Introduction to Medicines' Division Inspectorate
Visit to Impact BPL April 1979

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The Director made the following observations to the Inspectorate to assist them interpret findings during inspection of BPL in the current context of the Stop Gap programme and to enable practical advice and recommendations to be made which related to the short term. The main objective was to assess the processes, materials and products with the objective of making major contributions to building and plant design in any future redevelopment.

It was pointed out that the historical background of BPL within NBTS was extremely relevant to the present position. The laboratories comprising the NBTS had spent the past three decades mainly concerned with collection, preservation and fractionation of whole blood. These pursuits were entirely protected against any form of commercial competition and hence as a result, the service had not been exposed to the necessary essential considerations which maintain viability in production industries eg. costing of end product, overall accountability, ongoing comparison of budgetary needs versus growth of product, forward planning and capital investment. In fact, there was relative unawareness that the transfusion service paralleled the prot.

19/225

Sterile filled products

Manufacturing — no packaging or labelling w. little or laboratory side

↙

Microbiol.
Sterility pyrogen bacterial
Documentation & use of
pyrogen testing etc.

Submit interim report.

Further 3 days in July.

Duration of upgrading & implementation.

Going through process.

One person in attendance.

Short and long term recommendations

Go through operations

65m
15 3.8
50

19/226

Generalities

Material ← { specifications and acceptance
met in part.
Including compensatory

Raw material specifications
more complete
This in fact is not tested

Components
bottles vials labels cartons.
Specifications for labels which should
include supplier.
Sanzaki no real turnover.

General attitude to processing.

Open process criticised as expected
Approach to improved environment

Brist. v. pharmaceutical.

Standards of production process.

Personal influence
environmental differences
Standardization of cleaning.

lack of GGMP.

Cleaning procedures poor
Processing vessels Varcas responsibility of users.

14/22

Custom based cleaning.

No documentation for disinfect production containers.

No control on effectiveness of cleaning

Microbiological backup
environmental quality control.

variation in batches.

Need for production manager over heads of departments

In addition to prod. manager - quality controller separate to production manager

Engineering major deficiency in validation of equipment in use general lack of good piping and maintainance
Di-octyl phthalate test.
responsibility of overseeing of commissioning equipment

laminar flow benches
Aseptic filling operation better under horizontal than vertical —
Hepa air for final filling.

Engineer has v. little control 19/227
Lack of chief engineer
lack of job description - extent & limits of authority

Question of validating sterilization of tubing and equipment.

No overall standardization
formalized training programme

Criticism of way in which clothing was worn
trousers inside boots
gloves over of sleeves.
Signs training
washing of clothing — no washing just autoclaving

clothing use in sterile clothes. laundry for special clean room clothing
Question of particles.
worn once
washed
packed Double wrapped in approved materials

Production of PPF

Melting to fitting

Control of environment Air flow incorrect.
Cardboard + packets. flow onto cardboard.

After centrifugation → 2° room fungal contamination

Centrifugation - product exposed } to uncontrolled environment
and final fabrication

In clean room suite - not sterile - make up

19/228

Implementation

Replacement of equipment

Laminar flow benches.
Sterilization
Clothing + cleaning
Testing and validation

Outside cold rooms. Unknown environment outside

More cold room space.
Poor conditions of working.

Batching checking system does not exclude

Use of loading bay as stores.

Vials on loading bay open.

Increasing load on washing.

So much depends on a single operation that the matter of sterile filtration is of concern.

Coagulation

premises — inadequate air filtration

recirculation & temp. control.

filling classified at 16C no operations
at standard requirement
filtration & pressure inadequate

recommendation double sterile filtration

process time shorter

2nd filtration in sterile filling room
immediately after first

Cf products generally
Attire questions.
Cleaning and monitoring of areas

Standard operating procedures.

F.D.

ethylene oxide sterilization not validated
general thoroughness for product and
personnel

Short term improvements training now

Building totally inadequate for manufacturing
environment

v. little chance of environmental improvement.

19/2 3C

earrings etc.

v. little guarantee that bottling is aseptic

filter bubble tested at 6 lb because of tubing

test separately at 50 lb.

Double filtration

Environment in clean room deficient.

Pressurization in cleaning room irregular
opening to opening
Changing not in sterile area.

Microbiology lab. plasma filling room grossly
inefficient — 95% efficient at 5 fr

No direct protection of plasma filling
inadequate filling area
not clean no changing area
Cardboard

Some plasma tested in similar room grossly
contaminated

Freeze drying Packing room as for filling area

19/23

GMP Cleaning of equipment & environment

? frequency of cleaning moulds

General levels of contamination in future during
Unpleasant working conditions

→ frequency v. process time requirements

General decontamination

Inside preparation areas - use one can
enlarge

* Advisory Service in GMP
Hospitals. Regional Advisory Service on
Hospital Cleaning
Pharmaceutical Industry
Cleaning files

Dress spectacles earings.
Uniform dress.

Positive pressure Watch.

Access to cold rooms in ordinary footwear

footwear policy

Disposable clothing

General and safety footwear.