Documentation

Part 2

15

Documentation

Labels

- What must be labelled?
  - *Containers, equipment, premises*
- Label information?
  - *Clear, unambiguous, company format*
  - *Intermediates and bulk products*
- Colours can be used, e.g. green (accepted), red (rejected)

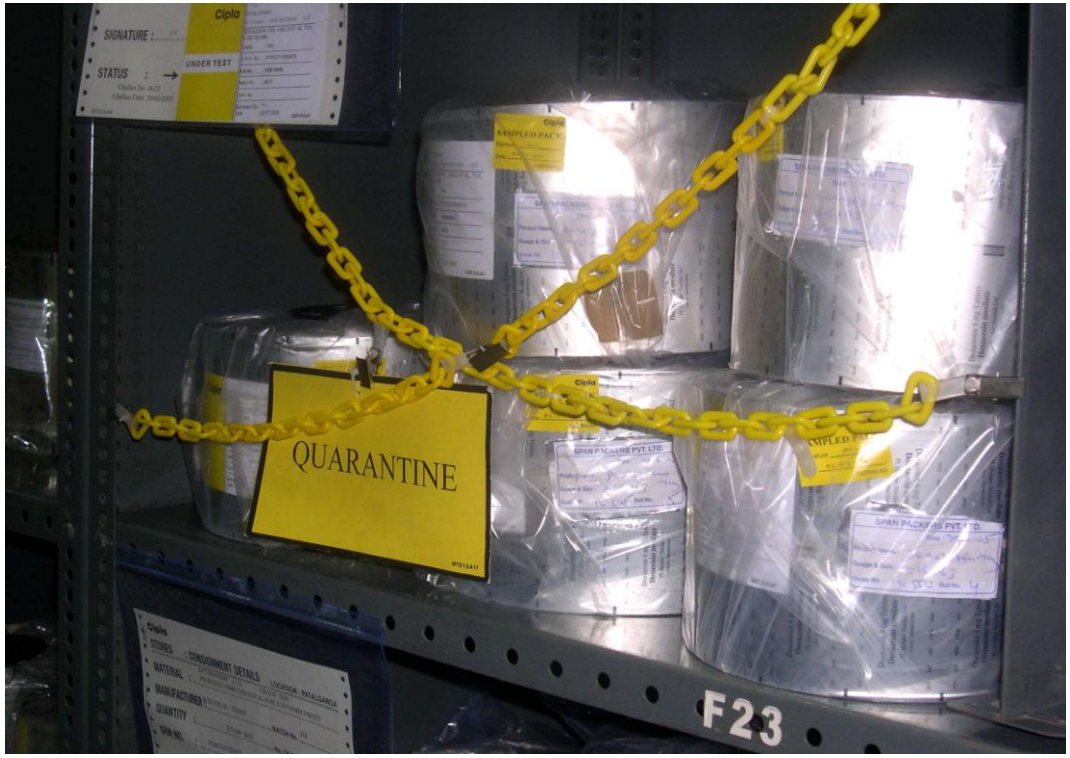
15.10

Basic Principles of GMP

- Different types of labels, e.g. cleaning status, production stage, status of materials
- Other types of labels?

Basic Principles of GMP

- Labels can indicate the status of materials such as "quarantine"



Documentation

Finished Product Label

National legislation, but includes:

- Name
- Active ingredients and amounts
- Batch number
- Expiry date
- Storage conditions, precautions if necessary
- Directions for use, earnings
- Name and address of manufacturer

15.11

Documentation

Reference standards

Label to include:

- Name
- Potency or concentration
- Date of manufacture
- Expiry date
- Date the closure is first opened
- Storage condition
- Control number

15.12

Documentation

Specifications

Specifications:

- Authorized, approved, signed and dated
  - *Starting materials and packaging materials*
    - *include tests on identity, content, purity, quality*
  - *Finished products*
  - *Intermediates and bulk*
  - *Water, solvents and reagents*
- QC, QA or documentation centre

15.14, 15.15

Documentation

Specifications and Test Procedures

Test Procedures:

- Validated (facility and equipment) before routinely used

Specifications:

- Periodic review
- In compliance with current pharmacopoeia
  - Pharmacopoeia, reference standards and spectra should be available

15.13, 15.16 -15.17

Documentation

Specifications: Starting and packaging materials

Include:

- Name (e.g. INN) and internal code
- Pharmacopoeia (if applicable)
- Qualitative and quantitative requirements and limits

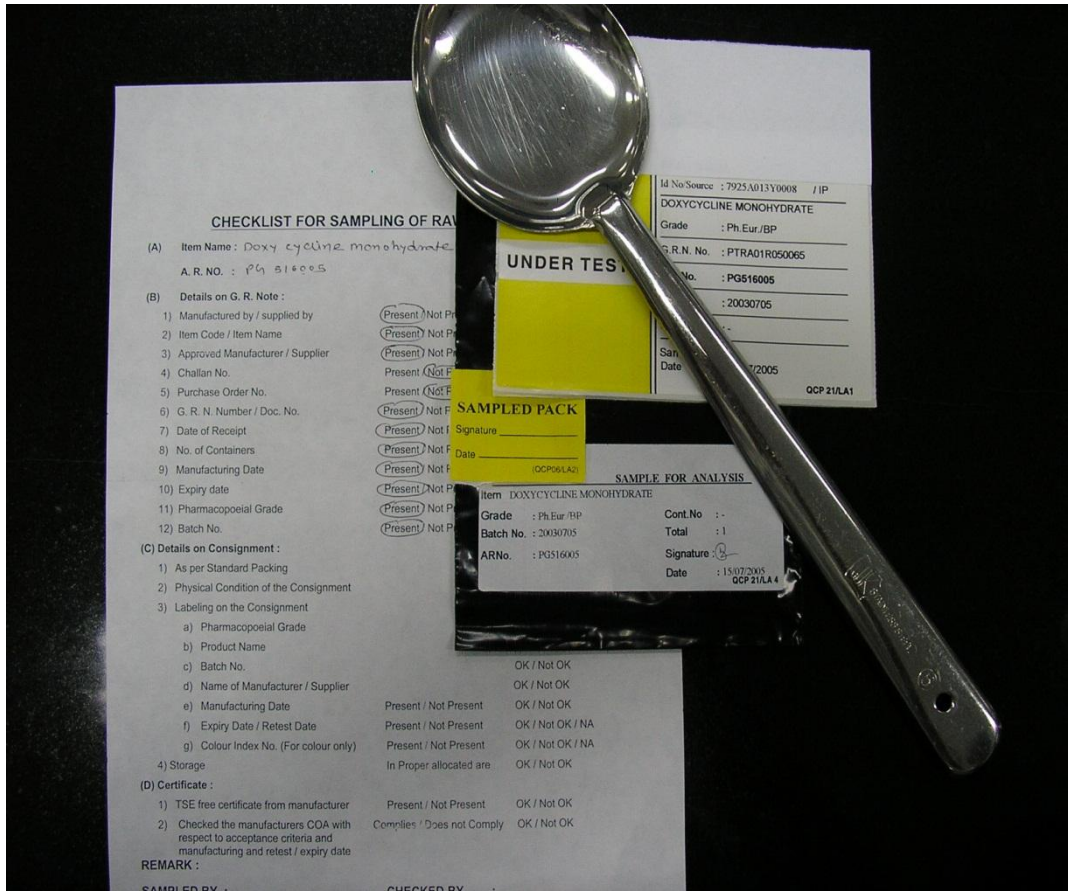
Other data may include:

- Supplier
- Sampling procedure or reference
- Storage conditions, precautions
- Retest date

15.18 -15.19

Basic Principles of GMP

- Can you list which documents are associated with / needed for sampling of starting materials?
- And for packaging materials?



World Health Organization

Documentation

Specifications: Finished products

Include:

- Name and code reference
- Names of actives (e.g. INN)
- Formula
- Dosage form, package details
- Reference to sampling
- Qualitative and quantitative requirements and limits
- Storage conditions and precautions
- Shelf life

15.21

Documentation

Master Formulae - I

- Master formula for each product and batch size
- Manufacturing instructions include:
  - *Name of product with product reference code*
  - *Dosage form, strength and batch size*
  - *List of starting materials including quantities and unique reference code*
  - *Expected final yield with acceptable limits (and intermediate yields)*
  - *Processing location and principal equipment*

15.22 – 15.23

Documentation

Master Formulae - II

- Manufacturing instructions - continued
  - *Equipment preparation (e.g. cleaning, assembling, calibrating, etc.)*
  - *Detailed stepwise processing instructions and checks, pre-treatments, sequence of additions, times, temperatures, etc.*
  - *In-process control instructions and their limits*
  - *Storage requirements and special precautions*
  - *Any special precautions if needed*

15.22 – 15.23

Documentation

Master Formulae - III

- Authorized packaging instructions for each product, pack size and type, and to include:
  - *Name of the product*
  - *Dosage form, strength and method of application*
  - *Pack size (number, weight or volume of product in final container)*
  - *List of all packaging materials (quantities, size, types and code number)*

15.24

Documentation

Master Formulae – IV

- Packing instructions - continued
  - *Examples of printed packaging materials, with location of batching information*
  - *Special precautions, including area clearance checks (before and after operations)*
  - *Description of the packaging operation including equipment to be used*
  - *In-process controls, with sampling instructions and acceptance limits*

15.24

DOCUMENT NO: GLUT/2
PAGE 2 OF 8

[redacted] PTY. LTD.

TABLETS

BATCH NUMBER:

SAFETY PRECAUTIONS:

a. Wear proper protective clothing at all times.
b. Wear gloves, disposable hat and face mask when weighing out and handling powders.
c. At all times keep hands and clothing clear of rotating machinery
d. If the operator has long hair then ensure it is tied up adequately.
e. Avoid materials coming into contact with the skin. Wash thoroughly.

Safety Instructions read and understood

Operators: **Date:**

EQUIPMENT REQUIRED

a. Mettler PE24 electronic balance.
b. Stainless steel scoop.
c. 20 mesh stainless steel hand screen.
d. 20 litre stainless steel bucket.
e. Stainless steel Bonser Anderson rotating mixer fitted with dust extraction.
f. 40 tray Weesburg Martin granule drying oven fitted with time clock and thermostatt.
g. Manesty Rotorgran oscillating granulator fitted with 20 mesh stainless steel screen.
h. Stainless steel 200 litre drum complete with lid and clamp.
i. Drum Tumbler.
j. Manesty Express Tabletting Machine complete with DCF/Vokes dust extracter.
k. 6 x 20 litre plastic pails lined with clean plastic bags and ties

All equipment clean and in working order.

Operator: **Date:** **Supervisor:** **Date:**

1 **Granulating Solution** **Date Commenced:**

Weigh into a 20 litre stainless steel bucket the following:

RAW MATERIAL	QUANTITY Decimal			ADDED BY
	7	500	kg	
	1	000	kg	

Stir until Povidone is completely dissolved and there are no lumps remaining.

Operator: **Date:**

Documentation

Batch Processing Record – I

- Record kept for each batch processed
- Based on the master or specifications (e.g. copied to avoid errors)
- Before start of process - check suitability of area and equipment
  - ↗ *clear of previous products, documents, materials*
- Checks recorded

15.25 – 15.26

Documentation

Batch Processing Records – II

Information recorded during processing include:

- Name of the product, batch number
- Dates and times (e.g. start, major steps, completion)
- Name of person responsible for each stage of production
- Name of operators carrying out each step (check signatures)
- Theoretical quantities for materials in the batch
- Reference number and quantity of materials used in the batch

15.27

Documentation

Batch Processing Records – III

Information recorded during processing include (cont.):

- Main processing steps and key equipment
- In-process controls carried out, person's initials, and results obtained
- Yield at each stage with comments on deviations
- Expected final yield with acceptable limits
- Comments on any deviations from process
- Area clearance check
- Instructions to operators

15.27

Documentation

CHECK LIST	SIGNATURE	DATE
COMPILED BY:	[illegible]	5/12/88
TECHNICAL MANAGER:	[illegible]	8/5/88
QUALITY CONTROL:	[illegible]	5/12/88
PRODUCTION MANAGER:	[illegible]	5/12/88
ISSUED BY:		

[illegible] PTY.LTD.
Manufacturing Batch Record For:

TABLETS

DOCUMENT NO: GLUT/2
PAGE 1 OF 8
BATCH NUMBER:

QUANTITY PER TABLET (mg)	% OVER-AGE	RAW MATERIAL CODE	G.I.N.	Raw Materials Checked By: RAW MATERIAL	THEORY QUANTITY USED Decimal	UNITS	ACTUAL QUANTITY USED Decimal	UNITS	WEIGHED BY	CHECKED BY
		AAK		[illegible]URED	500	kg		kg		
		POV		[illegible]	000	kg		kg		
		GAK		[illegible]	000	kg		kg		
		SBW		[illegible]	000	kg		kg		
		TAQ		[illegible]COLLOIDAL	500	kg		kg		
		CAS		[illegible]GEN PHOSPHATE FINE	000	kg		kg		
		MBM		[illegible]STEARATE	200	kg		kg		
		AAA		[illegible]'DER	300	kg		kg		
		AAK		[illegible]URED	000	kg		kg		
		CBC		[illegible]OCRYSTALLINE	000	kg		kg		
		MAJ		[illegible]RATE	400	kg		kg		
		TAB		[illegible]	500	kg		kg		
		SBE		[illegible]SULPHATE	200	kg		kg		

☐ Cross box and record any information affecting stock records on back of this page.
Affix any Machine or Product Labels to the back of the relevant page.

ALLOWABLE LOSS (%)	ACTUAL YIELD (%)	REJECT(%)	RECONCILIATION:							
± 1.0			TOTAL GRANULATION YIELD:	57	100	kg			kg	
			AVERAGE TABLET WEIGHT:	571	000	mg			mg	
± 2.0			TOTAL TABLET YIELD:	57	100	kg			kg	
			REJECT MATERIAL:	NIL		kg			kg	
± 2.0			FINAL TABLET YIELD:	100	000	Tabs			Tabs	

Documentation

Batch Packaging Records – I

- For every batch or part of a batch
- Based on approved packaging instructions
- Can be copied or computer generated
- Before start – checks that equipment and work station suitable and clean, no previous product
  - Line clearance (opening)
  - Recorded

15.28, 15.29

Documentation

Batch Packaging Records – II

Contents:

- Name of the product, batch number and quantity to be packed
- Batch number, theoretical quantity and actual quantity of finished product
- Actual quantity obtained – reconciliation
- Dates and times of operation
- Name of person responsible for packaging, initials of operators carrying out each step
- Checks, and in-process results

15.30

Documentation

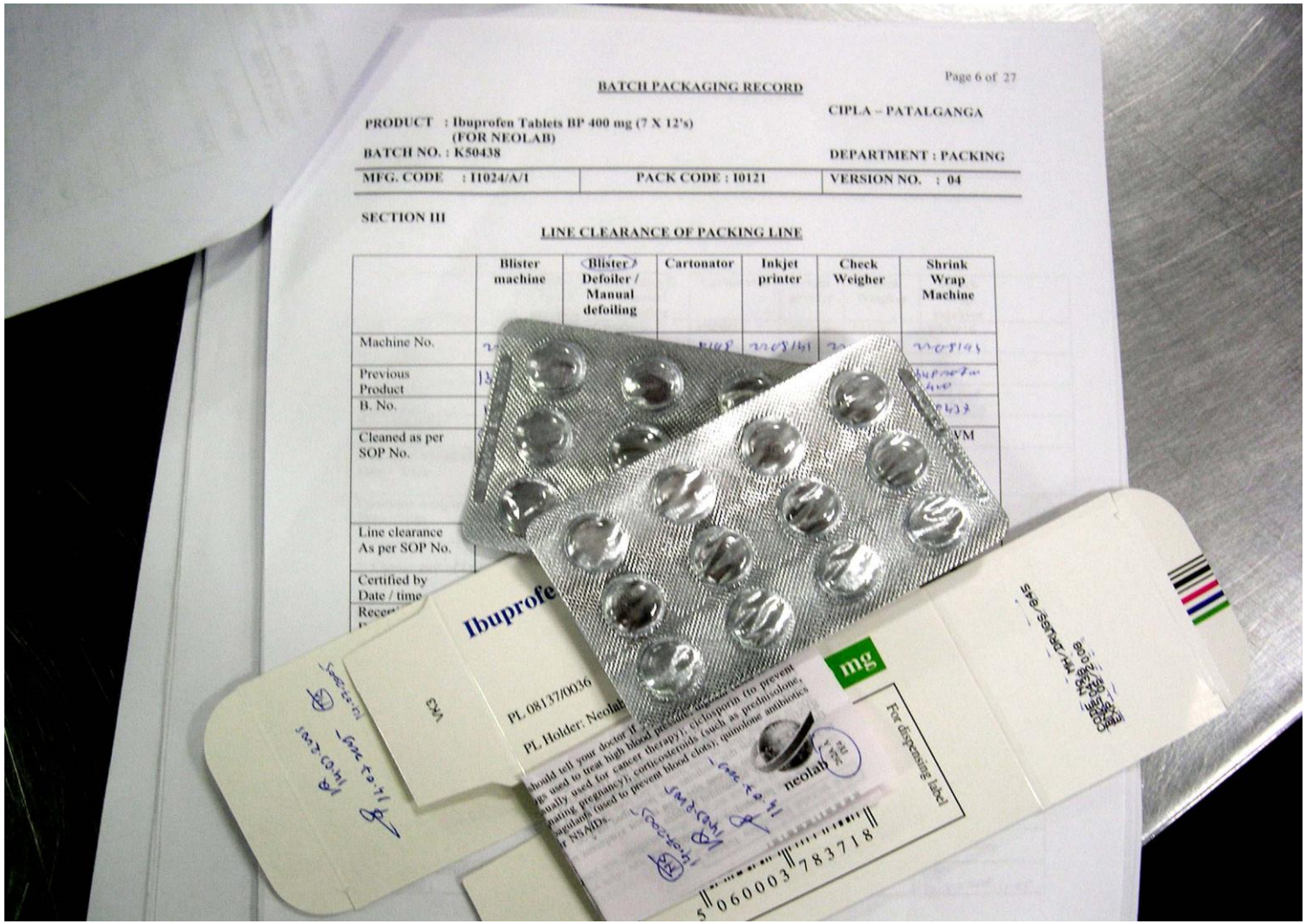
Batch Packaging Records – III

Contents:

- Details of packaging operation, including equipment and line used
- Returns to store
- Specimen of printed packaging materials, with batch coding approval (batch number and expiry date)
- Deviations and actions taken; and authorization
- Reconciliation of packaging materials, including issues, use, returns and destruction

15.30

Documentation



World Health Organization

Documentation

Standard Operating Procedures (SOP) - I

- What is an SOP?
- Who is responsible for preparing SOPs?
- What is the format for an SOP?
- Which activities require SOPs?
- Where should SOPs be stored?
- Are SOPs associated with records?

15.31

PHARMACEUTICALS

STANDARD OPERATING PROCEDURE "Confidential and Proprietary"

Procedure No:		Page No	1 of 7	Date Issued	
Revision No:		Supercedes:		Date effective:	

SECTION GENERAL OPERATING PROCEDURE

SUBJECT PRODUCT COMPLAINTS.

1. PURPOSE MAINTENANCE OF THE PRODUCTS COMPLAINTS REGISTER.

2. SCOPE THIS PROCEDURE APPLIES TO **ALL** PRODUCT COMPLAINTS **NO MATTER HOW TRIVIAL SOME MAY APPEAR.**

2A ABBREVIATIONS

EG., FOR EXAMPLE
QM QUALITY MANAGER
SOP STANDARD OPERATING PROCEDURE

3. RESPONSIBILITY

THE QUALITY DEPARTMENT MANAGER (QM) IS RESPONSIBLE FOR THE INVESTIGATION OF ALL PRODUCT COMPLAINTS AND IS RESPONSIBLE FOR ENSURING THAT MARKETING, MEDICAL AND FRONT LINE PERSONNEL SUCH AS TELEPHONISTS AND RECEPTIONISTS ARE FAMILIAR WITH THE COMPLAINTS HANDLING PROCEDURE.

PRODUCT COMPLAINTS MAY NOT BE RECEIVED AT FIRST CONTACT BY A TECHNICAL PERSON. IT IS THEREFORE IMPORTANT THAT ALL FRONT LINE PERSONNEL ARE FAMILIAR WITH THESE PROCEDURES AND FOLLOW THEM EXACTLY. THE QM SHALL TRAIN ALL SALES PEOPLE, RECEPTIONISTS AND TELEPHONISTS IN THESE PROCEDURES.

4. PROCESS DESCRIPTION

4.1 PRODUCT COMPLAINT CODES EXAMPLES

CRITICAL COMPLAINT	CATEGORIES
PRESUMPTIVE ADVERSE REACTION	1

Author:		Checked by:		Authorised by:	
Date:		Date:		Date	

Review date on or before 12 months from date of authorisation

Documentation

Standard Operating Procedures - II

Which activities require SOPs?

- Equipment and analytical apparatus:
  - *Assembly, validation*
  - *Calibration*
  - *Internal labelling, quarantine and storage of materials*
  - *Operation*
  - *Maintenance and cleaning*
- Personnel matters:
  - *Qualification*
  - *Training*
  - *Clothing*
  - *Hygiene*

15.31

Documentation

Standard Operating Procedures - III

Which activities require SOPs?

- Environmental monitoring
- Pest control
- Complaints
- Recalls
- Returned goods

15.31

Documentation

Standard Operating Procedures - IV

- SOP and records for receiving materials
  - *Name of material as on delivery note*
  - *Name and in-house code*
  - *Date of receipt*
  - *Supplier's and manufacturer's name*
  - *Batch number*
  - *Quantity and number of containers received*
  - *State of container and other information*

15.33

Documentation

Standard Operating Procedures - V

- Other SOPs include:
  - *Internal labelling, quarantine and storage of materials*
  - *Operation, maintenance, calibration and cleaning of all instruments and equipment – production and QC*
  - *Sampling of materials*
  - *Batch numbering systems*
  - *Material testing at all stages of production*
  - *Complaints, recalls*

15.31, 15.32

Documentation

Standard Operating Procedures - VI

- Which activities require SOPs? (Continued)
  - *Batch release or rejection*
  - *Maintenance of distribution records*
  - *Equipment assembly and validation*
  - *Maintenance, cleaning and sanitation*
  - *Personnel recruitment, training, clothing and hygiene*
  - *Environmental monitoring*
  - *Pest control*

…and many more…

15.31

Documentation

Standard Operating Procedures - VII

- SOP for sampling:
  - the method of sampling and the sampling plan
  - equipment to be used
  - precautions to avoid contamination
  - amount(s) of sample(s) to be taken
  - instructions for any required subdivision of the sample
  - type of sample container(s) to be used
  - specific precautions

…and many more…

15.37

Documentation

Records

- What should be recorded?
- Where should records be stored?
- Why are the records important?

Documentation

Records

- Different types of records should be kept
- For defined periods of time
- Production records and packaging records
- Quality control records
- Distribution records
- Equipment records

15.32

Documentation

Records

Records of receipt of materials

- Name of material, “In-house” name and/or code of material
- Date of receipt, supplier’s and manufacturer’s name
- Batch or reference number, quantity, and number of containers received;
- Comment (e.g. state of the containers).

15.33

Documentation

Records

- Analysis records to include:
  - Name of material / product
  - Batch number
  - Reference to specification and test procedures
  - Test results
  - Dates
  - Equipment references for traceability
  - Initials / names of analysts and supervisors who checked the data
  - Statement of release or rejection

15.43

Documentation

Records

Include also:

- Cleaning and use
- Qualification and validation
- Calibration
- Maintenance
- Preventive maintenance etc…

15.35

Documentation

Group Session II

- From your own experience of factory inspections, how do documentation systems in this country compare with the WHO model?
- Identify gaps and reasons
- What will help and/or hinder the process of eliminating these gaps?