ADITYA
PHARMACY COLLEGE

Documentation in Pharmaceutical industry - III

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Production documents

- Manufacturing Formula and Processing Instructions
- Packaging Instructions
- Batch Processing Records
- Batch Packaging Records

Manufacturing formula

- Formally authorised Manufacturing Formula and Processing Instructions should be available for each product and batch size to be manufactured and often they are combined in one document

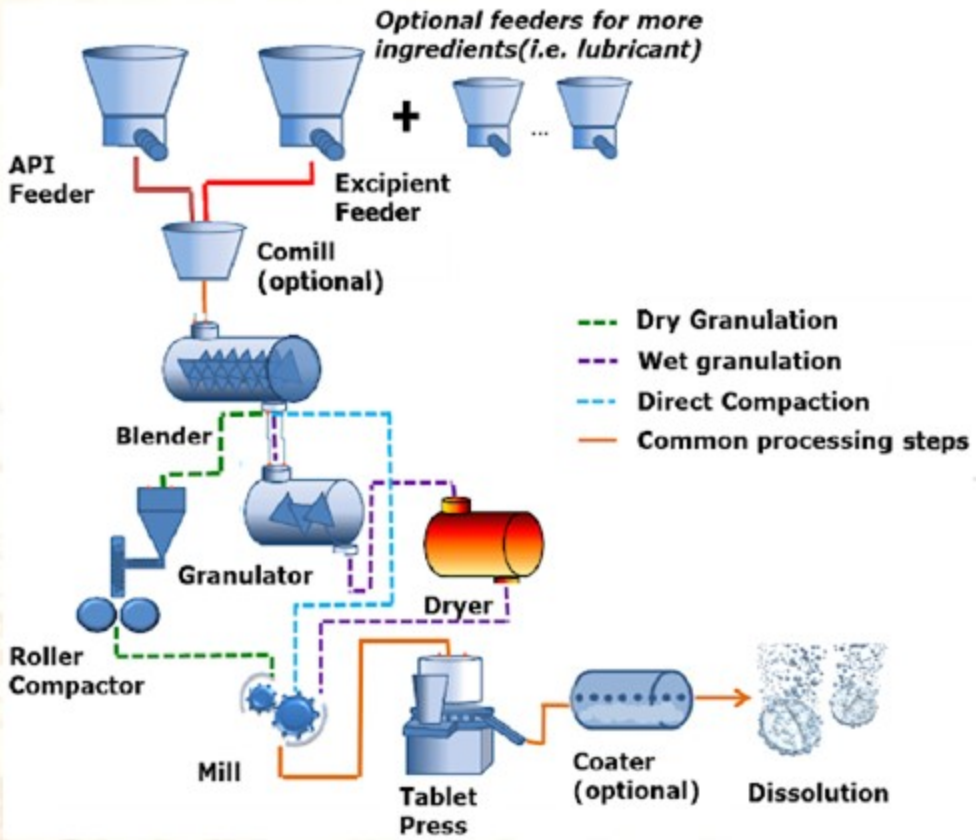
Shall include:

- Product name with reference code relating to its specification
- Description of product dosage form and strength, and batch size
- List of all starting materials
  - Amount of each
  - Designated name and reference which is unique to the material
  - Substance that may disappear during processing
- Statement of expected final yield with acceptance limits

Processing Instructions

- Statement of processing location and equipment used
- Method/SOP (or reference to methods) for setting up equipment e.g cleaning, assembling, calibrating
- Detailed stepwise processing instruction (e.g. Checks on materials, pre-treatments, sequence for adding materials etc)
- Instructions for any in-process controls with limits
- Requirements for bulk storage of products; include container, labelling, special storage conditions if applicable
- Any special precautions.

Processing instructions



- Shall describe the different operations carried out upon crude material such as: Sorting, Cleaning, Drying, Crushing and Sifting
- Shall include drying time, temperatures, and methods used to control fragment or particle size
- Shall also describe sieving process/other methods of removing foreign materials.
- In particular, written instructions and records, shall be available to ensure that each container of the product is carefully examined to detect any adulteration/substitution or presence of foreign matter, such as: metal, glass pieces, animal parts or excrement, stones, sand or rot and signs of decay.
- For product preparation, instructions shall include:
  - details of base or solvent
  - time and temperatures of extraction,
  - details of any concentration stages and
  - methods used

PROCESSING INSTRUCTION

Formula Card No :	**MASTER FORMULA**	Page : 2 of 3
Issued date :	**Product name (Powder)**	Mixing date :
Issued by :		Batch No :
		Batch size : kgs

Precautions & Safety Directions

1) Handling and weighing of raw materials should be aware.
2) The operators must wear protective equipment as appropriate.
3) Do not allow to swallow the raw materials.
4) Weighing process should be done by atleast two operators.
5) All of preweighed raw materials should have control number.
6) Preweighed raw materials should be separated.

Equipment

1) Ribbon mixer
2) Stainless steel beaker 5L
3) Stainless Steel Sifter
4) Storage Tank

Equipment Cleanliness

1) Ribbon Mixer No____ [ ] Cleaning date_____[ ] Consecutive used
SOP for cleaning & sanitizing :
Cleaned by_____ Checked by _____
Previous product_____ B.N._____

2) Sifter No____ [ ] Cleaning date_____[ ] Consecutive used
SOP for cleaning & sanitizing :
Cleaned by_____ Checked by _____
Previous product_____ B.N._____

3) Storage tank No____ [ ] Cleaning date_____[ ] Consecutive used
SOP for cleaning & sanitizing :
Cleaned by_____ Checked by _____
Previous product_____ B.N._____

Line Clearance	Operated by	Checked by
1) None of the unused raw materials are in the production area.		
2) Mixing tank, Premix tank and other equipments are cleaned.		
3) All of Raw materials are approved.		

Remark : Any deviations from the bulk product manufacturing record should be advised by the production supervisor & recorded.

Comment : _____

Production foreman Date

Prepared by:	Date	Checked by:	Date	Approved by:	Date

Reviewed by	Date	Batch approval	Date

F02-043 Rev 3

MASTER FORMULA RECORD

PRODUCT CODE: 001/1/2012	MASTER BMR No.: MFR/S.R.TAB/001	PAGE: 1

DICLOFENAC-Na TABLET(100 mg)

BATCH No. : _____

BATCH SIZE : 1,50,000 TABLETS

MFG. DATE : _____

EXP. DATE :

LABEL CLAIM : Each Uncoated Tablet Contains.

INGREDIENTS	QTY FOR EACH BATCH	OVERAGES ADDED
	40.00 Kg	
Powdered Sugar	47.00 Kg	
Cetyl Alcohol	25.00 Kg	
Aerosil	1.20 Kg	
Polyvinyl Pyrollidone	2.40 Kg	
Magnesium Stearate	1.20 Kg	

REFERENCE OF MASTER FORMULA RECORD : MFR/S.R.TAB/01

MANUFACTURING DATE :

REVISION No. :

REVIEW PERIOD : 2 YEARS

EXPIRY DATE

PACK : Blister Package

MFG. LICENCE No. :

BMR ISSUED BY & DATE

Q.A.: _____

BMR RECEIVED BY & DATE

PRODUCTION: _____

PREPARED BY	CHECKED BY	APPROVED BY	AUTHORIZED BY
QA OFFICER	PRODUCTION MANAGER	QA MANAGER	GM QA/QC

Batch Processing Record

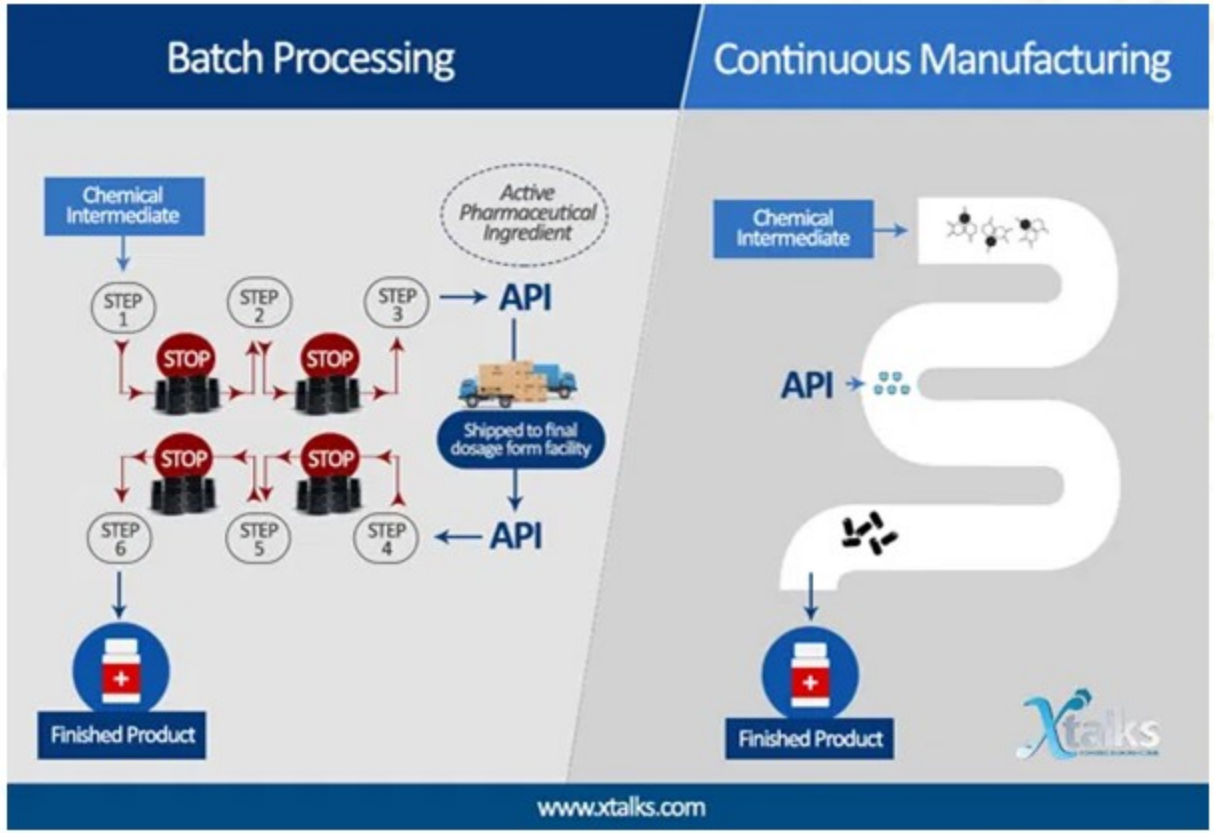
- Batch Processing Record is that part of Batch Manufacturing Record
- Should be kept for each batch processed
- Should be based on the relevant parts of the currently approved Manufacturing Formula and Processing Instructions.
- Method of preparation of such records shall be designed to avoid transcription errors.
- Record should carry the batch number of the product being manufactured.
- Before any processing begins line clearance should be done and documented:
  - Recorded verification that equipment and work station clear of previous products, documents or materials not required for planned process
  - Equipment clean and suitable for use

Batch Processing records

- During processing, the following should be recorded at time action is taken, and after completion, and the record shall be dated and signed by person responsible for processing operations:
- Product name
- Dates and times of
  - Initiation
  - significant intermediate stages and
  - Completion of production
- Name of person responsible for each stage of production
- Date and signature of operator of different significant steps of production and where appropriate, of the person who checked each of these operations (e.g. weighing, adding active material)

Batch Processing records

- Batch number and/or analytical control number include quantities of each starting material actually weighed
- Any relevant processing operation or event and major equipment used
- A record of in-process controls, date and signature of person carrying them out and results obtained
- Product yield obtained at different and pertinent stages of manufacture
- Notes on special problems including details, with signed authorisation for any deviation from the manufacturing formula and processing instructions



MFG Batch Record Header

MANUFACTURING LOG SHEET

M.F.# Title:

Date Approved: Approved by:

Date Checked: Checked by:

Replaces Page No.: Dated:

Date Written: Written by:

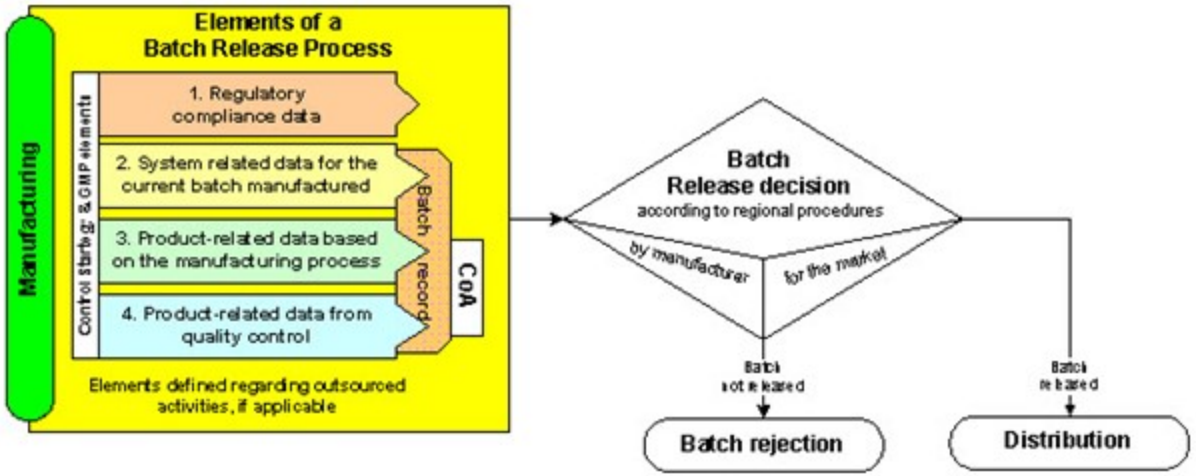
Mfg. Lot. No.: Mfg. Date:

Batch Size: Page: 1 of 10

Reproduction Reviewed for Accuracy: Date:

BATCH RELEASE DOCUMENT :

- All relevant paperwork for a particular batch, including samples of printed cartons, leaflet, shipper labels, Line Openings, Line Clearances records, etc. and collecting them together.
- There should be written procedure for the distribution of each batch of a product to facilitate recall of the batch



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 Watson Victor granule drying oven fitted with trolley 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:**

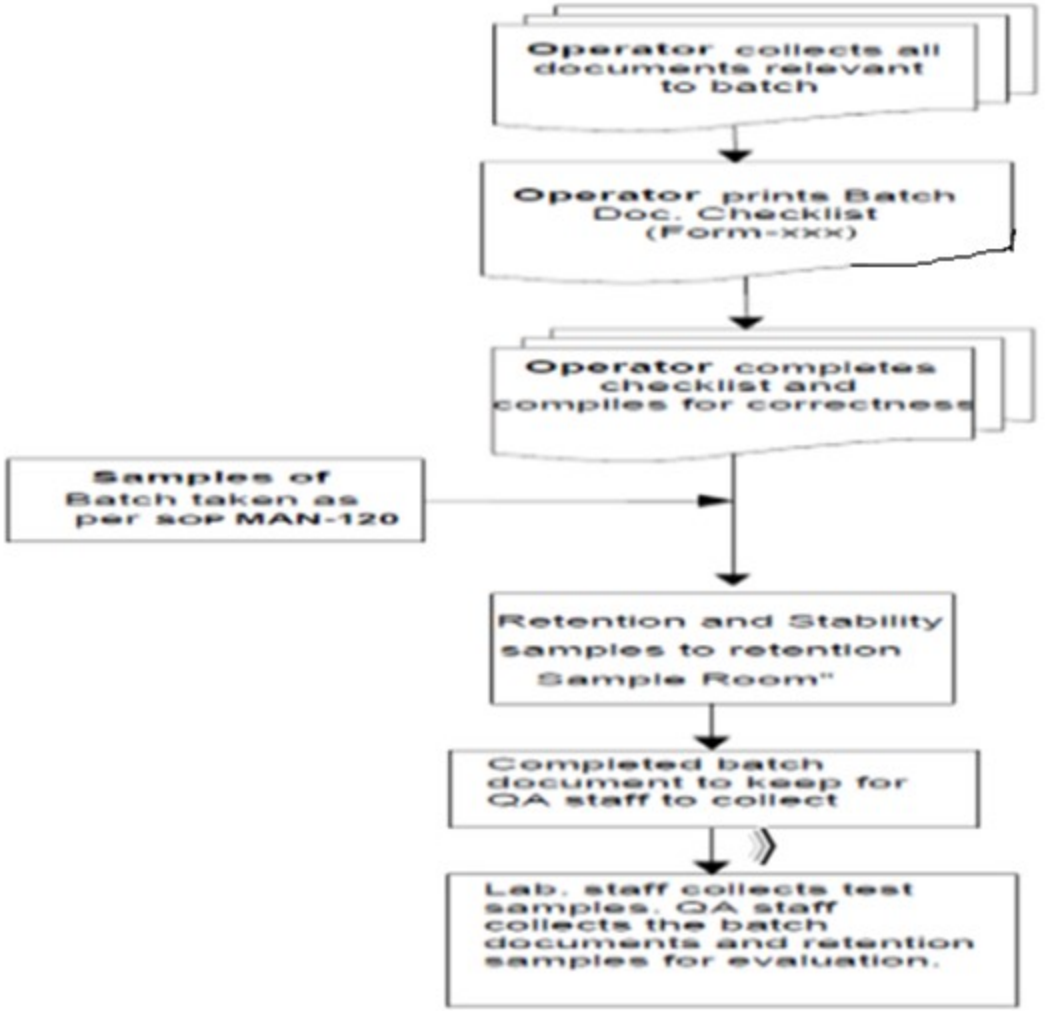
Weigh into a 20 litre stainless steel bucket the following:

RAW MATERIAL	QUANTITY Decimal			ADDED BY
[redacted]	7	500	kg	
[redacted]	1	000	kg	

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

Operator: **Date:**

BATCH DOCUMANTATION



Packaging instructions

- Formally authorised Packaging Instructions should be available for each product pack size and type.

Shall include:

- Product name
- Description of product dosage form, strength (if applicable)
- Pack size (expressed in terms of number, weight or volume of product in final container)
- Complete list of all packaging materials required for standard batch size including quantities, sizes and types with the code or reference number relating o the specifications of each packaging material
- An example/ copy of relevant printed packaging materials and specimens indicating where to apply batch number references, and shelf life of the product.
- Special precautions to be observed
- Description of packaging operation
- Details of in-process controls with instructions for sampling and acceptance limits

Batch packaging records

- Is part of Manufacturing Record and should be kept for each batch or part of batch processed.
- Shall be based on relevant parts of Packaging Instructions
- Method of preparation of such records should be designed to avoid transcription errors
- Record shall carry Batch Number (BN) and quantity of bulk product to be packed, as well as BN and planned quantity of Finished Products (FP) that will be obtained.
- Before any packaging operation begins:
  - Recorded checks that equipment and work station clear of previous products, documents or materials not required for planned packaging operations
  - Equipment clean and suitable for use


PHARMACEUTICAL
E-RECORDS
DASH BOARD
PLANNER
RPI
USER NAME
Department: Manufacturing
MANAGER
E-BMR
E-BPR
E-Masters
E-Log
QMS
AMS
Data Bank
Electronic Batch Packing Records
Product
Select Batch Number
Execute
Product Name
Amlodipine
Product Code
223456
Total
Batches Packed
102
WIP Batches
02
Product Name
Famotidine
Product Code
223457
Total
Batches Packed
122
WIP Batches
01
Product Name
Fluconazole
Product Code
223458
Total
Batches Packed
12
WIP Batches
00
Product Name
Gatifloxacin
Product Code
223459
Total
Batches Packed
222
WIP Batches
01
Product Name
Norethindrone
Product Code
223460
Total
Batches Packed
91
WIP Batches
02
Product Name
Omeprazole
Product Code
223461
Total
Batches Packed
256
WIP Batches
01

Batch packaging records

Information should be entered at time each action is taken, and after completion, and the record shall be dated and signed by person(s) responsible for packaging operations:

i. Product name

ii. Dates and times of packaging operation When there is risk of contamination, packaging activity should be done within the day itself

iii. Name of responsible persons carrying out packaging operation

iv. Date and signature of operators of different significant steps.

v. Records of verification for identity and conformity with Packaging Instructions including the results of in-process controls

vi. Details of packaging operations carried out, including references to equipment and the packaging lines used

vii. Samples of printed packaging materials used, which include the batch/lot number, expiry date and any additional overprinting

viii. Notes on any special problems or unusual events

ix. Quantities and reference no. or identification of all printed packaging materials and bulk product issued, used, destroyed or returned to stock and quantities of obtained product – for adequate reconciliation

Standard Operating Procedures

- A Standard Operating Procedure(SOP) is a set of written instructions that guide employees in their areas of responsibility.
- The development and use of SOPs are an integral part of a successful quality system as it provides individuals with the information to perform a job properly, and facilitates consistency in the quality and integrity of a product or end-result.
- The term "SOP" may not always be appropriate and terms such as protocols, instructions, worksheets, and laboratory operating procedures may also be used.

Record Documents :

Relationship between the Employees and the Work they perform.

- Ex: Protocols, Batch Production Records (BPRs), Log Books, Calibration Records etc.
- Protocol:-
  - Protocols are written records clearly defining the objectives and methods that will be used for the validation programs.
  - An important part of the protocol is the description of the testing method including who will test the system, how they will test it and what data is to be collected and reported.
- Computerized system protocols often include three distinct stages:
  - Installation Qualification(IQ), Operational Qualification (OQ), and Performance Qualification (PQ).

Life cycle of SOP

Test Procedure Standards

- It is important that test design standards are documented, communicated and followed by the whole development team.
  - This is so that the required test information is produced.
- These guidelines are necessary whether they are manual or automated test procedures.
  - The standards for manual test procedures should include an example of how much detail the procedure should go in.
  - The standards for automated test design are pretty similar to those of best coding practises.

Test Procedure Standards

- While it is important to maintain and mandate a test procedure template, it is worth noting that the template should remain in a generic manner, omitting test data which is too specific.
- This could lead to unnecessary duplication which could become both costly and time consuming.

SOP & Records

- Written procedures and records must be available for receipt of each delivery of each starting materials and packaging material.
- Records of receipt should include the following:
- Name of material on delivery note and containers
- In-house name and/or code of material
- Date of receipt, date and signature of receiving staff
- Name of supplier and manufacturer
- Manufacturer's batch/reference no.
- Total quantity and no. of containers obtained
- Batch Number assigned after receipt
- Any relevant comment (e.g State of containers)

SOP & Records

- SOPs should be available for the following:
- Internal labelling, quarantine and storage of starting materials, packaging materials and other materials as appropriate
- Operation of each equipment and placed in close proximity to instrument or equipment
- Sampling (which specify person authorised to take samples, sampling tools, and sampling instructions)

SOP & Records

- Describe details of batch/lot numbering system
- Objective – ensuring each batch of intermediate, bulk, or Finish Products is identified with a specific Batch Number
- Batch numbering procedures shall assure that same Batch Number will not be repeatedly used; this applies also to reprocessing.
- Batch Number allocation should be immediately recorded e.g. in logbook.
- Record should include date of allocation, product identity and size of batch.
- SOP for batch numbering that are applied to processing stage and to respective packaging stage should be related to each other.
- Quarantine, release and rejection of materials and products, in particular release for sale of Finish Products by authorised person.
- Records shall be maintained of distribution of each batch of product in order to facilitate recall of batch if necessary.

SOPs and associated records should be available for the following:

- equipment assembly;
- operation of analytical apparatus and calibration;
- maintenance, cleaning, and sanitisation of equipment and premises;
- personnel matters including qualification, GMP training, clothing, and hygiene;
- environmental monitoring;
- pest control;
- adverse product reactions, complaints and product recalls
- returns and recovered products, rejected products/materials;
- disposal and destruction of the rejected products/materials;
- self-inspection / quality audit
- change control , handling deviation, Corrective Action Preventive Action (CAPA)
- product quality review

SOP & Records

- Logbooks
  - Should be kept for major or critical equipment
  - Shall record the usage (name of products and batch number) and as appropriate, any calibrations, maintenance, cleaning, or repair operations, including dates and the identity of the people who carried out the operations
  - Should be recorded in chronological order (for use of equipment and areas where product been processed).
- Several of the mentioned procedures, specifications and/or records may be combined together in one specific document, e.g.:
  - Batch Processing Instruction and Batch Packaging Instruction; and
  - Processing Records and Batch Packaging Records can be merged into a single document.

GUIDE FORMAT FOR SOP

This SOP is for oral liquid filling machine.

Name of Company _____

Address _____

SOP FOR CLEANING OF LIQUID ORAL FILLING MACHINE

SOP NO. ..... Effective from ..... (Date)

Prepared by checked by Responsibility

Section Supervisor

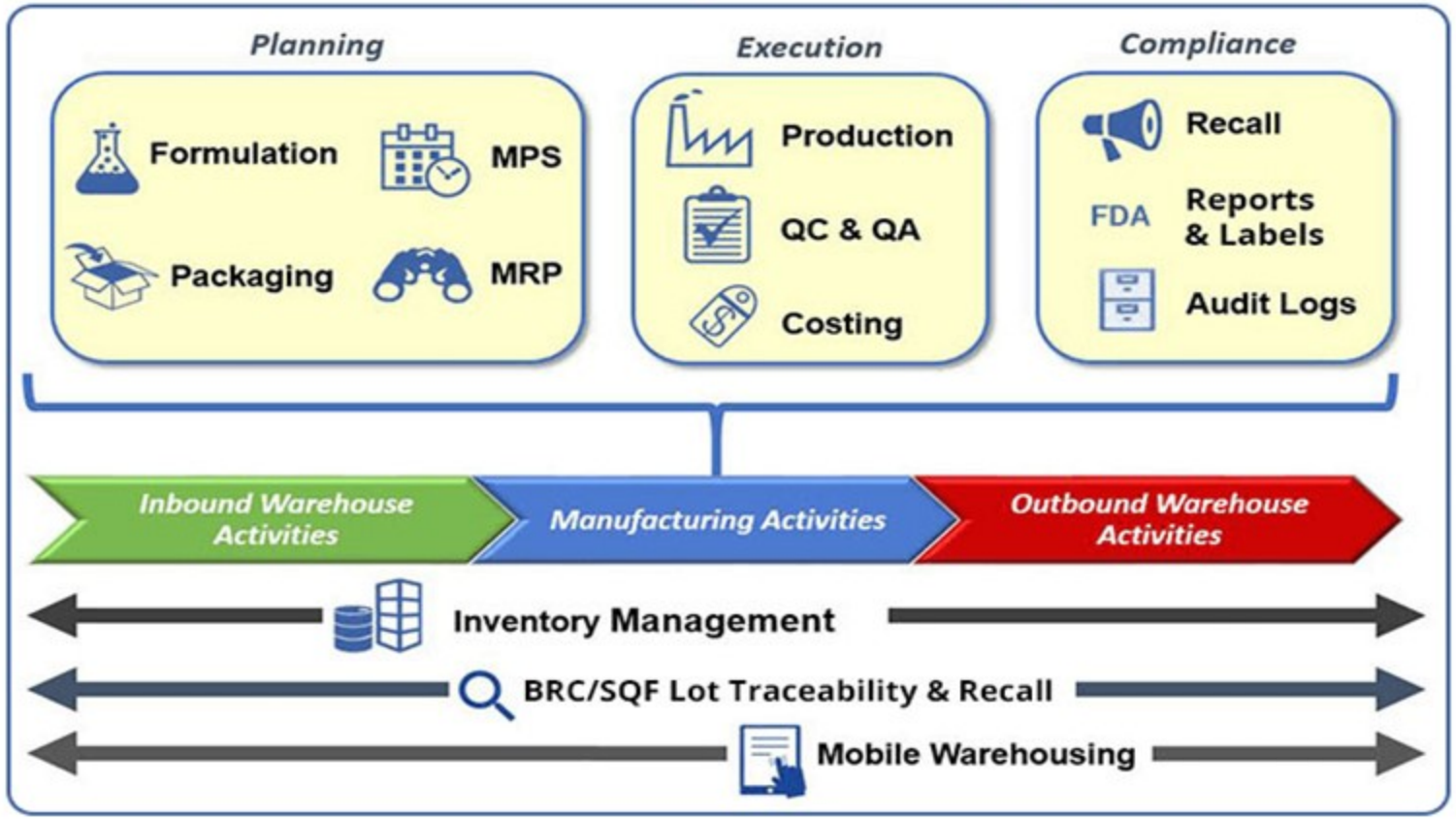
Approved by

In-charge In-charge

Production Quality control

1. Drain out holding tank of left overs, if any.
2. Fill the holding tank with water up to a height of _____ cm washing the internal surfaces and switch on filling machine. Run the machine till the water is removed from holding tank (as much as is possible).
3. Now open the drain valve of holding tank.
4. Disassemble nozzles and washer.
5. Remove tubing.
6. Clean all parts with jet of water for _____ minutes.
7. Soak parts and flexible tubings in antiseptic solution for 30 min. (0.5% cetrimide solution can be used for this purpose).
8. Wash these parts & tubings in running water.
9. Soak these in previously boiled & hot purified water.
10. If steam is available subject the parts to live steam. If steam is not available, use 70% Isopropyl alcohol and allow to dry.
11. Clean the flexible tubing in the similar way.
12. Cover ends of clean tubing with polyethylene sheets.
13. Clean the holding tank with previously boiled & hot purified water. If steam is not available, treat the holding tank with sodium hypochlorite solution (0.1%).
14. Assemble the equipment.
15. Label the equipment with status label e.g. "Ready for use".

Manufacturing & Warehousing



Front Office & Supply Chain

Continue.....