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Report on

# Operations of Industrial Affairs Site Sanofi-aventis

[ Training Program  
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## **East West University**

I want to thank my respective teacher Dr. Bidyut Kanti Dutta who inspired me to make the report. His inspiration helped me to get attached to the company, which in turn will help me in my professional life.

# Origin of the Report

## **Origin of the Report**

The study will help to gain work experience in the professional field. Thus the study relies on practical, real world situation to develop my skills and ability to analyze the working environment in which Sanofi-aventis operates.

## **Scope of the Study**

1. Understanding the basic concept of manufacturing quality products
2. Helping to develop control measures for various functions
3. Testing my skills in communicating analysis, conclusion and recommendation
4. Understanding the in-plant environment of the pharmaceutical industry

# Company Overview

## Introduction

Number one Pharmaceutical Company in France and in Europe, number three worldwide sanofi-aventis has been positioned as a key player in the healthcare. The Group was set up more than 30 years ago.

Their business consists of discovering, developing and providing physicians and patients throughout the world with innovative, effective, well-tolerated and high-quality treatments, whilst maintaining the economic performance levels that will permit them to continue this undertaking.

As a global industry leader Sanofi-aventis seek to conquer and prevent disease by bringing to market innovative pharmaceuticals, vaccines, therapeutic proteins and diagnostics. Aventis pharma was created as a part of the 1999 business combination of Hoechst and Rhone-Poulenc to form Aventis SA, one of the world's leading life sciences companies. Aventis Pharma concentrates its efforts on strategic brands that meet growing patient needs and contribute to a long-term sales growth. With 2001 sales of 15.168 billion euro (excluding sales of diagnostics), Aventis Pharma contributes three-quarters of the life sciences sales of Aventis SA. The Aventis Pharma prescription drug business is investing about 2.98 billion euro a year in Drug Innovation and Approval, one of the industry's largest R&D budgets.

## History of Aventis

In 1830 in London, John May, a young, talented employment seeker got a job with a chemist Charles Price. By 1834, he left the company and formed his own firm with partnership JI Picket and TS Grimwade. Next year Mr. Picket died and Mr. Grimwade retired in 1839. Same year, a few months later William Garrad Baker, 24 an apprentice in his



father's business and druggist joined May to start a new company and bought own premises at Golden Wharf. Baker started to look after manufacturing and dispatch while May was dealing with London Wholesale Market. Soon the introductory part of a future global company was founded. During First World War May & Baker became stronger through association with Poulenc Freres a reputed manufacturer of arsenic compounds. In 1927, Poulenc bought over 90% of May & Baker's ordinary share and ended up with 85% of May & Baker's total capital. Poulenc established its name in place of May & Baker. Shortly, Poulenc Freres merged with the Society Chemical des Usines du Rhone in France. In 1928, Rhone-Poulenc, became the largest manufacturer of organic chemicals in France with 3000 employees. In the following years, it became a story of mergers and acquisitions, the firm expanded all over the world under different names. In 1998 company decided to unify its global presence by the name of Rohne-Poulenc.

## Bangladesh scenario

### Tongi Site

**Site activities include production of drug products and distribution**

Site area	105600 m <sup>2</sup>
Plant area	18156 m <sup>2</sup>
Head count	396 nos.
Export	3 countries

### Capacity

Tablet	1850 mio
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Capsule	396 mio
Liquid	18.7 mio
Cream/ ointment	6.40 mio
Suppositories	10.4 mio
Liquid sterile	30.0 mio
Sterile powder	8.40 mio
Powder for suspension	9.80 mio

## Site History

- 1960 Incorporation as a joint venture company- Pakistan Pharmaceutical Industry with May & Baker owning 60% and Pakistan Industrial Development Corporation 40% shares.
- 1962 Production and marketing of Largacil, Flagyl, Stemetil, Phenergan etc
- 1971 Independence of Bangladesh
- 1972 Renamed as Bangladesh Pharmaceutical Industry
- 1981 Started animal health & nutrition and agrochemical business
- 1986 Renamed as Rhone-Poulenc Bangladesh Limited
- 1990 Development of sales of Profenid, Peflacin, Imovane etc.
- 1995
  - Renamed as Rhone-Poulenc Rorer Bangladesh Limited
  - Animal health & nutrition and agrochemical business reformed as a new company- Rhone-Poulenc Agrovet Bangladesh Limited
  - Acquisition of Fisons
- 1997 GMP upgrade and implementation of GMPs on site
- 1998 Started Qualification & Validation activities
- 1999 Merger of Rhone-Poulenc Rorer and Hoechst Marion Roussel to form a new company- Aventis Pharma

- 2001 Complete transfer of Fisions and HMR products on site
- 2002 Complete technology transfer of Amaryl and Tritace from Scopitto, Italy
- 2004
  - Commendable achievement of the site in IACS Audit- “Green Site”
  - New company – Sanofi - aventis

## **Background**

Sanofi Aventis is the 3<sup>rd</sup> largest pharmaceutical company in the world and no. 1 in Europe. In Bangladesh it has 3 legal entities and represents the largest multinational pharmaceutical manufacturing operation in the country.

Since its inception (45 years ago) the Tongi site with its new construction and up gradation has turned into an internationally GMP compliant recognized as a green site with its own glory and natural beauty.

Tongi industrial affairs team has put forth their best effort to achieve the goal and is ready to meet any future challenge.

## **Their Mission**

Aventis has a mission to become the **BEST** pharmaceutical company in the world by dedicating their resources, their talents and their energies to help improve human health and the quality of life of the people throughout the world

## **Their Objective**

Aventis has the objective to become one of the leading drug companies in the world through the success of strategic imperatives: Investment in research,

quality ,and innovation in the services provided to all their customer .Aventis aims to satisfy the specific needs of medical community

## **Their Goal**

The goal of sanofi-aventis is to involve every employee with its success and its commitment to health care by developing their professional skills and talents, and by helping them build their careers within the Group.

## **Their Values**

Sanofi Aventis has chosen to focus on seven key values in order to: create an environment where everyone is proud of the work of the employees and committed to Sanofi Aventis; capitalize on its cultural diversity and varied experiences; guide its behaviour in ways that build its competitive advantage by achieving excellence in performance.

## **Empowerment**

Sanofi Aventis

- ◆ A sign of respect of people
- ◆ Achieve through powerful mission and transparent process
- ◆ Encourage and reward self-confidence and initiative
- ◆ Require accountability.

## **Major Therapeutic Areas**

Their marketed product portfolio covers seven core therapeutic areas:

- Cardiovascular
- Thrombosis,
- Central nervous system,
- Oncology,
- Metabolic disorders
- Internal medicine

- And vaccines.

## **Strengths of Sanofi aventis**

- Strong leadership
- House keeping
- Traditional safety culture
- Good discipline
- Occupational health

## **Qualification and Vlidation**

1. Total no. of products 148: Level of process validation completeness
2. Total no. of process equipments 212: Level of process validation equipment qualification
3. Total no. of analytical methods 226: Level of analytical method validation
4. Total no. of lab equipments 82: Level of lab equipment qualification
5. Total no. of cleaning process 24: Level of cleaning validation completeness.

## **HSE compliances and site good practice**

Site is compliant to local and global HSE rules.

### **Site good practices include**

- A. Top management involvement in the development and implementation of HSE action.
- B. Excellent compliance check process against countries new laws and regulations.

- C. Well implemented and maintained internal audits and HSE inspection programs.
- D. Strong commitment of shop floor management in warehouse, correct use of PPE, good house keeping for technical areas and inside building.

## **Protection of environment**

- A. Waste water treated with effluent treatment plant before release into the outside environment.
- B. Solid wastes are processed externally by outside contractor.
- C. Emissions are within compliance.

## **Good practices**

- A. Site has automatic external defibrillator (AED) to attend emergency cardiac arrest problem.
- B. Installed public address system.
- C. Team for crisis management, emergency response, first aid and fire fighting.
- D. Emergency preparedness.
- E. Risk assessment review program.
- F. Process monitoring and controls.
- G. Review of HSE system.

## **HSE priorities**

- Industrial safety
  - o Implement explosive atmosphere (ATEX) directive regarding hazards.
  - o Training on individual safety to employee.
  - o Control occupational exposure.

- Environment protection
  - Reduction of solid waste by 1.6% from the baseline of 2004
  - Reduce use of water 10% from 2004 baseline
  - ISO 14001 certification.
  
- Property protection
  - Fire hydrant system upgrading.

# Industrial Technology



## IT deals with the following sectors

### A. Validation

Criteria required for the manufacturing of quality products. e.g. compression pressure , rpm etc are validated after 2-3 batch of successful production and establishment as standard procedure for the product..

### B. Qualification

Qualification is done on the basis of cGMP and HSE requirements.

### C. Calibration

To detect whether the temperature, rate, humidity, air flow etc displayed on the respective instruments are correct or not.

### D. Changing

Changing in any part of the procedure is done showing valid reason and then is approved in a meeting.

### E. Deviation

Any deviation is recorded and then by doing investigation the cause is uncovered and correction methods or suggestions are also noted.

## Functions of IT department

### A. Design qualification

It is done the basis of following the three factors:

- Requirements of production
- Facilities available
- HSE profile

### B. Installation qualification

Done the basis of protocol of the group. If any change occur, then it should be justified and conclusion should also be verified and approved.

### C. Calibration qualification

Regularly all the equipments are calibrated.

### D. Operational qualification

Trial batch is run, justified, verified and approved. On the basis of operational qualification SOP is prepared,

**E. Performance qualification**

Raw material (source, brand), weight (balance), batch manufacturing record, packaging materials, manufacturing instructions are under this qualification.

**F. Addendum qualification**

Every year calibration, maintenance or thorough checks up of the machines are done.

**Class I: Calibrated within 6 months.**

**Class II: Quality will not be hampered but time dependent.**

**Class III: Reference instruments.**

**Class IV: Not time dependent.**

**G. Cleaning qualification**

Microbial test and chemical identification tests fall under this category.

**H. Computer system validation/ software validation/ hardware validation**

**I. Process robustness**

It deals with statistical process control reducing the loss improving quality.

**J. Room qualification**

**K. Analytical method validation**

**L. Validation master plan**

**M. Site validation master plan**

**N. Change control validation**

**O. Preventive maintenances**

## **Training**

Training programs are carried out on the following subjects:

- Administrative
- Management
- Technical

# Information Solution

This system is present in the plant as well as in the head office. There is a special small room in the plant for IS, where the machines are kept from where the data are received from the head office and distributed and send to the head office.

There is a special software/ system in plant from where the data are automatically received by the server at particular time and then send to the head office.

Soft wares are also developed by this department and sometimes soft wares are also brought from abroad or from other companies.

# Production

Solid

## Two dosage forms are prepared in this section

1. Tablet
2. Capsule

### Tablet

Tablets are solid dosage form with or without excipients, which are prepared by compression. Excipients may include diluents, binders, disintegration agents, and lubricants, sweetening agents, flavoring agents and coloring agents.

Processes of tablet manufacturing:

1. Granulation
2. Compression
3. Coating

### Granulation

Granulation is the process in which powder particles are made to adhere to form large particles called granules. Granulation is carried out to confer fluidity, compressibility & uniformity of the powder systems.

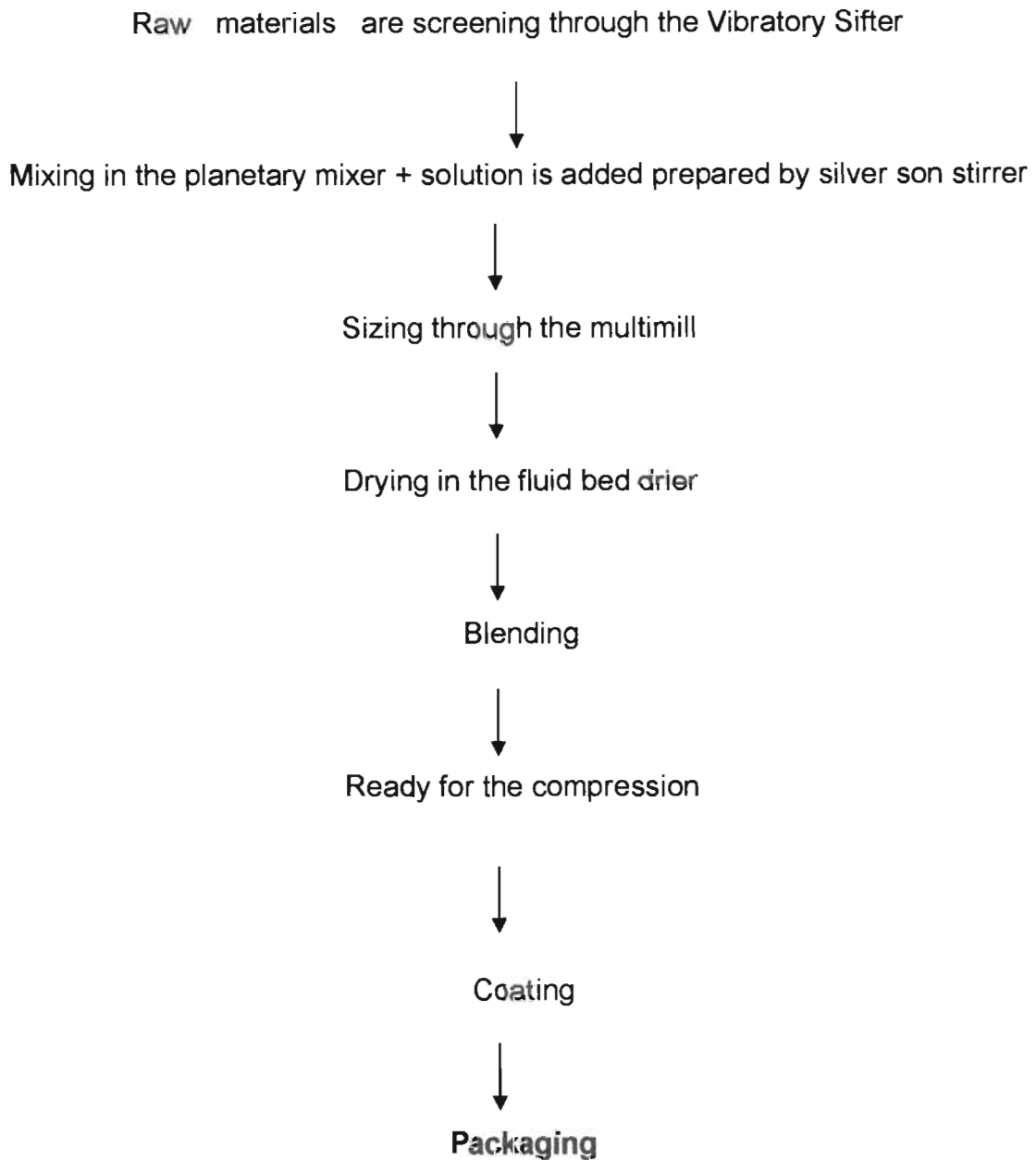
There are two methods for the manufacture of granules.

- Wet granulation methods (Most widely used method)
- Dry granulation method

There are many methods also to make the tablet dosage form. The methods are:

- ✓ Direct compression
- ✓ Slugging

## Flow chart of wet granulation



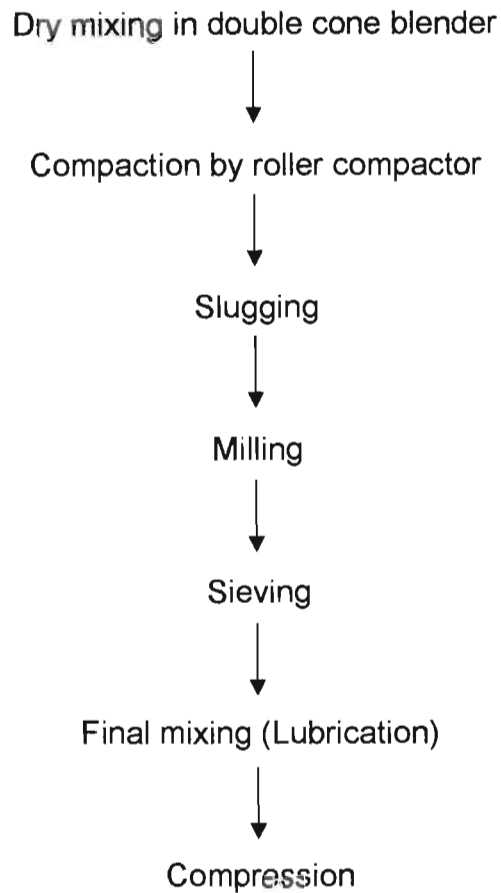
## Flow chart of dry granulation

This method is used for powders which require granulation and sensitive to moisture and water.

Raw material weighing

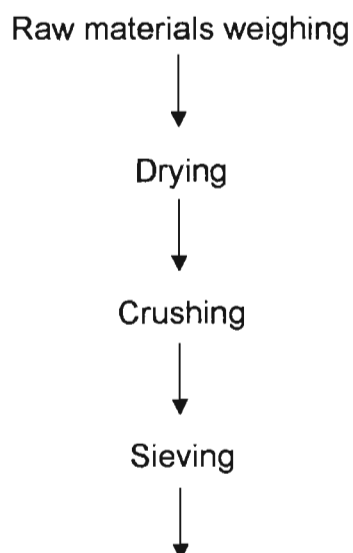
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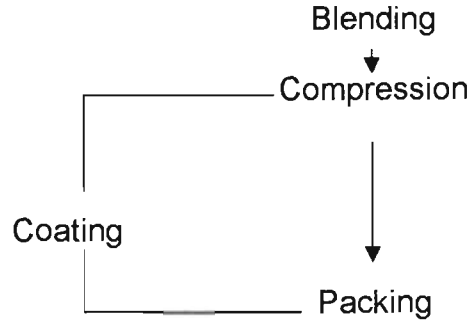




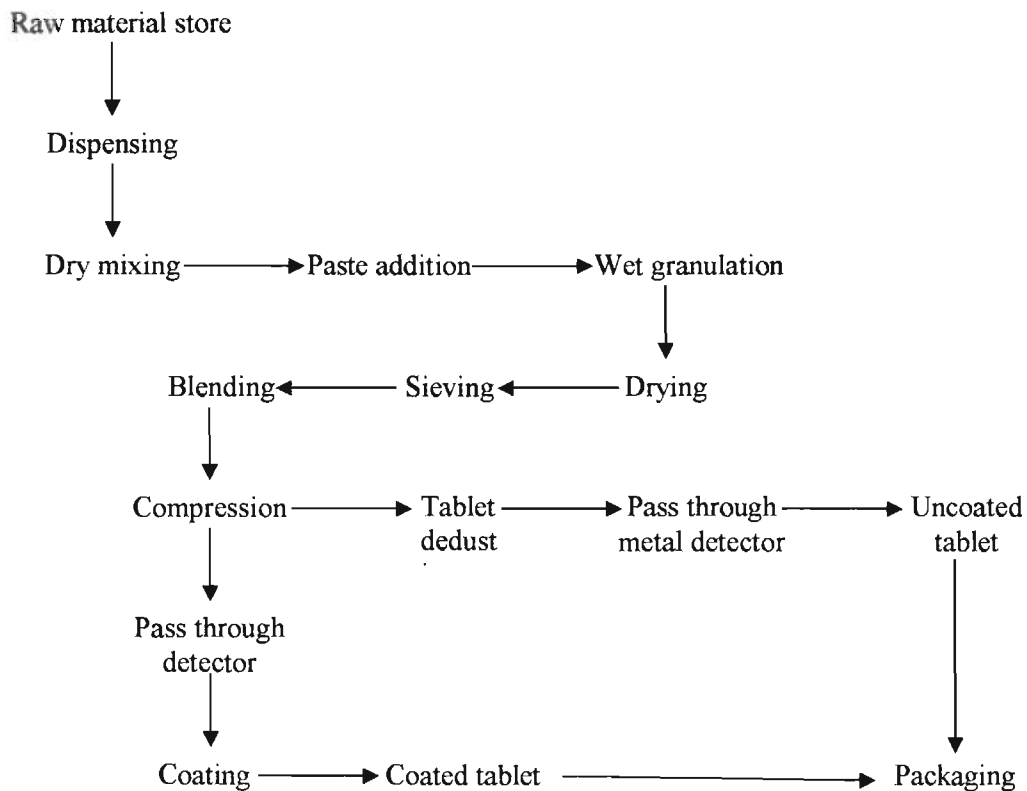
### Direct compression

This is the method used in Sanofi Aventis for manufacturing of tablet. The materials are directly compressed to form tables. The steps for direct compression are:





## Flowchart for overall tablet manufacturing practiced in Sanofi Aventis



## Basic requirements for successful tablet manufacturing

### a. Design:

- For separate operations, separate rooms are available
- Air lock door system available
- Separate entrances for personal and materials

- Floors and walls have no sharp edges preventing dust deposition.
- Floors and walls are painted by epoxy paint.

Rooms available in tablet section are:

1. Hand washing, shoe cover and gown wearing room
2. Office room
3. Solution preparation room
4. Coating room
5. Dispensing room
6. Store
7. Granulation room
8. Blending room
9. Equipment store
10. Compression room
11. Capsule filling room

b. Equipments:

List of equipments:

- Jaguar mixture granulator (India)
- Alliance fluid bed dryer (India)
- Apex mill (London)
- Rotopress compression machine
- Manesty BB3B compression machine (England, 38 punches, 2000 tab/min))
- Cadmach CMB4 compression machine (India, 36 punches, 1200 tab/min)
- Korcsh compression machine ( Germany , 30 punches, 2400 tab/min, 80 rpm)
- Sejong capsule filling machine
- Clinocone blender (700 L)

- Sopphire fluid bed dryer (India)
- Saizone mixture granulator (India)
- Manesty oscillating granulator
- Sejong SFC 170 coating machine ( Korea, 4-8 rpm)
- Sejong SFC 170 solution preparation tank

Following features are maintained for all the machines:

- Safety card (providing safety instructions to machine operators)
- List of authorized persons
- Labeling (describing state of operation, for example: machine label, to be cleaned, cleaned, under test etc)
- Machine log book
- Proper cleaning of the machine

c. Facility:

To maintain CGMP the following facilities are available:

- Adequate space
- PRW (purified water) supply
- HPS (high pressure steam) supply
- ICA (instrumental compressed air) supply
- Vacuum line
- Pressure differential gauge
- Positive air pressure

d. Personnel:

The workers operating the procedures are highly skilled. Some of them are even working here for 20-25 years.

They also properly maintain the PPI (personal protective equipment)

- Gowning
- Mask
- According to hazard of the product all the products are divided into 3 categories:
  - o OEB (operational exposure band)- 2: cotton mask
  - o OEB (operational exposure band)- 3: N-100 mask
  - o OEB (operational exposure band)- 4: PAPR (powdered air purifying respirator)
- For blending: HFNP (half phase negative pressure)

# Parameters checked prior to tablet manufacturing:

- Proper cleanliness of all materials and room
- Check the room temperature, humidity and air pressure
- Proper mixing to distribute all ingredients uniformly
- Proper drying of the wet granules to adjust the moisture content of the granules.
- Proper selection of die and punch
- Compression pressure, speed of the machine.
- The prepared coating solution should be used within 72 hours and the compressed tablets should be coated within 6 weeks.
- Tablet bed temperature, pan rotation, gun to bed distance, air temperature, atomized air pressure, pump speed and coating time.

### **Parameters checked during In-process quality check**

In case of tablet compression the following parameters are checked

- Weight

- Height
- Hardness
- Disintegration
- Appearance
- In case of coating
- Molting or any spot
- Sticking
- Capping
- Broken edge
- Roughness

### Flow chart for tablet coating



### Parameters checked prior to spraying coating solution

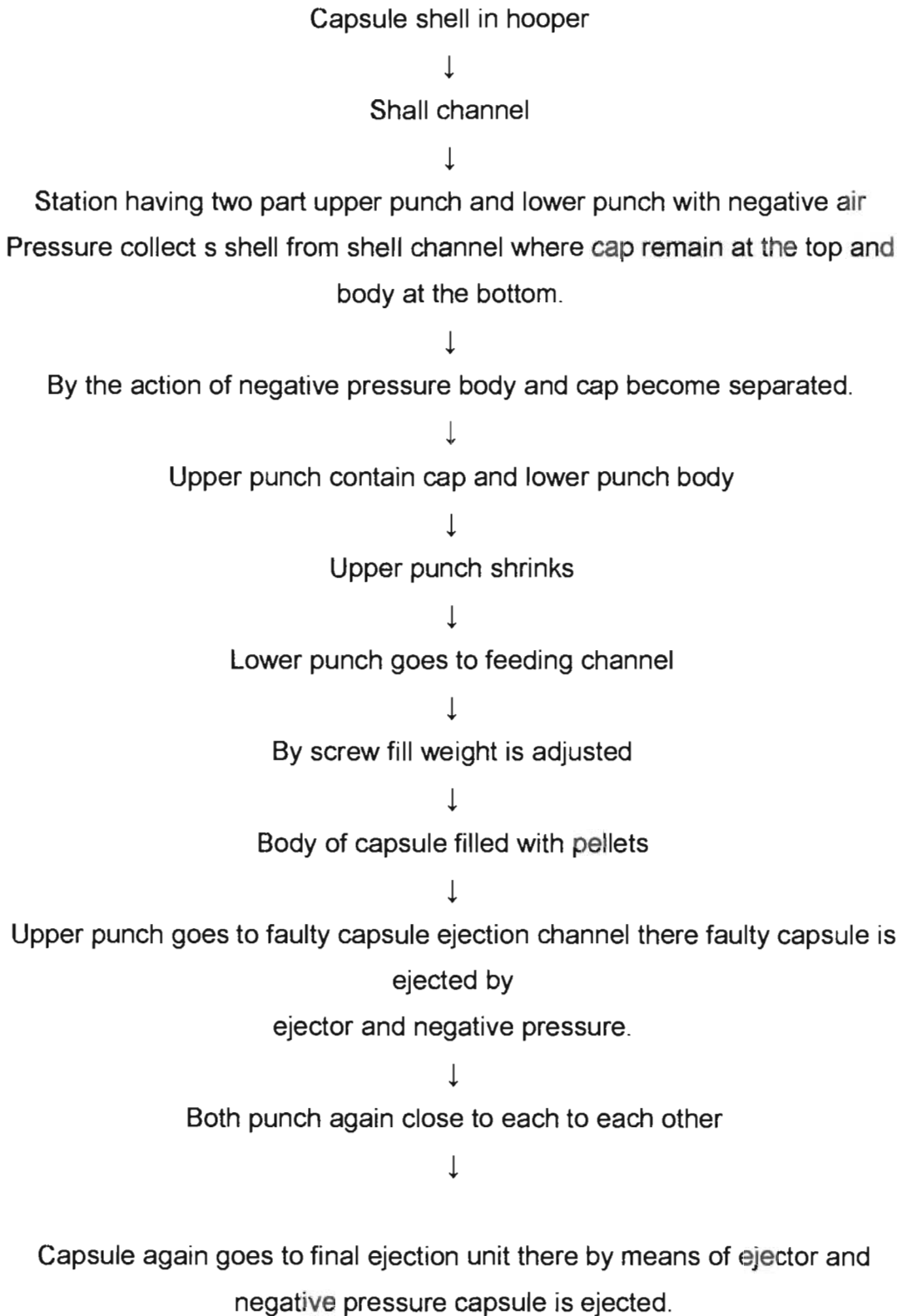
- Pan rotation
- Gun to bed distance
- Negative pressure
- Inlet air temperature
- Outlet air temperature
- Atomizing air pressure
- Fluid return volume
- Pump speed

### Capsule

Capsules are solid dosage forms in which the drug is enclosed in either a hard or soft gelatin shell. Gelatin shells are available in various sizes. Capsules shells have two parts; Body and Cap.

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PROCESS INVOLVES:



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## List of products manufactured in the Solid Production

Amaryl tablet 2×15×1 mg  
Amaryl tablet 2×15×2 mg  
Amaryl tablet 2×15×3 mg  
Avomine tablet 50×10×25 mg  
Flagyl tablet 50×10×200 mg  
Flagyl tablet 50×10×400 mg  
Imovane tablet 3×10×7.5 mg  
Largactil tablet 10×10×100 mg  
Largactil tablet 10×10×50 mg  
Largactil tablet 50×10×25 mg  
Macrocin tablet 10×10×250 mg  
Macrocin tablet 5×10×500 mg  
Macrocin granules for suspension 100 ml  
Peflacin tablet 3×10×400 mg  
Phenergan tablet 10×20×10 mg  
Profenid- CR capsule 5×10×100 mg  
Profenid- CR capsule 5×10×200 mg  
Profenid-E tablet 5×10×100 mg  
Profenid-E tablet 5×10×50 mg  
Rovamycin tablet 5×4×3 mg  
Secnidal granules for suspension 500 mg  
Secnidal-DS tablet 5×2×1 gm  
Spasmonil tablet 20×10×10 mg  
Stemetil tablet 25×20×5 mg  
Tritace tablet 2×14×2.5 mg  
Tritace tablet 2×14×5 mg  
Asec 3×10×10 mg capsule  
Asec 3×10×20 mg capsule  
Asec 3×10×40 mg capsule  
Amizide tablet 20×10×50 mg  
Asinar tablet 10×10×150 mg



Betanol tablet 10×10×50 mg  
Betanol tablet 10×10×25 mg  
Betanol tablet 10×10×100 mg  
Butapan tablet 50×10×10 mg  
Butapan tablet 10×10×20 mg  
Ficlou SR capsule 5×10×100 mg  
Ficlou tablet 10×10×25 mg  
Ficlou tablet 10×10×50 mg  
Fisat tablet 10×10  
Fisat DS tablet 25×4  
Firazin tablet 5×10×500 mg  
Folfecap-CR capsule 3×10  
Folfecap-CR plus capsule 3×10  
Folfetab tablet 1×100  
Folfetab tablet 1×1000  
Fiambutol tablet 10×10×400 mg  
Fiprox tablet 3×10×250 mg  
Fiprox tablet 3×10×500 mg  
Fiprox tablet 2×10×750 mg  
Inflam tablet 10×10×200 mg  
Inflam tablet 10×10×400 mg  
INH tablet 1×100×300 mg  
Meben tablet 5×6×100 mg  
Mepadis tablet 20×10×50 mg  
Metronid tablet 10×10×400 mg  
Motilon tablet 50×10×10 mg  
Salbutal tablet 50×10×2 mg  
Salbutal tablet 50×10×4 mg

Sterile

## **Sterile section consists of three units:**

1. Sterile area
2. Water plant
3. Packaging area

## **Criteria for sterile area**

- Free from microorganism; outside air inlet allows air through 0.2  $\mu$  heap filter.
- Airlock system for materials and personnel entry.
- Positive pressure within the room.
- HVAC system.
- LAF for aseptic works.
- Special gowning for the personnel.

## **Description of the sterile area**

Sterile areas are environmentally classified as A, B, C, D, 3, 2 and 1 area.

Area used laminar air flow is described as Class A.

Aseptic filling room is designated as Class B.

Aseptic manufacturing and terminal product filling area is designated as Class C.

Terminal product manufacturing, bottle washing and other area of class 10000 is designated as Class D.

Change room for entering to manufacturing area is designated as Class 3.

Material entry, inspection room, intermediate bulk store and packaging area are designated as Class 2.

Entry and exit procedure are described separately for different class area for maintenance of class environment and safety of personnel, equipment and products.

### Conditions required and maintained

- Temperature in manufacturing area is 17-25 ° C.
- Room air humidity is 30-60% RH.
- Room air pressure differential is  $\geq 15$  Pascal relative to surrounding area.
- Temperature, RH and differential pressure is checked at the beginning of any batch and at every 60 min interval.

### Filtration procedure used

100 L solution is filtered under nitrogen gas pressure at 0.5 bar. Gassing of storage vessel is performed before and after filtration.

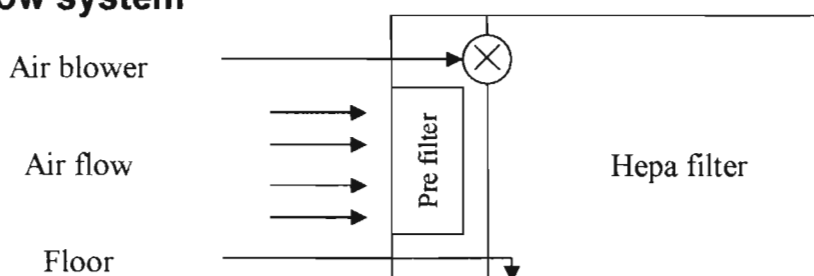
The filtered solution is taken in to two 50 LSS storage vessels in equal distribution.

The load is then sterilized.

Integrity test is of the used cartridge filter and gas filter is performed before and after filtration according to SOP.

Filter	Bubble Point Required
Cartridge Filter	3200
Gas Filter	1100

### Air flow system



## Parameters checked visual inspection of Ampules/ Bottles

1. Sealing
2. Volume
3. Fibers
4. Glasses
5. Foreign particles

Type	Shape
Glass large	Large irregular shaped particle, sink to the bottom of the solution very rapidly.
Spicules	Long shiny, thin particles, sink rapidly.
Flakes	Flat, very thin and irregular in shape.
Specks	Rounded, sink slowly and usually sparks.
Fibers	Long, thin, straight, may float or sink.
Dust	Usually of dirt, fine particles and nearly float in the solution.
Colored particle	Black, red & off-white, generally settle out but may float.

6. Sealing strength

### Equipments used

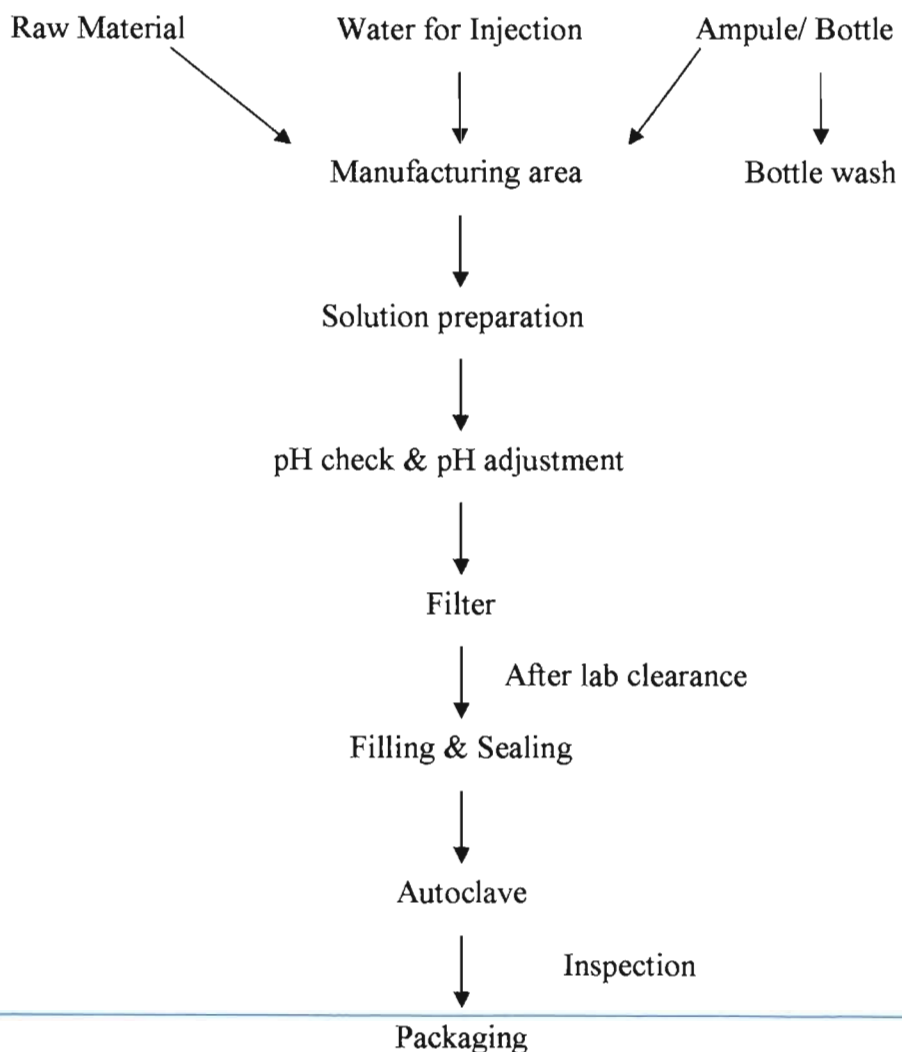
1. Rota ampule filling and sealing machine (Germany)
2. Linda steam sterilizer (Holland)

3. Getinge autoclave
4. Sanamij autoclave
5. Millipore filter
6. Greatide bottle washing machine
7. Hoong-A blister packing machine ( Korea)
8. Stobel & Bousch ampule filling and sealing machine
9. Cozzoli ampule filling and sealing machine

### Ampules or bottles are rejected when

1. Containing fibers, glass or any other foreign particles.
2. Having low volume, bad sealing, charring, and printing problem.

### Flow chart for overall sterile product manufacturing



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## Process description of the sterile section

- A. Receiving of RM
  - i. Cleanliness of incoming drums, containers and bags
  - ii. No materials entry except relevant to the product
  - iii. QA approval
  
- B. Dispensing of RM
  - i. All materials of previous are removed
  - ii. Shop is cleaned
  - iii. Balance are calibrated
  - iv. Temperature, pressure and humidity are checked every hour.
  
- C. Manufacturing
  - i. Mixing of WFT/ DW
  - ii. Nitrogen gas passed to dissolve oxygen
  - iii. pH adjusted (QA approval)
  - iv. Temperature, pressure and humidity are checked every hour.
  
- D. Filtration unit
  - i. Filtration through 0.2 $\mu$  sterilized cartridge
  
- E. Filter integrity test (bubble test)
  - i. Done before and after filtration
  
- F. Sterilization
  - i. Prevacuum
  - ii. Steaming
  - iii. Pulsing
  - iv. Warming up
  - v. Sterilizing
  - vi. Drying

vii. Air inlet

G. Filling

- i. Headspace oxygen content  $\leq 1.5\%$
- ii. Gas bulk solution with nitrogen gas
- iii. QC approval
- iv. Sample sent to microbiology lab

H. In process control

- i. Volume check
- ii. Nitrogen gas flow
- iii. Oxygen content

I. Shop clearance

J. Sterilization (product)

- i. Prevacuum three times
- ii. Heating
- iii. Sterilization
- iv. Post vacuum
- v. Pressure equalization

K. Leak test

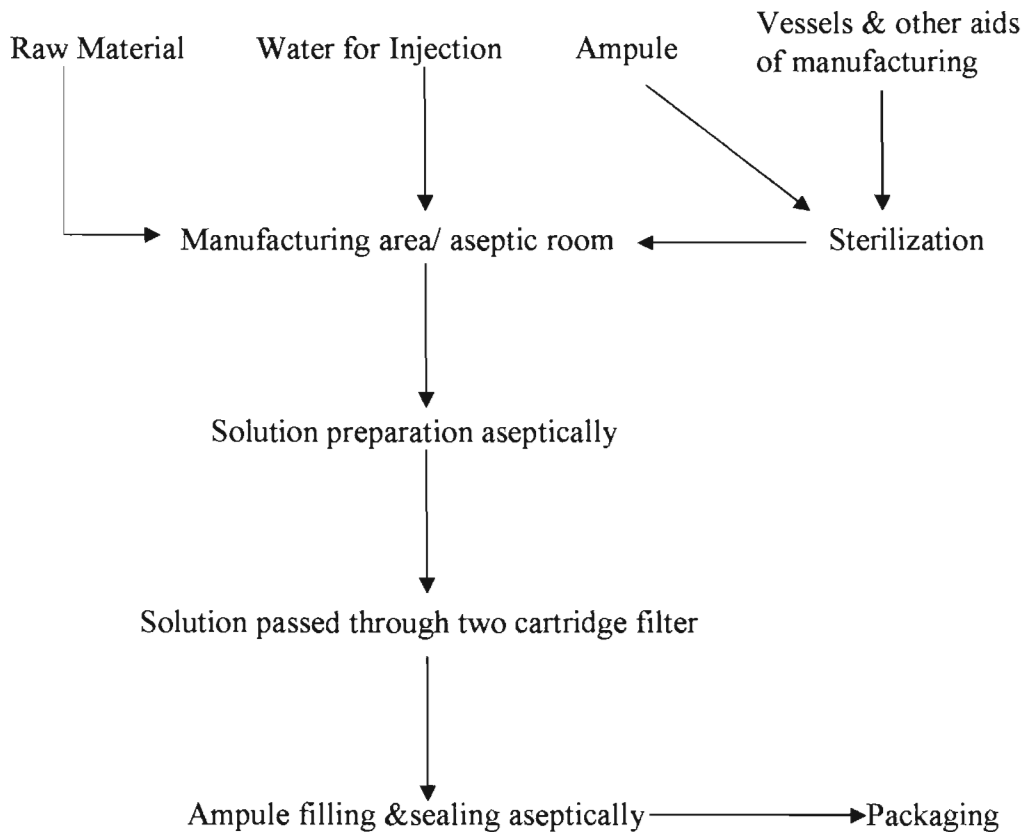
L. Inspection

M. Packaging

N. QA approval



## Flow chart for overall aseptic product manufacturing



### Some factors given importance

1. Proper sterilization of all containers, equipments and other things used in manufacturing.
2. Proper room condition for the products.
3. Integrity test of cartridge filter by bubble point test.
4. Maintain exact pH of the preparation.
5. Proper IPC for volume filled, nitrogen gas flow rate.
6. Leak test and proper inspection.

## List of products manufactured in sterile section

1. Water for injection 10 ml
2. Water for injection 20 ml
3. Water for injection 5 ml
4. Flagyl 100 ml
5. Peflacin 5 ml
6. Voltalin 3 ml
7. Phenergan 2 ml
8. Profenid 2 ml
9. Largactil 2 ml
10. Avil 2 ml
11. Lasix 2 ml
12. Novalgin 2 ml
13. Asinar 2 ml
14. Stemetil 1 ml
15. Motilon 2 ml
16. Butapan 1 ml
17. Lignocaine 2 ml
18. Doloran 2 ml
19. Zepac 1 ml
20. Zepac 10 ml
21. Zepac 30 ml
22. Ficlone 3 ml

# Liquid Packaging & Manufacturing

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**The following types of preparations are manufactured in this section**

- Syrup
- Suspension
- Emulsion
- Elixir
- Cream
- Suppository

**Factors which are given importance during manufacturing**

- Proper dispensing
- Proper mixing, adequate mixing time and speed of vortex mixture
- Carefully transfer and filtration of the liquid
- Attractive appearance, color and flavor.

**Name of equipments used**

1. Rotary bottle washing machine ( Taiwan)
2. Master bottle washing machine (India)
3. Bottle drying oven
4. Atomat liquid filling machine (India, 105 bottle/ min)
5. King cap sealing machine (Germany)
6. Myth cap sealing machine
7. King bottle labeling machine (England)
8. Ink jet printer
9. Sarong suppository filling machine ( Italy)
10. Sarong suppository sealing machine ( Italy)
11. SSSJ manufacturing vessel ( 2250 L & 500 L)
12. Vortex mixture
13. Mono pump

14. Meta filter
15. SS cream storage vessel
16. SS bucket
17. Bowl scoop
18. Premier colloid mill
19. Kalix Dupuy cream filling machine (France)

### List of products manufactured in this section

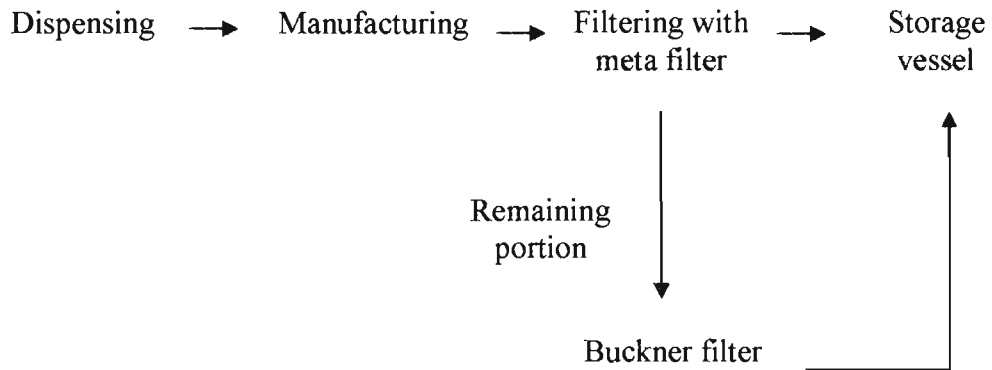
1. Anthisen cream 15 gm
2. Ascabiol emulsion 100 ml
3. Avil syrup 100 ml
4. Fisat suspension 60 ml
5. Flagyl suspension 60 ml
6. Infflam suspension 100 ml
7. Macrocin-T 2% lotion 30 ml
8. Metronid suspension 60 ml
9. Motilon pad. drops 15ml
10. Motilon syrup 100 ml
11. Pevaryl cream 10 gm
12. Pevison cream 10gm
13. Phenergan elixir 125 ml
14. Profinid gel 30 gm
15. Retin-A 0.05% cream 5 gm
16. Retin-A 0.05% cream 15 gm
17. Retin-A 0.05% cream 30 gm
18. Salbutal syrup 100 ml
19. Ficlou 12.5 mg suppository
20. Ficlou 50 mg suppository
21. Pevison cream 20 gm
22. Sandom drops 15 ml
23. Sandom suspension
24. Flagyl suppository 500 mg



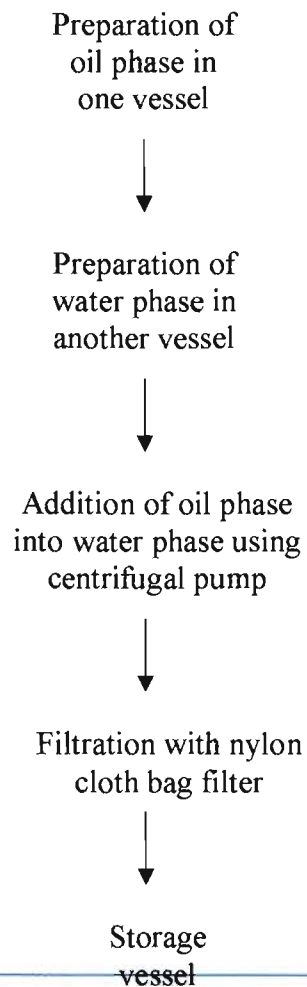
25. Flagyl suppository 1000 mg

26. Anthisan cream 5gm.

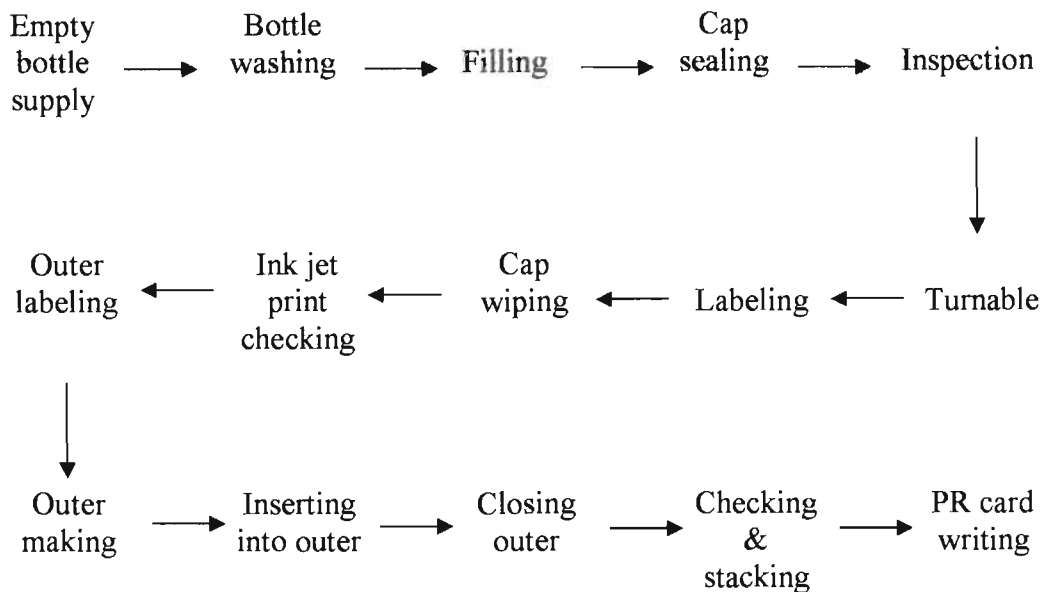
### Flow chart for oral syrup manufacturing



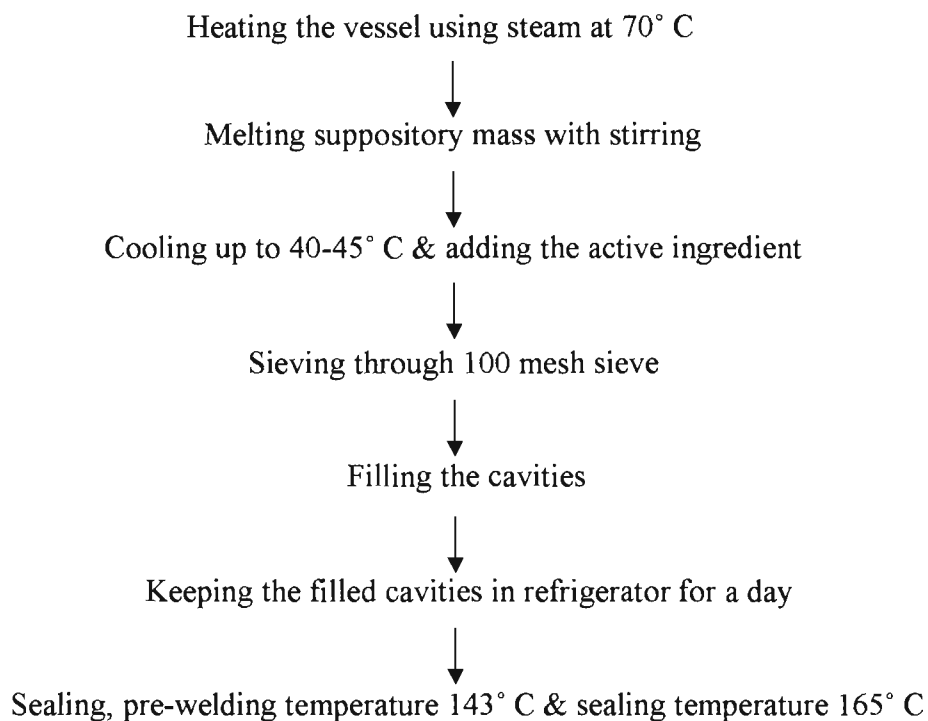
### Flow chart for emulsion manufacturing



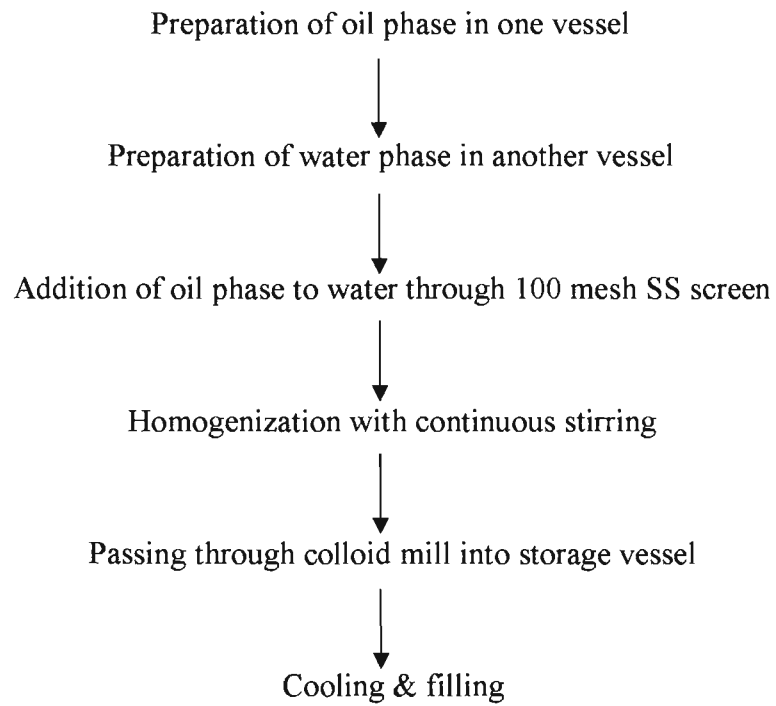
## Flow chart for oral liquid filling



## Flow chart for suppository manufacturing



## Flow chart for Cream Manufacturing





# Packaging

## **Packaging materials used**

Packaging materials are of two types:

**Primary Packaging materials and Secondary Packaging Materials.**

Primary Packaging materials used:

1. PVC
2. Aluminum foil
3. Clear & amber glass
4. Plastic spoon & syring

Secondary Packaging materials used:

1. Printed cartoon
2. Outer
3. Liner
4. Labels
5. Leaflet
6. Printed tape

## **Packing forms**

The following forms of packs available in this company:

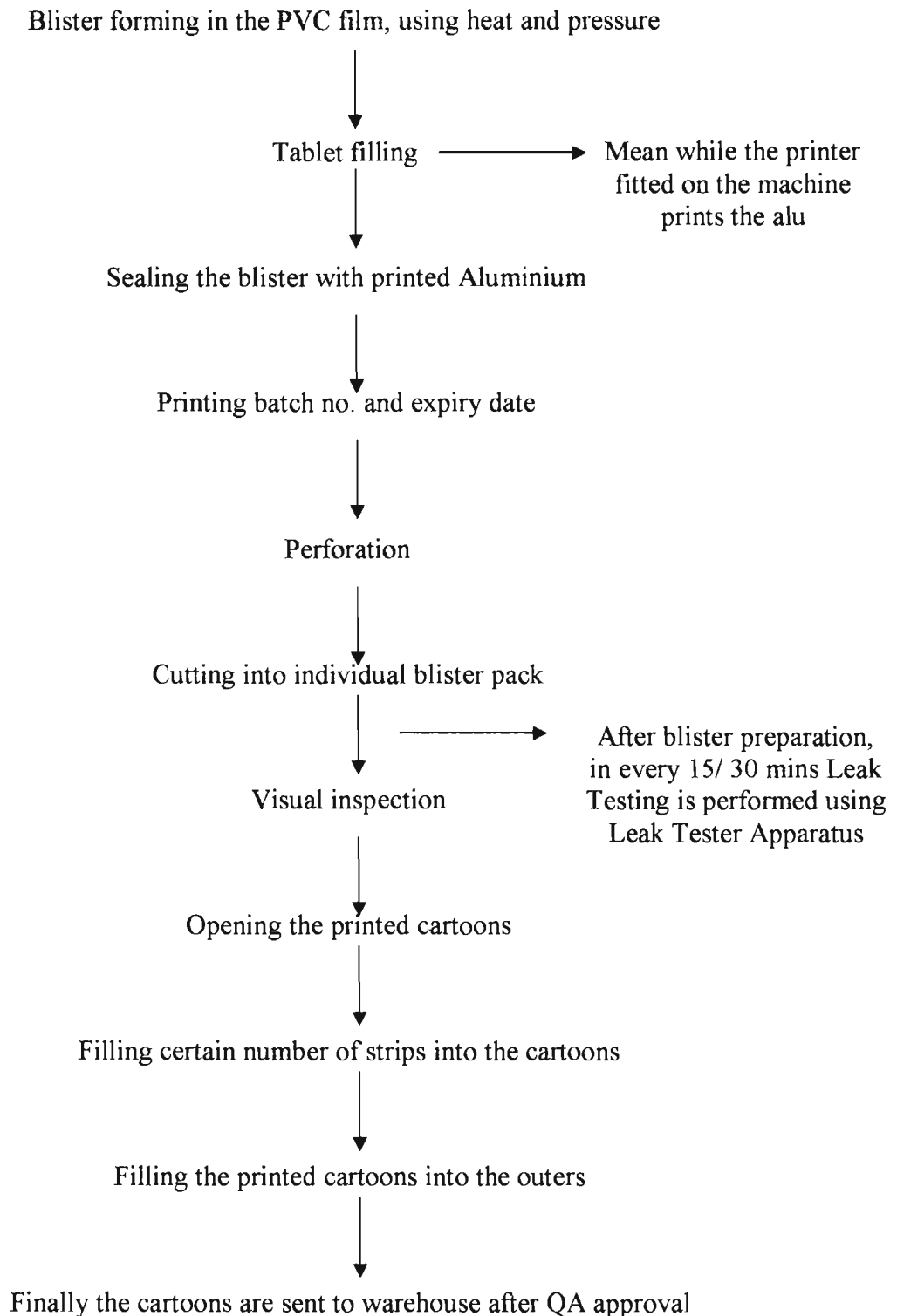
1. Blister pack, used for tablet, capsule, ampule and vial
2. Strip pack, used for tablet and capsule
3. Amber glass bottle and ampule, used for liquid and injection
4. Clear glass ampule and vial, used for injectables
5. Aluminium collapsible tubes, used for cream and ointment.

## **Equipments used**

1. Horn Noack Blister Packer (Germany)
2. E. TH Noack Blister Packing Machine ( Germany)

3. Klockner Hansel Blister Packer (Germany)
4. Hoong A Blister Packer

## Flow of Packaging procedure



## Printing

Printing unit is essential to print batch no., mfg date, exp date, MPR of each product on label, cartoon, outer label etc.

This unit consists of several overprinting machines that are semi automatic and manual:

1. Manna- Model- MAPL
2. Imprintamatic
3. MACs
4. Marico
5. Code-O – Matic

## List of imported finished products packed in this section

1. Act-HIB injectables: Hoemophilus type B conjugate vaccine
2. Actonal 5 mg tablet
3. Azmacort inhaler 20gm
4. Avaxim 80: Hepatitis A child vaccine
5. Avamix 160: Hepatitis A vaccine (inactivated)
6. BCG vaccine, freeze dried
7. Compto 40mg injection
8. Compto 100mg injection
9. Clexane 2000 anti-Xa i $\mu$ / 0.2ml
10. Clexane 4000 anti-Xa i $\mu$ / 0.4ml
11. Clexane 6000 anti-Xa i $\mu$ / 0.6ml
12. Clexane 8000 anti-Xa i $\mu$ / 0.8ml
13. Endoxan ASTA 200mg
14. Endoxan tablet 50mg
15. Endoxan ASTA 500mg
16. Endoxan ASTA 1gm
17. Granocyte 34
18. Haemacel infusion
19. Holoxan injection 500 ml

20. Holoxan injection 1gm
21. Holoxan injection 2gm
22. Honvan injection
23. Honvan tablet
24. Immucyst injection 81mg
25. Insuman Basal 100 i $\mu$ / ml
26. Insuman Rapid 100 i $\mu$ / ml
27. Insuman Comb 100 i $\mu$ / ml
28. Intal 5 inhaler
29. Lantus 100 i $\mu$ / ml solution for injection
30. Meningoccal A+C vaccine
31. Nasacort AQ nasal spray
32. Paluther 80mg injection
33. Streptase 1500000i $\mu$
34. Succinyl siccum 500mg
35. Taxotere 20mg
36. Taxotere 80mg
37. Tetavax injectable: Absorbed Tetanus vaccine
38. Tilade inhaler
39. Transamin 500mg tablet
40. Transamin 250mg injection
41. Transamin 500mg capsule
42. Trimovax: Measles, mumps and rubella vaccine
43. Uromitexan 400mg injection
44. Verorab injectable: Rabies vaccine (vero cell)

# CPR

Sanofi Aventis being a multinational pharmaceutical company in Bangladesh is renowned for manufacturing quality antibiotic products. It follows cGMP, and according to that the antibiotics has to be manufactured in isolated area from that of the non-antibiotics, to prevent cross contamination and resistance development. Sanofi Aventis has a separate building named CPR ( C= Cephalosporin, P= Penicillin, R= Refampicin) where three different types of antibiotics are produced in three separate premises. These three premises are completely isolated from each other regarding the following the features:

- Different HVAC system
- Three different water treatment plant
- Gowning
- Manufacturing area
- Packaging
- Ware house
- QC lab
- Waste management tank
- Non pharmaceutical activity
- Official activity

By following the above mentioned features Sanofi Aventis is able to maintain the quality of antibiotics. And that is why multinational company like Novartis and local company Beximco gave them the offer of toll manufacturing.

## Penicillin Section

### Types of products

1. Capsule
2. Tablet
3. Dry powder
4. Pediatric drops
5. Dry powder for injection

## Equipments used

1. Drum blender (England)
2. Clinocone ( India)
3. Cube mixture ( England)
4. J.G Jackson & croikatt granulator (England)
5. Apex Granulator ( England)
6. Manesty oscillating granulator ( England)
7. Manesty petrie dryer ( England)
8. Manesty B3B (16 punch) rotary tablet machine ( England)
9. Manesty B3B (23 punch) rotary tablet machine ( England)
10. Manesty D3A rotary tablet machine ( England)
11. Automatic film coating machine (Thailand)
12. Zanasi AZ20 capsule filling machine (Italy)
13. Zanasi AZ40 capsule filling machine (Italy)
14. Zanasi MG2 capsule filling machine (Italy)
15. Arenco auger filler
16. Hauser filling machine (Korea)
17. Getinge autoclave (Sweden)
18. Hot air depyrogenation oven (Taiwan)
19. Bottle dryer
20. Hoong A blister packer
21. Gansons strip packer (India)
22. E. Th Noack strip packer (Germany)
23. Imperial electric & gas appliances Co. dehumidifier
24. Automatic bottle labeling machine (Taiwan)
25. Rotary bottle washer
26. Strunck vial washing machine (Germany)
27. P+AM capsule filling machine ( India)



## Equipments used in Penicillin Lab

1. Polarimeter
2. Moisture analyzer
3. Chomato UV E cabinet
4. Hot water bath
5. Ultrasonic vibration
6. Karl fisher titrator
7. Disintegration tester
8. Dissolution tester
9. Friability tester
10. Vacuum oven
11. Unicom UV/ Vis spectrophotometer
12. Genesis series IR
13. HPLC
14. Electronic balance
15. Refrigerator

## Use of personal protection clothing and wears

A chart is made where the decisions are taken which parameters are to be maintained in which operations:

### Solid Manufacturing

Shop	Operation	Cap	Mask	Arm Cover	Gloves	Shoes	Safety Glass	Ear Muff
Granulation	Dispensing	√	√	√	√	√		√
	Mixing	√	√	√	√	√		√
	Solution preparatio	√	√	√	√	√		√

	n							
	Drying	√	√	√	√	√		√
	Sieving & blending	√	√	√	√	√		√
	Cleaning	√	√			√		
Compression	Hopper charge	√	√	√	√	√		√
	Compression	√	√	√	√	√		√
	In process test	√	√	√	√	√		
	Cleaning	√	√			√		
Coating	Solution preparation (aqueous)	√	√	√	√	√		√
	Solution preparation (organic)	√	√	√	√	√	√	√
	Charging/Discharging	√	√	√	√	√		
	Cleaning	√	√			√		
Capsule filling	Hopper charging	√	√	√	√	√	√	
	In process test	√	√	√	√	√	√	
	Cleaning	√	√			√		

### Liquid & Cream Manufacturing

Shop	Operation	Cap	Mask	Arm Cover	Gloves	Shoes	Safety Glass	Ear Muff
Oral liquid	Dispensing	√	√	√	√	√		
	Syrup preparation	√	√	√		√		√
	Mixing	√	√	√	√	√		√
	Filter setting	√	√			√		
	Filtration of syrup/ elixir	√	√			√		
	Filtration of suspension	√	√	√	√	√		
	Cleaning	√	√			√		
Topical liquid	Dispersion of oil phase	√	√	√	√	√	√	
	Dispersion of aqueous phase	√	√	√	√	√	√	
	Emulsification	√	√	√	√	√	√	
	Transfer	√	√	√	√	√	√	
	Cleaning	√	√			√	√	
Cream & suppository manufacturing	Dispersion of oil phase	√	√	√	√	√	√	√
	Dispersion of aqueous phase	√	√	√	√	√	√	√
	Emulsification	√	√	√	√	√	√	√
	Homogenization	√	√	√	√	√	√	
	Transfer	√	√	√	√	√	√	√
	Cleaning	√	√			√	√	√

### Sterile Manufacturing

Operation	Cap	Mask	Arm Cover	Gloves	Shoes	Safety Glass	Ear Muff
Distilled water plant	√	√			√		
Solution preparation	√	√	√	√	√		
Mixing	√	√	√	√	√		
Filtration	√	√	√	√	√		
Sealing	√	√	√	√	√		
Sterilization	√			√	√		
Inspection	√				√		

## Cleaning of Penicillin manufacturing area

### Special Instructions followed for the cleaning purposes

1. Freshly prepared disinfectant or detergent solutions are used in the same day of preparation.
2. Non shedding materials are used for any cleaning purpose.
3. The safety of all equipment and products are ensured from dirt, water, detergent or disinfectant at the time of cleaning.

### Types of cleaning and preparation of disinfectant solutions

- a. Savlon solution (17.5 % v/v)

To prepare 1000 ml solution 175 ml of Savlon is added into 825 ml of PW

Dettol solution (2.5 % v/v)

To prepare 1000 ml solution 25 ml of Dettol is added into 975 ml of PW

Sodium Hypochlorite solution ( 0.25 % v/v)

To prepare 1000 ml solution 0.25% solution from a 5% solution, 50 ml of the 5% solution is mixed with 950 ml of PW.

- b. The containers of the detergent or disinfectant solution are labeled properly with name, strength and date of preparation.
- c. Cleaning is of two types: A) Normal B) Gross.

## **Critical and acceptable parameters**

Savlon, Dettol, Hypocholite and IPA solutions are prepared with care. Acceptable percentages are 17.5, 2.5, 1 & 70% respectively.

# Frequency:

Savlon is used in first and third week and Dettol is used in second and fourth week in the month. Sodium hypochlorite solution is used in case of gross cleaning.

## **Room inspection checklist**

Parameters observed in case of room inspection are:

1. No insect dents etc within the room.
2. No dust, shoot, cob web, fungus etc on
  - a. Equipment/ furniture/ cabinet
  - b. Floor/ wall/ ceiling
  - c. Door/ glass
  - d. Extinguisher/ fire hose
  - e. Diffuser/ return air grill
3. No crack, dent, blister, rust, deterioration of paint on:
  - a. Equipment/ furniture/ cabinet
  - b. Floor/ wall/ ceiling
  - c. Door/ glass
4. Function of smoke detectors
5. No leakage from
  - a. Water/ steam/ compressed air/ vacuum/ gases/ lubricant
6. No broken
  - a. Electrical phev socket/ swich

- b. Conduit/ light cover
7. Proper label on equipment
8. Overall tidiness

## Cephalosporin Section

### Types of products

1. Capsule
2. Tablet
3. Dry powder for syrup
4. Pediatric drop
5. Dry powder for injection

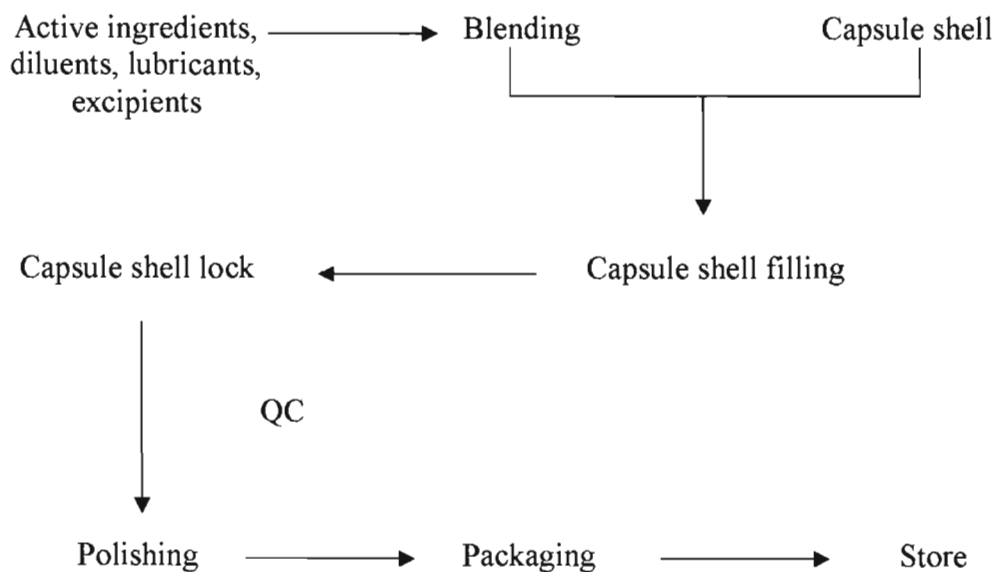
### Equipments used

1. Drumm blender (England)
2. Rotogran
3. Rotary bottle washing machine
4. Bottle dryer
5. Rotary vial washer (Taiwan)
6. Getinge autoclave (Sweden)
7. Hot air oven
8. Imperial electric and gas oven
9. Zanasi AZ20 capsule filing machine (Germany)
10. Gansons strip packer
11. OTTO Hansel vial blister packer
12. Jaganberg Wene AG labeling machine (Germany)
13. Automatic bottle labeler

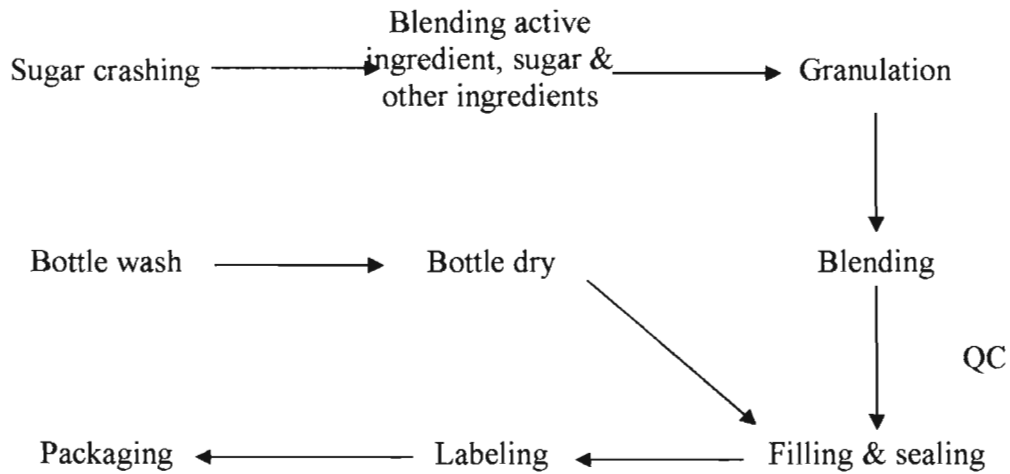
### Equipments used in Cephalosporin Lab

1. UV/ vis spectrophotometer
2. Analytical balance
3. Dissolution tester
4. Thermonic DT machine
5. Oven
6. Kerry ultrasonic bath
7. Thermonic bulk density apparatus
8. Dissolution tester six vessels
9. Refrigerator
10. Karl fisher titrator
11. Thermonic friabilator
12. HPLC
13. pH meter

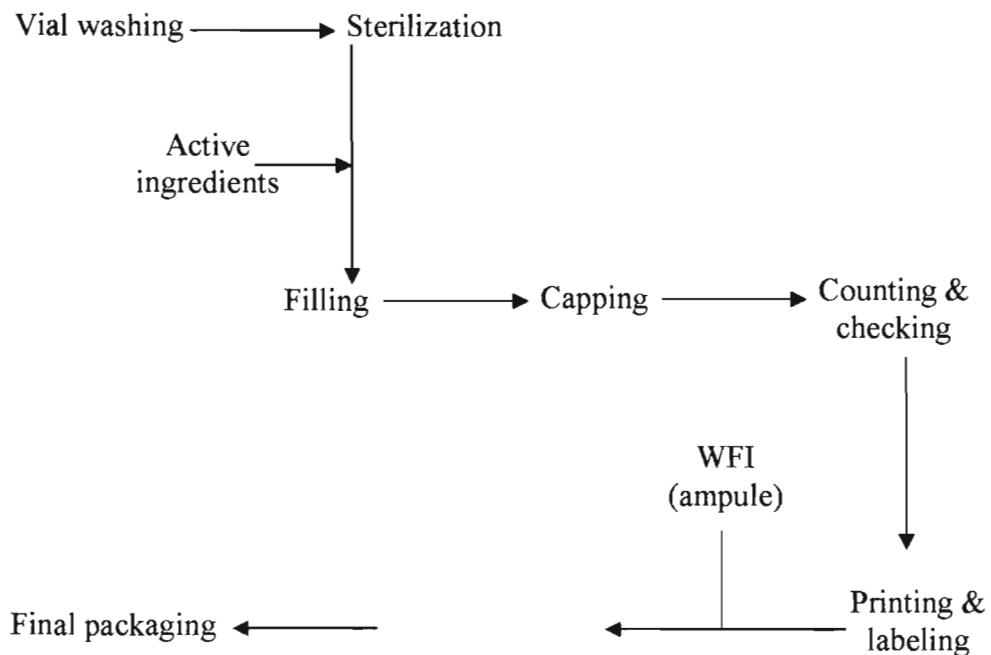
### Flow chart for capsule manufacturing and filling



## Flow chart for manufacturing of dry powder for syrup



## Flow chart for manufacturing of dry powder for injection and pediatric drops



## Cleaning of Cephalosporin manufacturing area



**Preparation of solution:**

- Savlon solution ( 17.5% v/v)

2L of PW was taken in a bucket and 880 ml Savlon was added. And then the volume was made upto 5 L with PW.

- Dettol solution ( 2.5% v/v)

3 L PW was taken in a bucket and 125 ml of Dettol was added. And then the volume was made upto 5 L with PW.

- Sodium Hypochlorite solution ( 1% v/v)

192 ml of the 3.25% solution was mixed with 808 ml of PW to make the volume 1 L.

- Sodium Lauryl Sulfate solution ( 0.5% w/v)

500 ml of Sodium Lauryl Sulfate was mixed with 1 L PW.

- Sodium bicarbonate solution (10% w/v)

10 gm of Sodium bicarbonate powder was mixed with 1 L PW.

- IPA (Iso propyl alcohol) solution ( 70% v/v)

700 ml of IPA was mixed with 1 L PW.

**Container:**

Disposable drum, polyethene bag etc are cleaned by 10% sodium bicarbonate or 3% ammonia.

**Gowning:**

100 ml of 10% sodium bicarbonate or ammonia in washing tank, MOP solution and IPA is sterilized by 0.2  $\mu$  cartridge filter.

**Some special features:**

Fumigation: To revalidate the aseptic area fumigation is done by 37% formaldehyde with water in 1:1 ratio. As fumigation is highly carcinogenic fumigation is done at least twice in a year according to corporate guideline. Sanofi Aventis is able maintain the aseptic area by taking precaution other than fumigation such as proper HVAC, LAF, personnel etc.

Decontamination: Antibiotic molecules present in the waste is treated by; first it is decontaminated, i.e. the  $\beta$ -lactum ring is broken down by adding 1.5 L of 25% ammonia solution twice daily on working days.

## **Parameters checked in Cephalosporin Lab to maintain the quality of the product**

In case of syrup/ suspension/ cream/ injectables:

1. Appearance
2. Odor
3. Identity
4. Color/ particulate matter
5. Average weight/ volume
6. Preservatives
7. pH
8. Miscibility with water/ consistency/ viscosity
9. Nitrate/ RI
10. Weight per ml
11. Microbial content/ Endotoxin test
12. Moisture/ water
13. Assay

In case of Raw Materials:

1. Appearance
2. Solubility
3. Identification
  - a. IR test
  - b. Sodium test
4. Clarity and color of solution
5. pH
6. Water (Karl Fisher Method)
7. Reconstituted solution
8. Assay

9. Sterility test
10. Bacterial endotoxin test
11. Particulate matter test
12. Particle size:
  - a. 100% pass \_\_\_\_ mm sieve
  - b. 73% pass \_\_\_\_ mm sieve
  - c. 55% pass \_\_\_\_ mm sieve
13. Specific optical rotation
14. Absorbance
15. Sulphated ash
16. Related substances
17. N,N-Dimethylamine

In case of Capsule:

1. Appearance
2. Identity
3. Disintegration time
4. Weight of 20 capsules
5. Individual weight of 20 capsules
6. Weight % deviation from average weight
7. Moisture content
8. Assay
9. Chemical potency
10. Stated dose
11. Uniformity of weight

## Rifampicin Section

### Types of products

1. Capsule (no longer manufactured)
2. Tablet

## **Equipments used**

1. Cadmill (India)
2. Drum blender
3. Rotogran MK III (England)
4. Sapphire fluid bed dryer
5. Jaguar high speed mixer granulator (India)
6. RAMA COTA coating machine (Thailand)
7. Manesty RD3 (16 punch) rotary tablet machine (England)

## **List of products manufactured in CPR section**

1. Enocéf injection + Ligno 500 mg IM vial
2. Enocéf injection + Ligno 250 mg IM vial
3. Enocéf injection + Ligno 1 gm IM vial
4. Enocéf injection + Ligno 1 gm IV vial
5. Enocéf injection + Water 250 mg IV vial
6. Enocéf injection + Water 500 mg IV vial
7. Epilim chrono 200 tablet
8. Epilim chrono 300 tablet
9. Epilim chrono 500 tablet
10. Epilim syrup
11. Ficillin cap 250 mg
12. Ficillin paed drop
13. Ficlox cap
14. Ficlox inj + water
15. Ficlox paed drop
16. Ficlox syrup
17. Fimoxyclav inj 0.6 gm
18. Fimoxyclav inj 1.2 gm
19. Fimoxyclav syrup
20. Fimoxyclav tab 375 mg
21. Fimoxyclav tab 625 mg

22. Fimoxyl 250 mg tablet
23. Fimoxyl 500 mg tablet
24. Fimoxyl cap 250 mg
25. Fimoxyl cap 500 mg
26. Fimoxyl DS syrup
27. Fimoxyl inj + water 500 mg
28. Fimoxyl inj + water 250 mg
29. Fimoxyl paed drop
30. Fimoxyl syrup
31. Firifam tab 450 mg
32. Firifam tab 150 mg
33. Firifam cap 250 mg
34. Fluxon cap 500 mg
35. Oracin 'k syrup
36. Oracin 'k tablet 250 mg
37. Oracin 'k tablet 500 mg
38. Pen-V 500 mg tablet
39. Pen-V syrup
40. Pen-V tablet
41. Rifazid 300 + Z tablet
42. Rifazid 450 + Z tablet
43. Rifazid tablet 300 mg
44. Rifazid tablet 450 mg
45. Rifazid tablet 150 mg
46. Sefdar cap 500 mg
47. Sefdar cap 250 mg
48. SefdarDS syrup
49. Sefdar inj + water 500 mg
50. Sefdar inj + water 1 gm
51. Sefdar inj + water 250 mg
52. Sefdar paed drop
53. Sefdar syrup
54. Sefrox 750 inj

- 55. Sefrox syrup
- 56. Sefrox 125 tablet
- 57. Sefrox 250 tablet
- 58. Sefrox 500 tablet

**List of products manufactured in this section for other companies**

**Product list of Beximco**

Product name	Dosage form	Active ingredient
Arixon	IV injection 250 mg IV injection 500 mg IV injection 1 gm IM injection 250 mg IM injection 500 mg IM injection 1 gm	Ceftriaxone Sodium Sterile
Enytracef	Injection 250 mg Injection 500 mg injection 1 gm	Cephradin with Arginine Sterile

**Product list of Novartis**

Product name	Dosage form	Active ingredient
Megion	IV injection 250 mg IV injection 500 mg IV injection 1 gm IM injection 250 mg IM injection 500 mg IM injection 1 gm	Ceftriaxone Sodium Sterile

# Hoechst Marion Roussel

The Hoechst Marion Roussel building is a complete unit for solid dosage form. Mainly tablet is manufactured here, with includes compression, coating, packaging, and the sugar coated tablets are manufactured in only this section of the company. HMR building is well equipped with proper production facilities.

### **Equipments used**

1. Sruti dry/ wet granulating machine (India)
2. Sapphire fluid bed dryer (India)
3. Diosna mixture granulator
4. Alexander wet screening machine
5. Electric dryer
6. Frewitt-Zimmermann oscillator
7. Cadmach roll compactor
8. Manesty rotapress MKII compression machine (England)
9. Cadmach CMB 4 tablet compression machine (India)
10. Heracus TU 2 drier
11. Leak test apparatus (India)
12. Colloid mill
13. UPS blister packer machine
14. Jaguar strip sealing machine (India)

### **List of products manufactured in this section**

:

1. Avil tablet 22.7 mg
2. Avil retard tablet 75 mg
3. Daonil tablet 5mg
4. Lasix tablet 40 mg
5. Frisium tablet 10 mg
6. Trentol tablet 400 mg



# Industrial Quality & Compliance

IQC Department is very important for a pharmaceutical industry to maintain **GMP**. The concept of total quantity management and total quality control refers to the process of striving to produce a perfect product by a series of **measures** requiring an organized **afford** by the entire company to prevent or eliminate errors at every stage in production.

Although the responsibility for assuring product quality belongs principally to IQC, it involves many departments and disciplines within the company. To be effective it must be **supported** by a team effort.

The IQC dept. is a vital part for a pharmaceutical industry since it controls and assures for quality of the products starting from the raw materials to the finished product till the customers consume it.

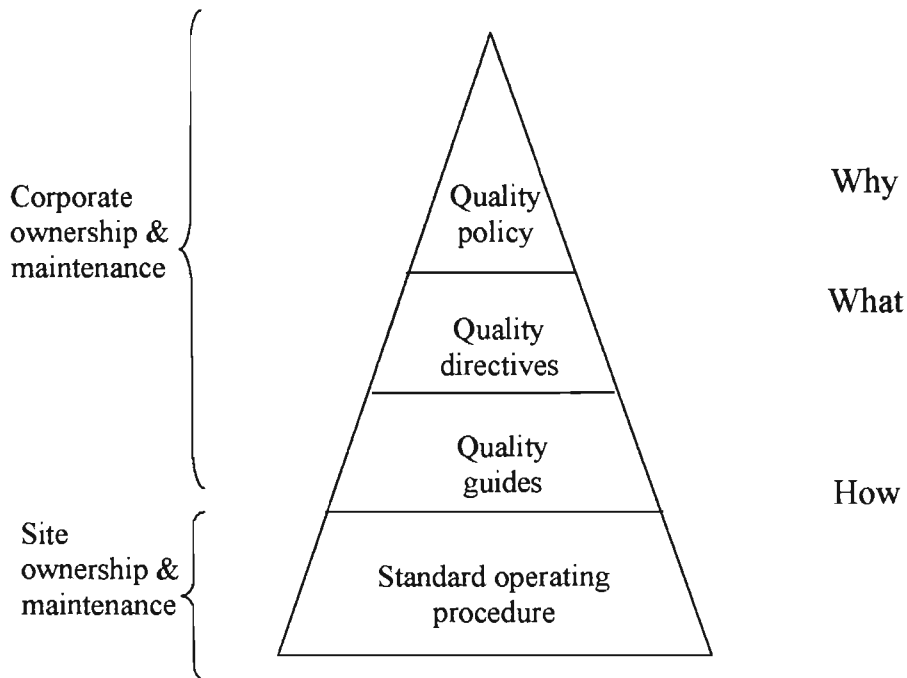
All kinds of necessary steps are **taken** by this department to serve a quality product to the end users.

A pharmaceutical product must **satisfy** certain standards to claim its quality.

The main criteria of any drug, in dosage form are:

- a. Safety
- b. Potency
- c. Efficiency
- d. Stability
- e. Acceptance
- f. Regulatory compliance

## Industrial quality manual



## IQC performance

- KPI: Right first time
- KPI: Validation achievement
- KPI: Product technical complaint
- KPI: Quality cycle time
- KPI: Quality cost

## The IQC department is divided into 5 sections

1. Quality control
2. Quality assurance
3. Analytical support and analytical development
4. Quality assurance regulatory liason
5. Microbiology

## Equipments used in IQC Lab

1. Hardness tester
2. Friability
3. Automatic refractometer
4. Vacuum oven
5. Total organic carbon analyzer
6. Total organic carbon generator
7. Water purifier
8. Conductivity meter
9. Dissolution tester
10. Disintegration tester
11. Analytical balance
12. Karl fisher
13. Viscometer
14. Potentiometric titrator
15. Electromagnetic sieve shaker
16. TLC
17. Centrifuger
18. Alliance HPLC
19. Shimadzu HPLC
20. Vacuum pump
21. Moisture balance
22. FTIR
23. Micro melting point apparatus
24. UV/ vis spectrophotometer
25. Electric oven
26. Refrigerator
27. Hotspot furnace ( oven sulfated ash)
28. Drying oven
29. Muffle furnace
30. Magnetic stirrer hotplate
31. Dissolution oxygen meter

32. Stability chamber
33. Ultrasonic bath
34. Compactometer
35. Eight channel plastic counter
36. LAF cabinet
37. Fume cupboard

## **Quality Control Department**

QC is one of the vital factors in any pharmaceutical company. Quality control can be defined broadly as the regular control of quality ensured by pharmacist, and technicians responsible for the acceptance or rejection of incoming **raw materials and packaging components**, in the Q.C for in-process tests and inspections, to assure that systems are being controlled and monitored.

Quality control, therefore, includes not only the analytical testing of the finished product, **but also the assessment of all operations beginning with the receipt of raw materials and continuing throughout the production and packaging operations, finished product testing, documentation, surveillance.** QC must select vital points to include parameters for effective quality assurance.

### **QC is responsible for**

1. Analytical testing of RM
2. Inspection of PM
3. In-process control (IPC)
4. Testing of finished products

### **Analytical tests performed for RM**

1. Appearance
2. Odor
3. Solubility
4. Identity
5. pH
6. Water content
7. Residue on ignition
8. Heavy metals
9. Sulfates
10. Assay
11. Limit of fluoroquinolonic acid
12. Chromatographic purity
13. Refractive index
14. Acidity/ alkalinity
15. Viscosity

## **Packaging material control**

For ensuring quality of the end product the packaging components must be of right quality. For this the following parameters are checked:

- A. PVC/ PE/ PVdC film for blister packing
  1. appearance
  2. visual inspection
  3. dimensions
  4. adhesion of PVdC coating
  5. presence of PVdC coating
  
- B. Unprinted polythene laminated aluminum foil
  1. Appearance
  2. Visual inspection
  3. Dimensions
  4. GSM of foil
  5. GSM of polythene film

---

## 6. Adhesion of polythene film

### C. Label

#### 1. Appearance

#### 2. Visual inspection for detection

- Critical:
  - Layout, color or text not as approved at work
- Major:
  - Printing missing, print smeared, partial print
- Minor:
  - Shade variations outside agreed tolerance
  - High print outside agreed tolerance
  - Light print outside agreed tolerance
  - Sport or streaks in print outside agreed tolerance
  - Partial print
  - Print blurred

#### 3. Text

#### 4. Dimension

#### 5. Material

### D. Printed cartons

#### 1. Appearance

#### 2. Visual inspection

- Critical:
  - Foreign carton, layout, color or text not as approved at work
- Major:
  - Printing missing, print smeared, partial print
- Minor:
  - Shade variations outside agreed tolerance
  - High print outside agreed tolerance
  - Light print outside agreed tolerance
  - Sport or streaks in print outside agreed tolerance

- Partial print
- Print blurred

- 

3. Text
4. Dimension
5. Material
6. Squareness of carton
7. Performance work
8. Color fastness

#### E. Leaflet

1. Appearance
2. Visual inspection for detection
  - Critical:
    - Layout, color or text not as approved at work
  - Major:
    - Printing missing, print smeared, partial print
  - Minor:
    - Shade variations outside agreed tolerance
    - High print outside agreed tolerance
    - Light print outside agreed tolerance
    - Sport or streaks in print outside agreed tolerance
    - Partial print
    - Print blurred

3. Text
4. Dimension
5. Material

#### F. Printed aluminium/ polyethylene foil:

1. Appearance
2. Visual inspection for detection
  - Critical:



- Layout, color or text not as approved at work
- Major:
  - Printing missing, print smeared, partial print
- Minor:
  - Shade variations outside agreed tolerance
  - High print outside agreed tolerance
  - Light print outside agreed tolerance
  - Sport or streaks in print outside agreed tolerance
  - Partial print
  - Print blurred

3. Dimensions

4. GSM of foil

5. GSM of polythene film

6. Adhesion of polythene film

G. Alu collapsible tubes:

1. Appearance

2. Text

3. Visual inspection for defects

- Critical:
  - Incorrect print color, foreign tubes, incorrect cap
- Major A:
  - Badly dented or damaged tube
  - Caps internal contamination with foreign matter
  - Thread metal nozzle containing loose metal shivers or particles
  - External enamel cracking or flaking
  - Internal contamination of tube with dirt or foreign matter
  - Cap missing
- Major B:
  - External contamination with dirt or foreign matter
  - Unevenness on outer surface

- Minor:
  - Minor dents in tube bodt
  - Color or print outside agreed tolerance
  - Decorating defect visible on close examination
  
- 4. External lacquered
- 5. Cleanliness check
- 6. Dimension
- 7. Average weight
- 8. Capacity
- 9. Material
- 10. Sealing condition of nozzle top
- 11. Crimping condition of tube
- 12. Performance check
  - Spike
  - Cap
  
- H. Ampule closed, clear, type 1 glass printed
  - 1. Appearance
  - 2. Symmetry and firmness check
  - 3. Text
  - 4. Visual inspection for defects
    - a. Mfg defects
    - b. Printed defects
  - 5. Dimensions
  - 6. Hydrolytic resistance
  - 7. Break force
  
- I. Bottle for Flagyl 100ml injection type II glass
  - 1. Appearance
  - 2. Visual inspection
  - 3. Dimensions
  - 4. Weight

5. Capacity
6. Hydrolytic resistance

**J. Vials, clear type 1 glass for antibiotic injection (tubular)**

1. Appearance
2. Visual inspection
3. Dimensions
4. Weight
5. Capacity
6. Hydrolytic resistance

Other than these, tests are also performed on several other materials (according to Standard Methods):

1. Ampule closed, amber, type I glass printed
2. Unprinted alu foil, coated for blister packaging tablets and capsules
3. R. O. P. P alu cap for pharmaceutical bottles
4. Glass bottle for oral preparation and vial for injection, type III glass
5. HDPE plastic container
6. PVC film for blister packing
7. Rubber plug for injection/ bottle vial
8. Flip off seal for injection Flayyl bottle/ vial
9. Printed alu. foil, coated for blister packing tablets, capsule and injection
10. Plastic plugs
11. Disposable plastic syringe with needle
12. Unprinted PVC/ alu./ OPA foil for blister packers

## **In Process Control**

IPC is done during the course of manufacturing which aims to ensure that products manufactured complies with the specifications of Sanofi Aventis:

- A. Tablet section:
1. Weight variation
  2. Disintegration

3. Friability
4. Dissolution
5. Hardness
6. Thickness
7. Diameter

B. Capsule section:

1. Moisture content
2. Weight variation
3. Sealing

C. Sterile:

1. Supervised by operators whether they complies or not with the SOP's

D. Packaging section:

1. Label check
2. Carton check (randomly)
3. Blister sealing check/ leak check

E. Syrup section:

1. Flavor
2. pH
3. Viscosity
4. Assay
5. Microbial counts
6. Volume
7. Weight per ml at 20° C

## Quality control for finished products

These tests are performed to determine compliance with specifications and hence are critical factor for the QA department. These testing procedures are

established in on an equally sound and recognized basis, and the entire system is enormous. In Sanofi Aventis the following parameters are checked:

1. Lot no./ Batch no.
2. Date of receive
3. Date of test
4. Appearance
5. Odor
6. Identity
7. Length/ diameter )mm)
8. Thickness (mm)
9. Presence of coating
10. Friability
11. Percent stated dose
12. Calculated weight (gm)
13. Total weight of 20 tab/ cap content (gm individual)
14. Average weight (gm)
15. Maximum individual deviation
16. Disintegration
17. Dissolution
18. Related substances
19. Moisture content
20. Assay

## Quality Assurance Department

Drugs which do not comply to the given standards, are considered as substandard. Drugs become substandard due to

- (1) Faulty formulation,
- (2) Faulty processing,
- (3) Unsatisfactory packaging and unfavorable conditions of handling during transportation or storage. because drugs are used in human beings, Therefore their quality assurance is essential.

Quality assurance program is the devise and implement systems and procedures that provide a probability that each dose or package of a product will have homogenous characteristics and properties to ensure both safety and efficacy of the formulation.

In order to achieve the quality objective a wide range of activities are involved

- A. Ensuring fulfillment of regulatory requirements
- B. Establishment specification and control procedures for all starting materials, intermediates and finished products
- C. Arranging quality audit visits to suppliers and self inspection
- D. To ensure implementation of GMP
- E. Establishing manufacturing methods and SOP's and their regular up gradation
- F. Communication of every aspects relating to quality to all relevant persons for early positive action
- G. IPC and their implementations
- H. Identification of high risk areas of contamination or action
- I. Batch determination system, reviewing data and assaying problems
- J. Working closely with relevant department for validation of equipment, process, control procedures and critical systems
- K. Marketing complaints for actions
- L. Rejection trend analysis and actions
- M. Identifying problems and positive actions for error cause removal
- N. Ensuring adequate training programs

## Documentation

During the course of producing a pharmaceutical product, numerous documents and records are generated. Each batch is assigned a specific code or lot numbers which include data on each significant phase of production, control and distribution.

The batch record provides a historical blueprint of every step, starting from the receipt of chemical raw materials and packaging components. Recording charts or computer printouts of significant operations such as autoclaving, drying, air-particulate monitoring, lyophilizing, etc; all are the part of the batch history.

Each required document must be checked for completeness and accuracy. When the batch is released, accurate shipping records must be maintained.

Documentation is a vital part of GMP to get approval from not only our country but also to get approval from FDA. In Sanofi Aventis first a Process Order (material list) is prepared then at last from QA a transfer note is given for release. After that all the documents are kept for more than one year than the expiry date of the product.

Parts of documentation:

- PTC (product technical complaint)
- Change control
- Deviation
- OOS (out of specification)

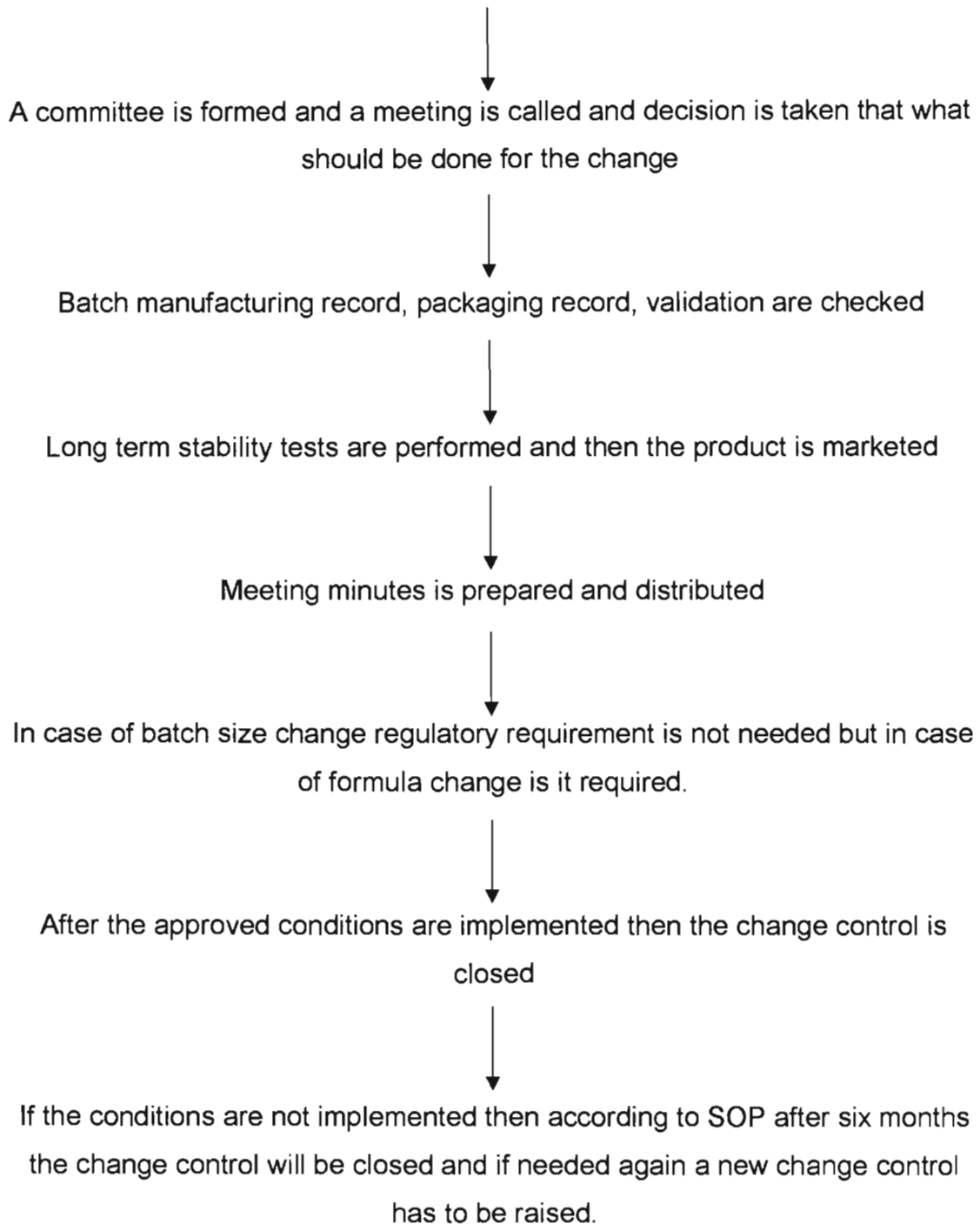
## Change control

### Operation procedures of change control

It is done for any permanent change

According to need a change order can be raised by any department (for example: solid section wants to reduce batch size of product from 120 kg to

70 kg)  
↓  
Sent to QA



## Product technical complaints (PTC)

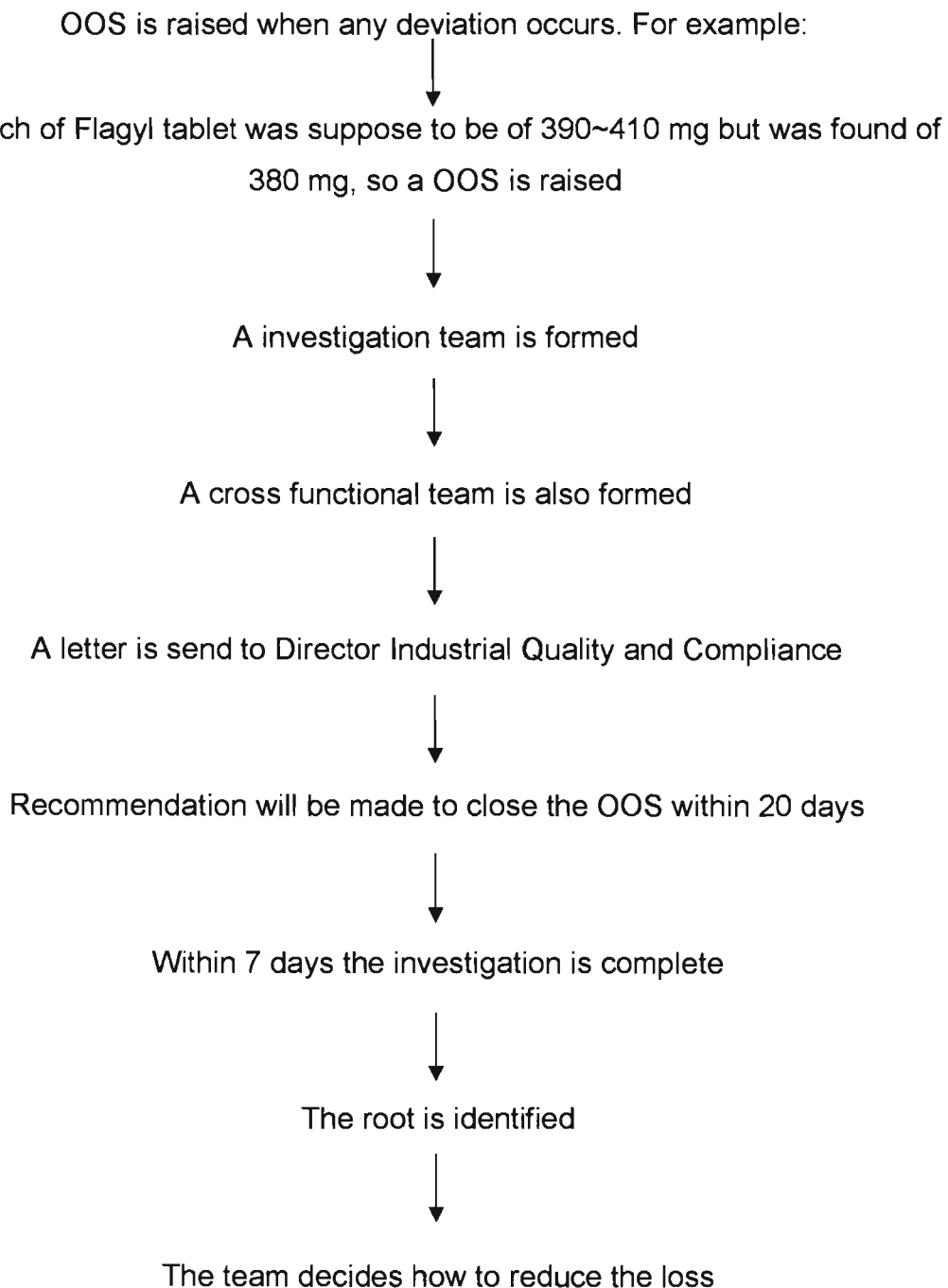
In case of a problem in printing or any other example: the batch no. is not clear on the strip and was detected by IPC and then those are checked thoroughly. Then by doing statistical analysis the percent is verified and if it is within the limit then the batch can be marketed.

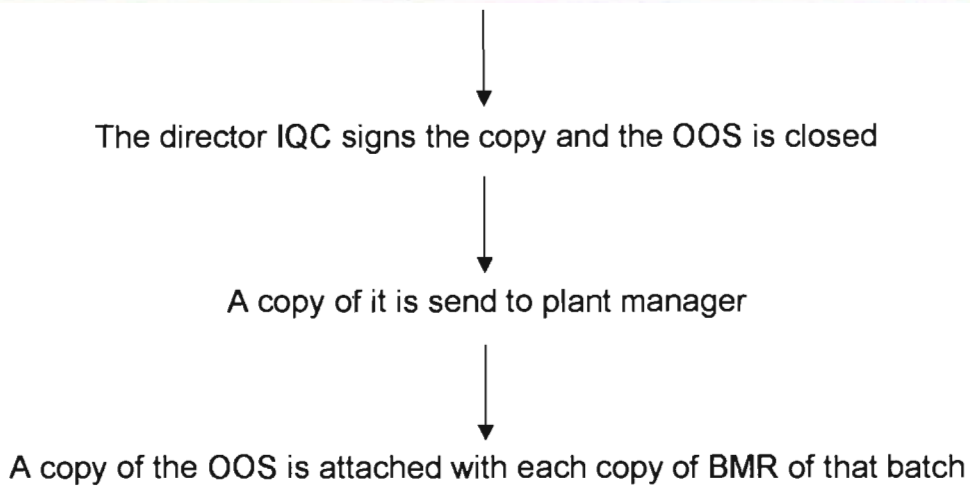


Now, if any complaint comes from market then a form is filled and team of two is formed combining a person from QA and one from production. And all the documents are filed and distributed to the respective/ related authorities.

## Out of Specification (OOS)

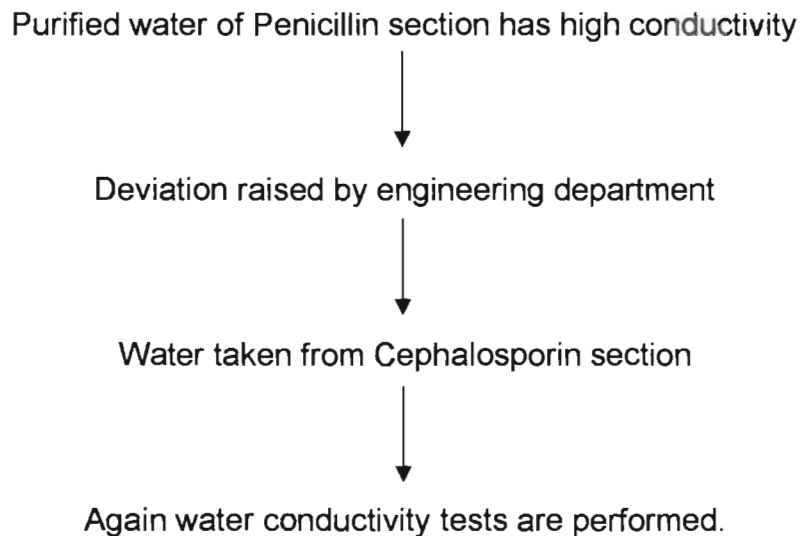
### Operation procedures of OOS





## Deviations

If a punch or a hopper breaks or a machine becomes out of order or any other this type of problem occurs then deviation rises. For example:



## Quality Assurance Regulatory Liaison

QARL is a very important section of QA department. Major responsibilities of this section are:

- A. Establishing drug administration license for five years.
- B. Elixir formula control
- C. Recipe control
- D. Formulation change control
- E. Microbiological system control

To grant permission for the production of drugs a pharmaceutical companies need a license, from Drug administration.



One company can have two license numbers, one for the biological products (vitamin, injectables, and antibiotics) and another one for non-biological products.



Every two years the license is renewed. When a product is included under a license it is validated for five years. And after five years it is renewed.



Now, if any product's formula is changed then amendment is done. And the paper of the new formula's stability tests also has to be submitted to drug administration. If the size of the pack has to be changed then also permission has to be granted.

## Operations performed to take permission for new product

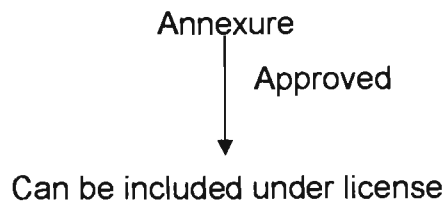
Recipe (if from BP or USP then no sample has to be submitted but if from some other source sample has to be submitted)

↓ Approved

↓ Stability study

↓ Packaging documents





When the product is marketed then from the 1<sup>st</sup> batch samples has to be sent to drug administration.

Drug administration comes for inspection and may give some terms and conditions for the improvement of GMP, manufacturing facility etc.

## Analytical Support and Analytical Development

It is also a very important section in IQC. This department does liaison with the research and development staff in the introduction of new products and solving of production and testing difficulties. It can be done by following two methods:

1. Stability testing
2. Analytical method development

Purpose of stability testing:

1. What is the condition of the product?
2. Increase the shelf-life

These tests are done on the follow types of products:

1. Marketed products
2. New products
3. Products under change control

Functions of ASAD:

1. New product method development
2. New product stability

3. Marketed product stability
4. Analytical method development

## Stability programs

Categorization of stability programs:

1. Development of new products
2. Routine support of a currently marketed products
3. Change control and/ or failure investigation when required

1. Development of new products:

Selection of batches:

- a) For conventional dosage form (immediate release solid dosage forms, solution) and when the active ingredient are known to be stable, stability data on at least two pilot batches are acceptable.
- b) For critical dosage form (prolonged release form) or when the active ingredient are known to be unstable, stability data on at least three pilot batches are required.

Test frequency and duration:

Frequency of testing should be sufficient to establish characteristics of the drugs substance. Testing under the defined long term condition will normally be every three month, over the first year every six months over the second year and then annually

1<sup>st</sup> year: 0, 3, 6, 9, 12 months

2<sup>nd</sup> year: 18, 24 months

3<sup>rd</sup> year: 36 months

Storage test conditions:

The duration of studies and storage condition required are normally:

	Conditions	Minute, time period at submission
Long term testing	30° C ± 2° C/ 75% RH ± 5%	6 months 12 months
Short term testing	40° C ± 2° C/ 75% RH ± 5%	

The duration of studies and storage conditions required for temperature sensitive finished products are:

	Conditions	Minute, time period at submission
Long term testing	5° C ± 3° C	6 months
Short term testing	25° C ± 2° C/ 60% RH ± 5%	6 months

For liquid preparations in semipermeable containers the duration of studies and storage conditions are:

	Conditions	Minute, time period at submission
Long term testing	30° C ± 2° C/ 75% RH ± 5%	6 months
Short term testing	40° C ± 2° C/ 75% RH ± 5%	6 months

## 2. Routine support of a currently marketed product:

Test frequency and duration:

Minimum sampling and testing frequency

Category 1 Pharmaceutical products		Category 2 Pharmaceutical products	Category 3 New product on site/ products with variations	
Well proven stability. Real time data for more than three years. No more than minor degradation of potency during shelf life. No significant change of specification testing results. Site has produced routinely for at least three years. No major changes occurred during last three years.		For all other product not in category 1 or category 3.	Minor changes	Major changes
Sampling frequency	One lot per year. Two lots per year in case of high volume of products.	One lot per year. Two lots per year in case of high volume of products.	Minimum one lot	As required first three lots for new products or products new to the site
Long term stability testing frequency	At time 0 and expiration date	At time 0 and then annually until the expiration date	At time 0 and then annually until the expiration date	At 0, 3, 6, 9, 12, 18, 24, 30, 36, 48 and 60 months and at expiry date
Accelerated testing frequency			Not applicable	At 3 and 6 months

Storage test conditions:

The duration of studies and storage conditions required are normally:

	Conditions (retention room)	Minute, time period at submission
Long term testing	Temperature: 18° C - 40° C Humidity: 40-80 %	Shelf-life

2. Change control and/ or failure investigation when required:

Test frequency and duration:

Category 1 Pharmaceutical products		Category 2 Pharmaceutical products	Category 3 New product on site/ products with variations	
<p>Well proven stability. Real time data for more than three years. No more than minor degradation of potency during shelf life. No significant change of specification testing results. Site has produced routinely for at least three years. No major changes occurred during last three years.</p>		<p>For all other product not in category 1 or category 3.</p>	<p>Minor changes</p>	<p>Major changes</p>
Sampling frequency	<p>One lot per year. Two lots per</p>	<p>One lot per year. Two lots per</p>	<p>Minimum one lot</p>	<p>As required first three lots for new</p>



	year in case of high volume of products.	year in case of high volume of products.		products or products new to the site
Long term stability testing frequency	At time 0 and expiration date	At time 0 and then annually until the expiration date	At time 0 and then annually until the expiration date	At 0, 3, 6, 9, 12, 18, 24, 30, 36, 48 and 60 months and at expiry date
Accelerated testing frequency			Not applicable	At 3 and 6 months

Storage test conditions:

	Conditions	Minute, time period at submission
Accelerated testing	40° C ± 2° C / 75% RH ± 5%	6 months

## Validation of analytical procedures

Validation characteristics:

Validation characteristics	Minimum no.	Identification	Impurities		Assay
Specification	Not applicable	+	+	+	+
Linearity	5	-	+	-	+

Range	Not applicable	-	+	-	+
Accuracy	9	-	+	-	+
Precision					
Repeatability	6 or 9	-	+	-	+
Intermediate precision/ reproducibility	2 series	-	+	-	+
Detection limit	Approach dependent	-	-5	+	-
Quantization limit	Approach dependent	-	+	-	-

(+) normally evaluated

(-) normally not evaluated

#### Revalidation:

Evaluate the need for revalidation in case of change, for example: during transfer of an analytical procedure, significant variation in the active pharmaceutical ingredient sourcing, variation in the finished product, composition of the analytical procedure.

## Microbiology Department

For implementation of GMP microbiology department is very important. In Sanofi Aventis this department performs the followings

- a. Sterile products
  - i. Sterility testing
  - ii. Endotoxin testing
- b. Air velocity
  - i. Flow rate

- c. Laminar air flow system
  - i. Filter integrity testing
- d. Media test
  - i. Growth promotion test
- e. HVAC system
  - i. Heating condition
  - ii. Ventilation system
  - iii. Air conditioning system
- f. Estimation test for microorganisms
  - i. Control test
  - ii. Media test
  - iii. Sensitivity test
  - iv. Sterility test

## To ensure safety following operations are performed

### First

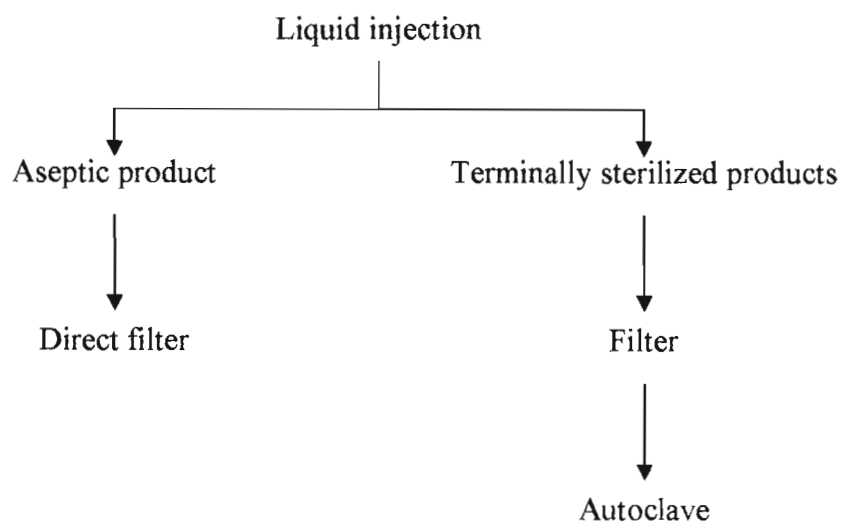
- ES (environmental safety)

Settle plate → Room soft test → Reinforce centrifugal sampler (RCS)

### Second

- Media test
  - o Fungus: dextrose, agar, soya agar
  - o Bacteria: TS (Triptosoya assay), agar

- **Sterility test**
  - Sterility testing ( bacteria 30-35° C in TGM, fungus 20-25° C in TSB)
  - Microbial count
  
- **Bioassay**
  - Minimum inhibitory count (MIC)
  
- **Water count**
  - Routine analysis
  
- **Bacteria**
  - Endocrine test by LAL test
  
- **Injection**
  - Free sterilization test



- **Oral preparations**
  - Allow 10,000 colony pathogenic organism

- Topical preparations
  - o Allow 100 colony non-pathogenic organism
  
- Machine test
- Appearance test
  - o Color and clarity
  
- Conductivity test
- pH
  - o pH within 5-7
  
- Nitrate
  - o Nitrate of all sample must be  $\leq 0.2$  mg/L

### **Equipments used**

1. Incubator
2. Air sampler
3. Anaerobic jar
4. Centrifuge machine
5. pH meter
6. Microscope
7. Laminar air flow machine
8. Autoclave
9. LAL testing kit
10. Water bath
11. Hot oven
12. Colony counter
13. Dust collector
14. Balance

# Warehouse

A centralized warehouse function is responsible for the receipt and storage of components in whatever stage of the process they are in. store is the transit point of any pharmaceutical industry, as it is the place where raw material first enter, goes to manufacturing and finished products after manufacturing are also temporarily stored here before releasing to the market.

## **Description of the warehouse observed in Sanofi Aventis**

There are several sections for the storage of separate materials

- In T4 building for non-antibiotic products:

Warehouse 1: finished products are stored here.

Warehouse 2: finished products are also stored here. Two separate zones are also present here for the storage of rejected products and promotional samples.

Warehouse 3: packaging materials are stored here. (both antibiotics and non-antibiotics)

Warehouse 4: raw materials of Aventis ltd and HMR are stored here.

Warehouse 5: raw materials of FBL are stored here.

Cool store: there are two cool stores. One for RM and another for finished goods which are heat sensitive and the temperature is maintained below 20°C.

Foster store: here temperature is maintained between 2-8°C. Antibiotic active ingredient, vaccines (imported), Insoman etc are stored here.

For glass bottle and shipping cartoon storage, there is a separate storehouse.

- In CPR building for antibiotic products:

Warehouse 6: active ingredient and finished products of Penicillin section are stored here. Temperature maintained below 30°C. Dispensing of RM are also

done. There is a separate RM store for antibiotic section where temperature is maintained between 15-18°C.

Warehouse 7: active ingredient and finished products of Cephalosporin section are stored here and temperature is maintained below 30°C.

## **Distribution of products in raw material stores**

### **1. Quarantine:**

The materials that has just entered into the warehouse and QC tests has not been performed are stored here.

### **2. Sampled:**

The materials from which, samples has been taken for QC tests are stored here.

### **3. Approved:**

The materials which, passed the QC tests and are ready to be used for manufacturing are stored here.

In this type of materials QC attaches the expiry date. So, that the use of the material become restricted after the expiry date.

### **4. Rejected:**

The materials which fails the QC tests and must be discarded are stored here.

## **Types of products in finished product stores**

### **1. Awaiting for approval:**

After manufacturing, finished products are labeled as "awaiting approval" are stored here.

### **2. Approved:**

QA approved products which are ready for distribution within the warehouse are stored in separate and identified zone for easy and proper identification.



## Some important factors

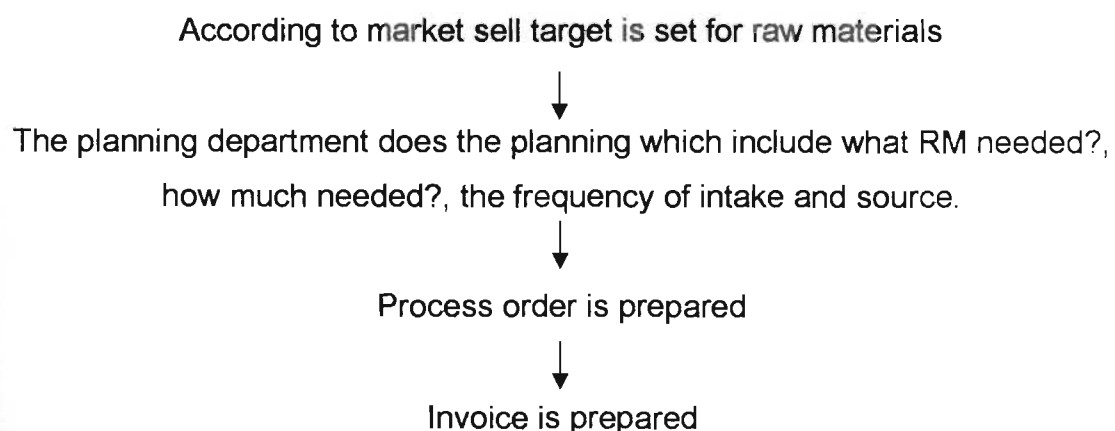
1. FIFO (first out first in)/FEFO strategy is followed for the release of RM to manufacturing.
2. Although materials are always taken from approved source; batch no. of the renders, manufacturing date, expiry date etc are checked before entry.
3. Complete security and prevention of pilferage of every material including the promotional materials are said to be confirmed.

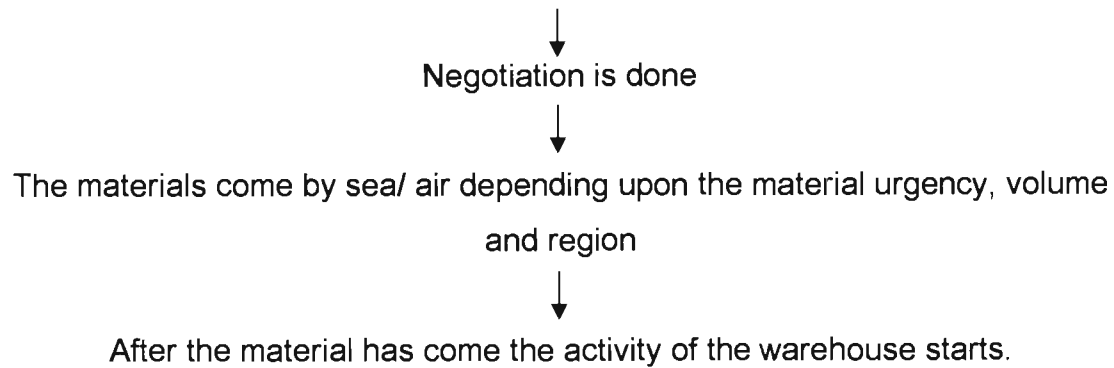
## Central dispensing room

According to cGMP guideline Sanofi Aventis has started a very modern and sophisticated Central Dispensing Unit. It is a specially designed area from which accurately weighed RM according to process order are dispensed to production floor. According to need RM from warehouse are taken into the central dispensing unit and then weighed under laminar air flow cabinet to prevent any type of contamination. Before weighing, the area is inspected and certified as clean.

## Activities of Warehouse

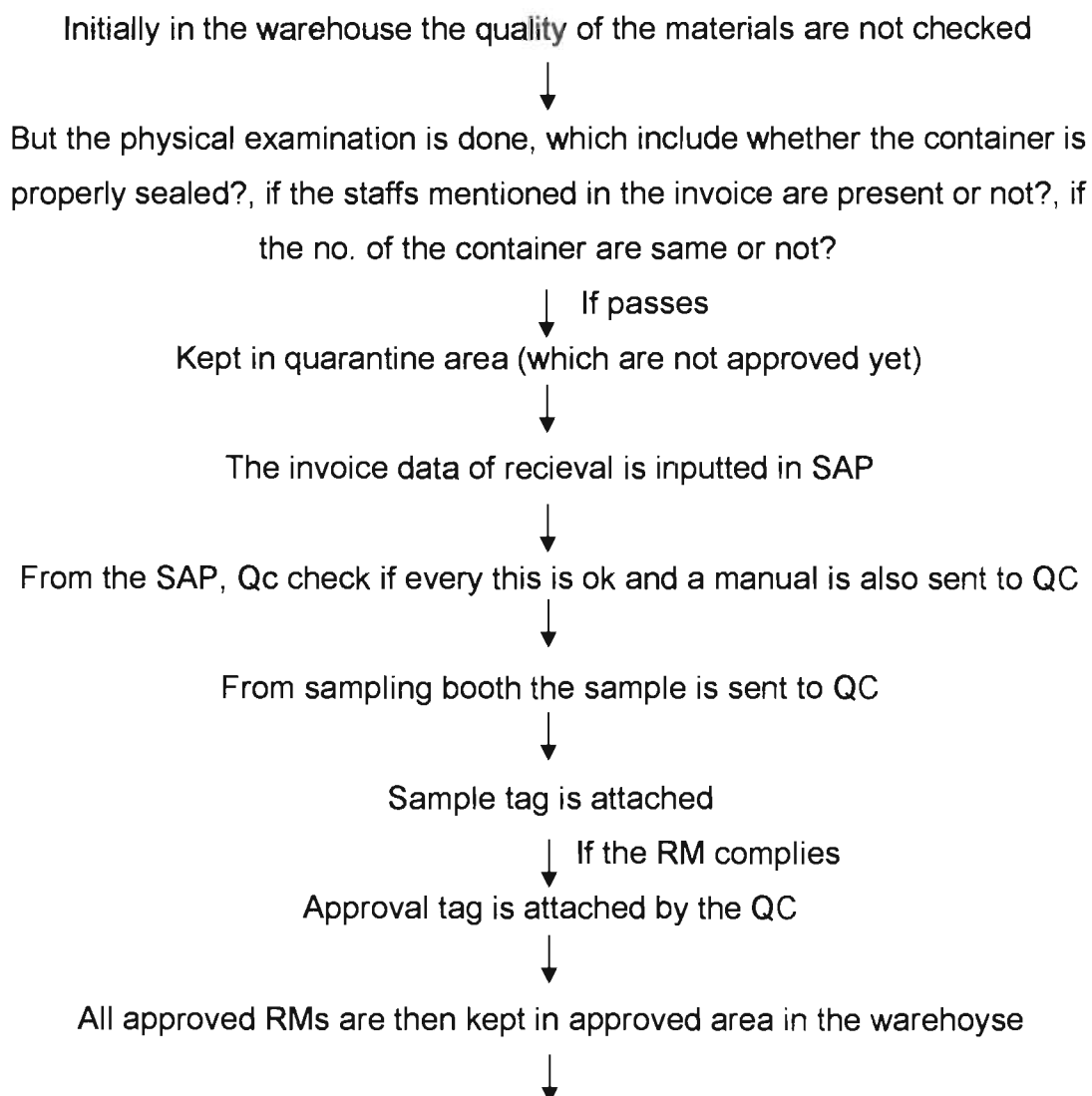
Beginning of the activity:





*Important note: due to the use of SAP software no material falls short.*

### Working procedures:



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All the data are uploaded in SAP



From there production unit can see and ask according to need



Warehouse follows FEFO and does the dispensing in the dispensing unit

## **Distribution of products from warehouse**

Distribution department



Makes a Stock Transport order to warehouse according to need of depot



Picking slip is prepared by warehouse and in this case also FEFO is maintained.



According to picking slip the products are picked and from there transported to the depots by proper transportation system.

# Engineering

The engineering department of Sanofi Aventis consists of a group of engineers, technicians and workers.

## **The activities are divided into two parts according to their function**

1. Maintenance
2. Project

### **1. Maintenance of the existing system:**

The function of this section is to separate the utilities and services in the plant. They also perform the maintenance function. The utilities and services handled by this section include:

1. Electricity
2. Portable or drinking water
3. Steam boiler
4. Air compression
5. HVAC system
6. Central vacuum system
7. Calibration

### **Calibration section:**

This section is responsible to calibrate all the instruments and machines to ensure performance and effectiveness. The general process is to calibrate the instruments and machines against a standard which is also standardized against international standards.

According to product quality management the instruments used are divided into four authentic classes:

Class	Description	Calibration
Class-1	These instruments are directly related to product quality of any deviation will harm the product	Calibrated three to six times monthly.
Class-2	These are standard instruments which are used to calibrate other instruments	Calibrated once yearly
Class-3	These instruments are indirectly related product quality and deviation will not harm the product.	Calibrated once yearly
Class-4	Tools, instruments used for various purposes.	

**Electricity:**

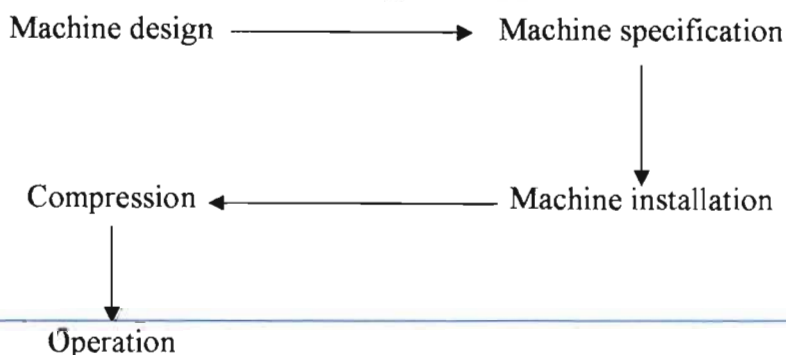
There are three substations to provide continues electricity in the plant.

1. 500 KVA
2. 1250 KVA
3. 2000 KVA

**2. Project:**

The personals involved in this section design new facilities as per requirement, generation, and setup of the facilities. This section also prepares the initial documents such as design outlet, capital expenditure for machines, building or any other facilities. After completion of the project it is hand over to the maintenance department for further services.

**Main functions of the project section**



Health Safety  
Environment

The concept of HSE is a modern and dynamic one. In a third world country like Bangladesh the implementation of HSE concept is rare. Among the pharmaceutical industry leaders of Bangladesh, Sanofi Aventis adopted the policy successfully.

## Mission

The mission is to integrate HSE in all function to build a safe and healthy workplace and to ensure sustainable environment.

## HSE Policy

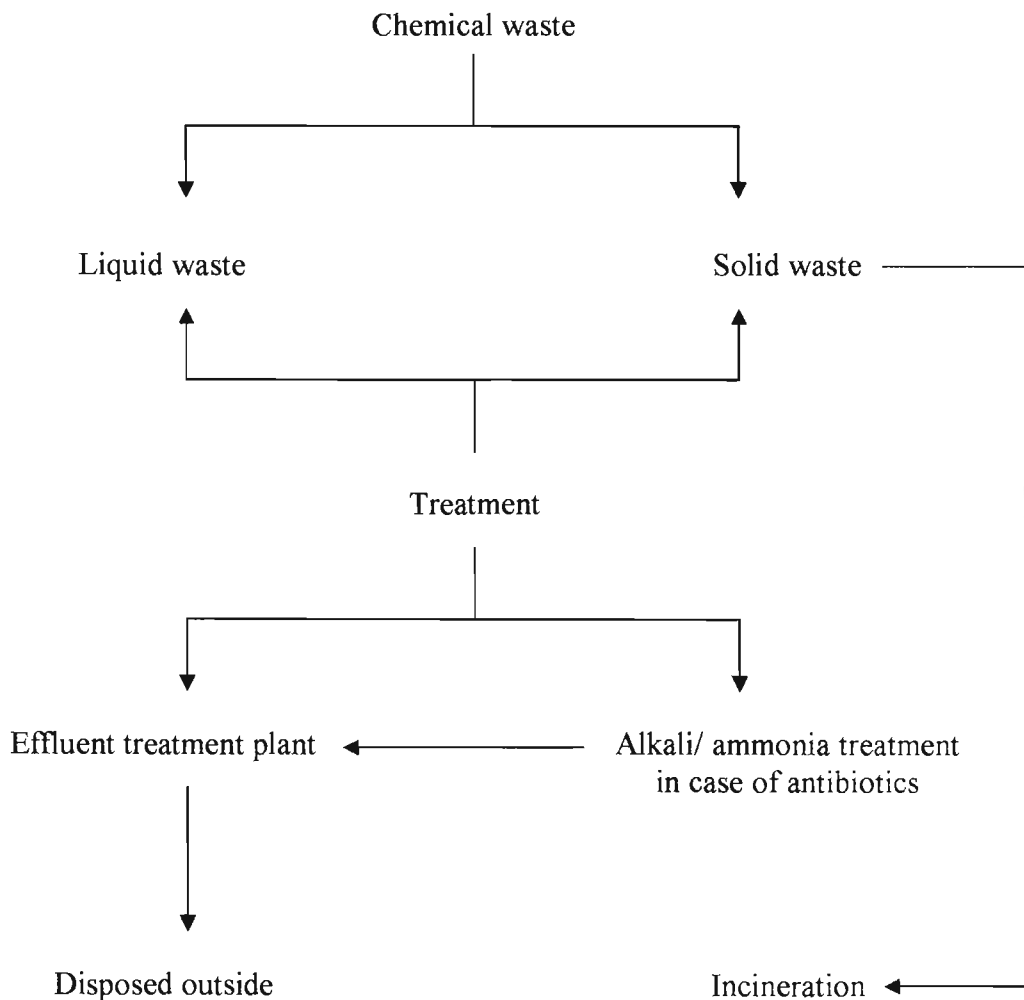
The HSE policy is based on 8 guiding principles which define a framework of actions with respect to their group of employees and external partners.

1. The HSE policy is an integral part of the general policy of the group.
2. The management and the employees of the group apply the policy at all levels. Each person is aware of their roles and their personal responsibilities with regard to the prevention of accidents, risk of health and damage to the environment.
3. In all places in which the group operates it respects the applicable laws and regulations, applies expert recommendations and uses the best industrial properties.
4. Sanofi Aventis operates management system related to safety, health at work and protection of environment adapted by implementing action plans called PASS with associated control system. The process depends on basic understanding, learning from experience, working together and training.
5. Every development project and every product launch will be subjected to a safety, health and environment risk assessment integrating all the scientific and technical knowledge of the group. Such project will be developed using the best available technology throughout a product half-life.



6. Sanofi Aventis take care of economics on natural resources to minimize the residual impact of atmospheric emission of effluents or of a waste in all its industrial activities in order to preserve the natural environment.
7. With regard to its suppliers, contactors and subcontractors, Sanofi Aventis aims to promote the applications of the rules of safety and protection of environment and considers the adoption of those rules as criterion to be applied to suppliers, contactors or subcontractors.
8. Sanofi Aventis has a constructive attitude of transparency and dialogue with regard to third parties with respect to their safety, health and environmental protection policy, its achievements and its commitments.

### Flow chart of chemical waste management



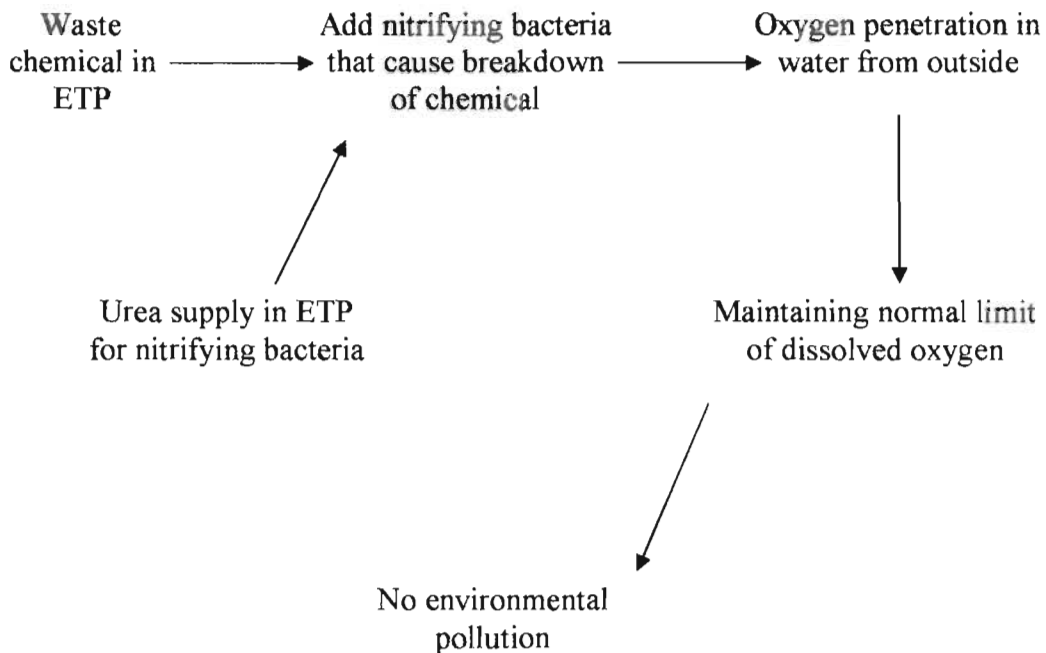
## Effluent treatment plant

ETP is maintained properly in Sanofi Aventis, for the prevention of environmental pollution. Waste chemicals of any pharmaceuticals are responsible for the reduction of dissolved oxygen and water by increasing

- BOD (biological oxygen demand)
- COD (chemical oxygen demand)
- TDS (total dissolved solid)
- TSS (total suspended solid)
- Chlorine
- pH
- Conductivity

Waste chemicals cause environmental pollution by decreasing dissolved oxygen by oxidation.

The oxygen demand is maintained by the following method



# Human Resource Management

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## HRM activities

- Planning
  - o Mission statement
  - o Organization
  - o Policy formation
  - o Staff strength
  
- Management
  - o Recruitment
  - o Orientation
  - o Transfer/ promotion
  - o Leave
  - o Discipline
  - o Salary & wage administration
    - Increments
    - Bonus
    - Provident fund
    - Gratuity
  - o Welfare
    - Insurance
    - Loans
    - Grievance
    - Handing
    - Motivation
    - Counseling
    - Canteen facilities
    - Transport
  - o Separation
    - Retirement
    - Termination
    - Dismissal

- Exit formalities
  - Resignation
- 
- Development
    - Approval
    - Training
    - Rewards
  
  - MIS
    - Record keeping
    - Reporting
    - Compensation

# Findings

The people of Sanofi-aventis are very cooperative

The personal protective equipments are used properly as per requirement

All equipments are validated and the expiry dates of validation are frequently checked by the officers so, that revalidation is done timely

Safety card (providing safety instructions to machine operators) is present on all equipments

List of authorized persons, the names of the ones who are only permitted to operate the machine are also present on the equipment

Labeling (describing state of operation, for example: machine label, to be cleaned, cleaned, under test etc) are attached to machine

Machine log book is maintained properly to avoid any deviation

Cleaning of room and machines are done after each batch manufacturing and the room is labeled cleaned, to be cleaned

Even the name of the previous product is mentioned on the room so that specified cleaning procedure can be applied.

Regular inspection is done from QA to see whether the environment to right

Sample are regularly sent to the IQC for IPC and also people from IQC come to take samples

Proper protective growing system for all operating procedures

SOPs are present in the production areas and they are maintained and followed properly

They have internal audit as well as from other companies (whose drugs are manufactured in this site) frequently

As the site is a very old one the layout is not an ideal one but yet GMP maintained and the employees follow the requirements properly

Three separate premises for the three antibiotics as per GMP requirement

Different gowning system for different antibiotic production

Two separate lab system for Cephalosporin and Penicillin, to avoid contamination

All the labs are well equipped and proper maintenance is also present

Officers/ analysts must wear lab coat, eye protector before entering the working area in the labs

COD, BOD etc tests are performed before the waste disposal

All the chemicals in the lab are kept separately in group according to their use and character and all are labeled, for example

- Hazardous chemicals
- Working chemicals
- Mobile phase and indicators
- Inflammables solvents
- Corrosive liquids

While running some specific equipments (for example particle counter) laminar air flow is used to get accurate result

Eye wash shower is present in the lab as well as in production area



The site map is present in almost every area to avail quick exit in case of any emergency

The exit signs with arrows indicating the direction are present and the signs also glow in the dark to facilitate evacuation

Every work is documented to practice GMP

Good food facilities and interval between works helps the employees to remain motivated and work properly

Training programs are arranged quite frequently to improve the quality

Safety places are present in the site so people can gather there in case of any emergency

Sanofi-aventis provide good transport facility for all the employees

Up to date official books (USP, BP etc) are present in the IQC department

The site is very green, also has ponds which makes it an environment friendly site

The company treats its workers as asset

It has a very sophisticated and modern central dispensing center

It provides proper in plant medical facilities and a medical center is also available

# Conclusion

Sanofi-aventis has a really strong goodwill. The company provides and ensures quality medicines. They maintain GMP properly and believe in documentation. They have a very strong quality control, engineering, storage system helping them to maintain the quality of the drugs. Sanofi-aventis also has proper system for disposal of the wastes to protect the nature.

So far the company is in good condition and they can reach even higher rank among the leading multinational companies if they continue to provide proper service and quality drugs.