained by converting the plasma pooling process into a more closed system (plans to provide a cleaner method of stripping of plastic, pooling and crushing of plasma have been discussed).

3.3 Preparatory Area (G66/G68) (ref 3.20 of PFC response)

Critical handling points should meet BS 5295 class 2 conditions. A general air supply of HEPA (0.5 micron) filtered air is recommended, and provision of air locks and changing facilities.

Staff are not wearing hats necessary in order to avoid the shedding of particles onto components and equipment.

The area is used as a general throughfare by staff not working in this area. A satisfactory area cannot be maintained under these conditions.

3.4 Solution Preparation and Filling Area (G67)

The proposed equipment layout (drawing 169) as detailed in the PFC Responce to the Draft Report of 11 and 16 June is acceptable.

The surface finishes of the walls and the crevice between wall and ceilings is still not acceptable.

3.5 Clean Room G104 (Preparation for Aseptic Area G77) (ref 3.8 of PFC response)

Critical handling points is this area should meet BS 5295 Class 2. The installation of HEPA filters (0.5 micron) is recommended for this area.

Air locks and changing facilities should be provided.

3.6 Freeze Drying Areas (G83/G94) (ref 3.10 of PFC response)

Installation of a LAF module over the entrance to the freeze dryers is scheduled for early completion. This is considered to be an interim solution and will be reviewed once it has been installed.

3.7 Inspection and Labelling Area (G98/G96) (ref 3.17 of PFC response)

The labelling area (G98) and the corridor outside is chronically overcrowded, and product flow is not easily controlled.

As a matter of urgency, the use of roll fed labels should be instituted to immediately alleviate the risk of mix up of labels and/or product.

3.8 Label Stores and Bag Printing (G63)

The storage area required for "cut" labels in this small room means that the space available for printing of PVC bags for large volume parenteral (LVP) solutions is very restricted.

Old printed PVC bags were on a shelf near to the printing equipment. This is a serious breach of GMP and a check list for change over of products and batches should be instituted immediately.

With the very cramped conditions provided, the implementation of upgrading of room G67 to accommodate bag printing must be a priority (see 3.4).

3.9 Autoclaves

These have now been brought up to a better standard by PFC but replacements should be planned for the early 1980's to ensure greater reliability and safety.

4 Conclusions

4.1 Progress towards implementing necessary standards of GMP in general Quality Assurance matters including provision of standard process documents and standard operation procedures is generally acceptable.

A major effort regarding these aspects is now coming to fruition

Two major exceptions to this were noted.

(i) 3.7 of this report. Labelling room G96.
(ii) 3.8 " " Old PVC bags left in Bag printing/store room G63. Lack of SOP to cover this aspect

4.2 Firm proposals to remedy those deficiencies regarding buildings and facilities as reported in the first inspection are still awaited, with dates of implementation.

These deficiencies are as defined in section 3 of the report.

4.3 The present buildings and facilities continue to fail to reach minimum standards of GMP, and a licence would not be recommended for an industrial equivalent unless agreed upgradings were instituted as a matter of urgency

Possible satisfactory alterations to the buildings and facilities have been discussed, on site, but provision of detailed plans by you is still awaited.

4.4 The use of a closed system for plasma stripping, pooling and crushing would substantially upgrade this part of the operation and lead to clearer starting material for extraction of coagulation factors and fractionation products.

4.5 Staff responsibility regarding autoclave validation and control is unusual in that the Section Manager is very actively involved. The total assurance given by his involvement with the Engineering Department does however provide a high general overall standard in this field, and is therefore quite acceptable.

5. Recommendations

The report should be forwarded to the appropriate Authority for remedial action as a matter of urgency.

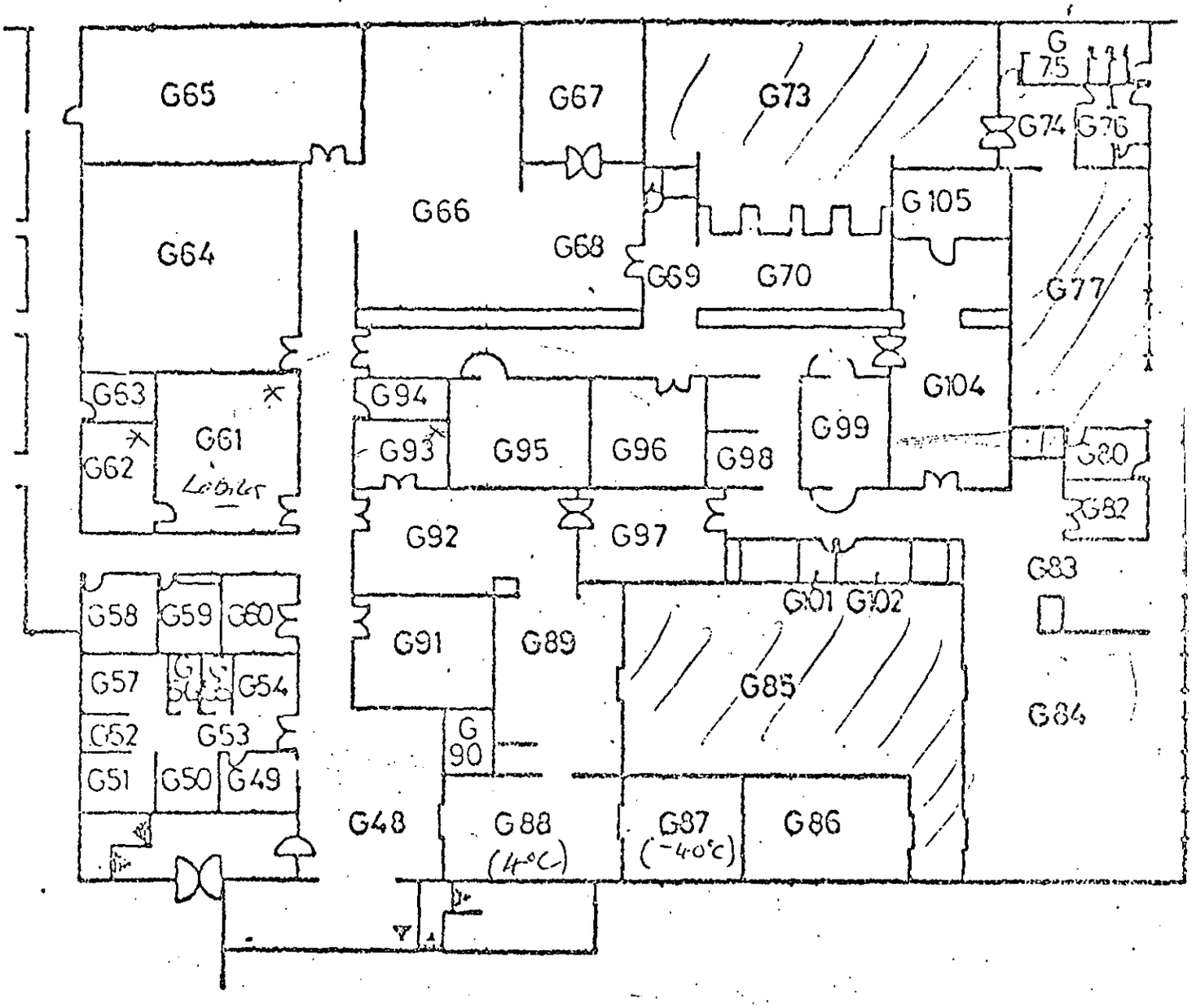
Where complete solutions to the deficiencies are not immediately available, then the interim proposals should be specified, and a timetable provided for implementation.

The Medicines Inspectorate is prepared to discuss on site or at SHHD any draft proposals so that unnecessary delays are avoided.

D HAYTHORNTHWAITE
K J AYLING

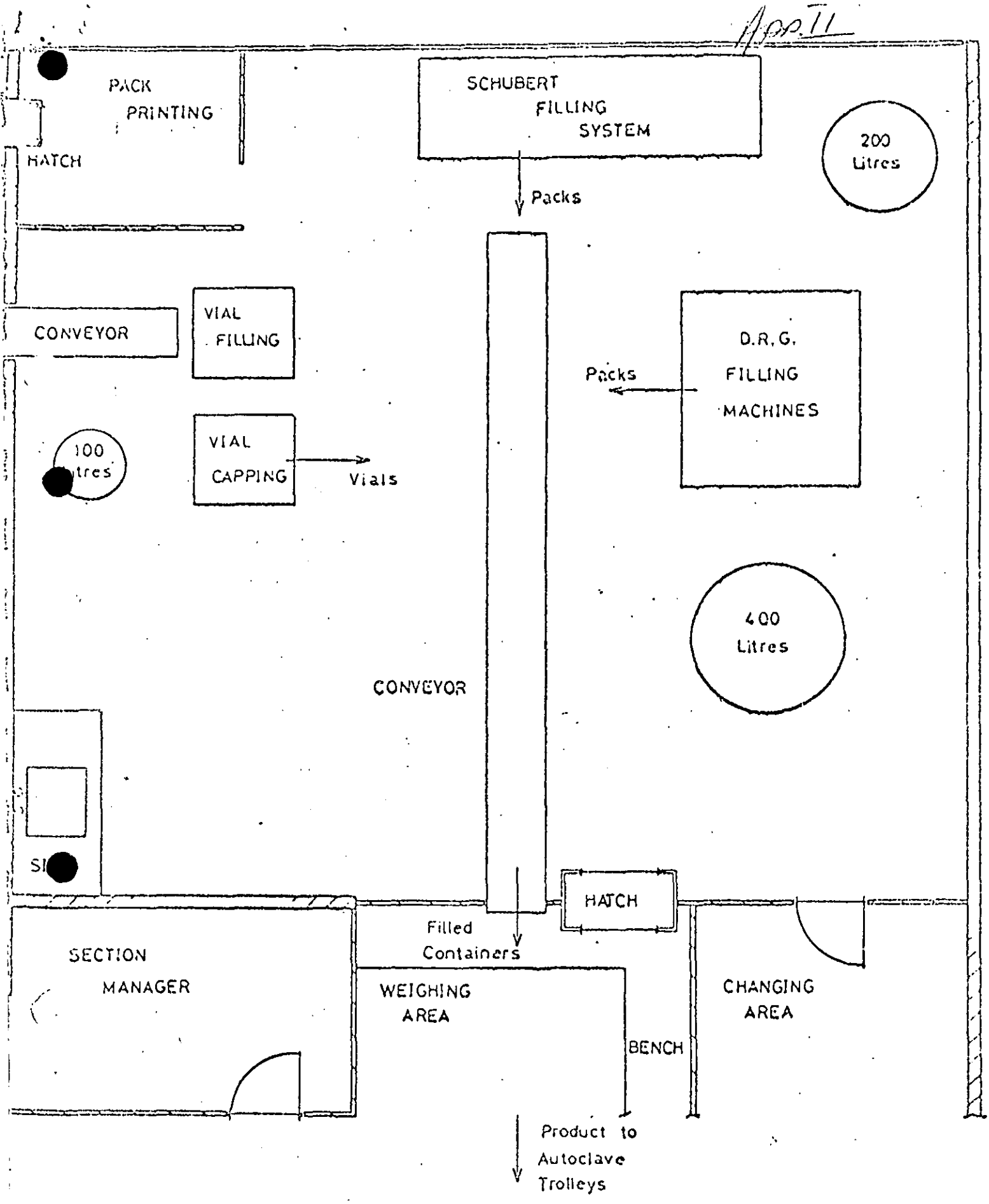
26 Oct 1981

refs K J A - 121081 (D1)
- 201081 (D2)
261081 (DF)



PRODUCTION BUILDING – GROUND FLOOR PLAN

App II



Original Date 2-9-81 Drawn SK				Protein Fractionation Centre EDINBURGH
Date	REVISIONS	Date	Name	
SCALE NTS	Title PREP FILLING AREA (G.67) –			Drg. N° 169