A

INDUSTRIAL TRAINING REPORT

Submitted

In Partial Fulfillment of the Requirements for the award of

Degree of
Bachelor of Pharmacy (B.Pharm) 6th Semester

Session -2023-24

Submitted by

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MEERUT INSTITUTE OF ENGINEERING & TECHNOLOGY, MEERUT

DECLARATION BY GUIDE

This is certify that the project entitled "Industrial training Report" is a bonafide and genuine training work done by **Mr. Govind Gupta (Roll No.-2100680500036)** B.Pharm III-Year, VI-Semester, session-2023-24 under my guidance.

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Date:-

Place:- MIET, Meerut

DECLARATION

I Govind Gupta, hereby declare that work presented in the industrial training report entitled in INDUSTRIAL TRAINING PERFORMED AT Plot no - 35-36, Sector -6A, SYNOKEM PHARMACEUTICAL.

It is an authentic record of work carried out by me during 21.02.2024 to 22.03.2024 at Plot no 35-36, sector no -6A SYNOKEM PHARMACEUTICAL, Haridwar (uttarakhand).

Is being submitted for partial fulfilment of the requirement for the award of bachelor degree in B. Pharm.

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TO WHOM SO EVER IT MAY CONCERN

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This is to certify that **Mr.Govind Gupta S/O Vijay Kumar Gupta** student of Bachelor of Pharmacy 3rd year,6th Semester **Roll No-2100680500036** from Meerut Institute of Engineering and Technology, Meerut Uttar Pradesh, has completed his **Industrial Training** from 21-02-2024 to 22-03-2024 in QC, QA and Production Department at our Manufacturing Unit Situated at Plot No.56-57, Sector 6A, IIE (SIDCUL), Haridwar-249403.

During his training, he has shown keen interest and sincerity and we wish him all the success for his bright future.

For,**Synokem Pharmaceuticals. Ltd.**

SYNOKEM LTD.

Authorized Signatory

ACKNOWLEDGEMENT

It is a matter of pleasure and happiness to make and submit this industrial training report during course of the completion of this industrial work. Many of the persons have offered their valuable and enormous support.

I'm thankful to all my teachers of M.I.E.T. For their blessings and encouragement.

I would like to express my special thanks and gratitude to

synokem pharmaceutical .

And Mr. PRASHANT KUMAR for providing all the essential facilities which were required for this training.

Finally, I express my regards to my beloved parents who inspired me throughout my studies and completion of this training.

Thanking You

Govind Gupta
B. Pharm 3rd Year
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INDEX

INTRODUCTION

Synokem pharmaceutical is a leading pharmaceutical company with over 3 decades of experience in developing, manufacturing, & Exporting high-quality generic & branded medicines. Our 7 state-of-art manufacturing units are equipped with in-house testing, to ensure that our products meet global quality standards.

FACILITIES

Production Units

UNIT -I Synokem Pharmaceutical

Synokem was incepted in 1993 and maintained its benign presence ever since. It started its first manufacturing unit in National Capital Region of India situated at just 150 Km away from Delhi International Airport. This unit is WHO-GMP Certified manufacturing plant having facilities for Tablets, Capsules, Liquid (orals), Dry Syrups & External Preparations and having extended facilities to manufacture Herbal Medicines. It is an EOU.

UNIT -II Synokem Pharmaceutical

Synokem second pharmaceuticals manufacturing unit became operational in the year 2005, in the tax free industrial zone of Himachal Pradesh at Paonta Sahib, with the latest and well equipped technology which is further 125 km away from its First unit. This unit is GMP Certified manufacturing plant having facilities for Injection, Tablets, Capsules, Liquid (orals), Dry Syrups & External Preparations. This unit is catering domestic market demand as well as manufacturing medicines for overseas markets.

UNIT -III Synokem Pharmaceutical

The Third and the largest pharmaceuticals manufacturing unit of Synokem Pharmaceutical came into existence in the year 2009, at Paonta Sahib, Himachal Pradesh, with the latest and well equipped technology as per USFDA & European GMP Standards in which the company has added separate manufacturing facilities for Oncology Drugs (Anti-Cancer drugs) and soft gelatin capsules. Synokem has further added the facility for FFS/BFS fluids, Eye Drops & WFI in a separate block.

The expansion for Vaccines manufacturing plant is also under way in full swing, where the company intends to manufacture Anti Rabies, Tetanus Toxoid and other vaccines for human use.

UNIT -IV Synokem Pharmaceutical

The Fourth unit of the group was commissioned in the year 2010 in the tax free industrial zone of Himachal Pradesh at Paonta Sahib with the latest and well equipped technology and dedicated to exclusive manufacturing of Cosmetics and Nutraceuticals preparations.

Forthcoming Ventures:

Synokem is further expanding its wings to the other categories, like vaccines, I.V. Fluids. The separate plant for manufacturing of I.V fluids & Anti Rabies Tetanus Toxoid & Other vaccines at Karnal.

PRODUCTS

- Synokem **Divisions: Tablets**

  In Synokem Pharmaceutical 219 tablets were made some common examples are-

S. No.	PRODUCT NAME	PRODUCTS COMPOSITION	PACKING
1	ACIV-200	Acyclovir 200 mg.	10X10 Tabs.
2	ACIV-400	Acyclovir 400 mg. Tablets	10X10 Tabs.
3	ACIV-800	Acyclovir 800 mg. tablets	10X10 Tabs.
4	ALCOVIN - 250	Disulfiram 250 mg. Tablets	4X5X10 Tabs.
5	ALESE®	Allyloestrenol 5 mg.	10X10 Tabs.
6	ALFEX-BT	Alfacalcidol + Calcium Carbonate + Beta carotene Tablets	05X03X10 Tabs.
7	ALTEC-400	Albendazole 400 mg.	10X05X01 Tabs.
8	ALTIN	Alprazolam 0.25mg. + Fluoxetine 20mg	10X10 Tabs.
9	ALZY® 0.25	Alprazolam 0.25 mg.	02X05X10 Tabs.
10	ALZY® 0.5	Alprazolam 0.5 mg.	10X10 Tabs.
11	AMZEL®-EL	Amlodipine 5mg.+ Enalapril Maleate 2.5mg.	10X15 Tabs.
12	ANCE® PLUS	Diacerein 50 mg. + Glucosamine 750 mg. Tablets	3X10 T. Alu/Alu Pack
13	ARTEZER-LF	Artemether 80 mg. + Lumefantrine 480 mg. Tablets	10X1X6
14	ASONAC® FORTE	Aceclofenac 100 mg. + Chlorzoxazone 250mg. + Paracetamol 500 mg. Tablets	10X10 Tabs.
15	ASONAC® -100	Aceclofenac 100 mg. Tablets	2X5X10 Tabs.
16	ASONAC® -200SR	Aceclofenac 200 mg. Sustained Released Tablets	2X5X10 Tabs.
17	ASONAC® -PLUS	Aceclofenac 100 mg. + Paracetamol 500 mg.	10X10 Tabs.

		Tablets	
18	ASONAC® -SR	Aceclofenac 100 mg. + Serratiopeptidase 15 mg. Tablets	10X10 Tabs.
19	ASONAC® -SR PLUS	Aceclofenac 100 mg. + Serratiopeptidase 15 mg. + Paracetamol 500 mg. Tablets	10X10 Tabs.
20	AVON	Dried Extract of Ginkgo Biloba 40 mg. eq. to Ginkgoflavone Glycosides 9.6 mg	2X5X10 Tabs.
21	AZITH-250	Azithromycin 250 mg	10X1X6 Tabs.
22	AZITH-500	Azithromycin 500 mg	10X1X3 Tab
23	BETNEVIN	Betamethasone Sodium Phosphate Tab 0.5 mg.	40X10 Strip Pack
24	BRACE-800	Piracetam 800 mg. Tablets	10X10 Tabs.
25	CALORICH-M	Calcium Citrate 1000 mg. + Calcitriol 0.25 mcg. + Mecobalamin 750 mcg.	10X02X15 Tabs.

Synokem **Divisions: Capsules** (Some common examples-)

S. No.	PRODUCT NAME	PRODUCTS COMPOSITION	PACKING
220	ALCEE	Calcitriol + Calcium + Zinc Capsules	10X02X15 Cap.
221	LYCORICH PLUS	Lycopene 5000 mcg. with Antioxdants	10X01X10 Cap.
222	SEYES®	Cyproheptadine 2 mg. + Dried Yeast 100 mg. Capsules	10X02X15 C.
223	SILBEX	Silymarin+ B-Complex Capsules	10X02X15 C.
224	FEROZINC	Haematinic with Zinc, Vitamin B12 & Folic Acid	10X02X15 Cap.
225	ORICH® PLUS	A complete Anti-Oxidant	10X02X15 Cap.
226	OXCEE PLUS	A complete Anti-Oxidant + Minerals	10X02X15 Cap.
227	ZINCOGLOBIN	Protein + Iron + Zinc + Multivitamin.	10X02X15 Cap.

S. No.	PRODUCT NAME	PRODUCTS COMPOSITION	PACKING
228	LANZEE®-30	Lansoprazole 30 mg.	10X02X15 Cap.
229	LANZEE®-DM	Lansoprazole 30mg. + Domperidone 10mg.	10X02X15 Cap.
230	UDXIC-450 SR	Ursodeoxycholic Acid 450 mg. Sustained Released Capsules	10X02X15 Caps.
231	THIOLIN-D	Thicholchicoside 4 mg. + Diclofenac Sodium 50 mg. Capsules	10X10
232	WINPHYLIN-100	Acebrophylline 100 mg Capsules	10X10
233	RABERTREX-DX	Dexrabeprazole 10 mg. + Domperisone (SR) Capsules	10X10 Alu/Alu Pack
234	ACIPHYNE-100	Acebrophylline 100 mg. capsules	10X10 C.
235	MONACLOX® PLUS	Amoxycillin 250 mg. + Dicloxacillin 250 mg.	10x10 C.
236	RACEX	Racecadotril 100 mg. Capsules	10X10 C.
237	CLOSPIRAN-50	Clofazimine 50 mg. Capsules	10X10 C.
238	RB CARE - IT	Rabeprazole 20 mg. Itopride hcl 150 mg. (SR) Capsules	10X10 C.
239	MONAMOX®-500	Amoxycillin 500 mg.	10X10 Cap.
240	FLUZE®-20	Fluoxetine 20 mg.	10X10 Cap.
241	MONACEF-250	Cephalexin -250 mg.	10X10 Cap.
242	MONACEF-500	Cephalexin 500 mg.	10X10 Cap.
243	MONAMOX®-250	Amoxycillin 250 mg.	10X10 Cap.
244	MONAMOX® BR	Amoxycillin 500 mg. + Bromhexine 8 mg.	10X10 Cap.
245	MONAMOX®-250BR	Amoxycillin 250 mg. + Bromhexine 8 mg.	10X10 Cap.
246	GLOBEX® FORTE	Protein + Iron + Zinc + B-Comp.	10X10 Cap.
247	DBS	Calcium Dobesilate 500 mg. Capsules	10X10 Caps.
248	CANDINIL-100	Itraconazole 100 mg.	10X1X04 cap
249	SHERIC®	Iron Carbonyl 100 mg. + Folic Acid 1 mg. + Vitamin B12 5 mcg. + Zinc 25 mg.	10X2X15 Cap.

S. No.	PRODUCT NAME	PRODUCTS COMPOSITION	PACKING
250	ZINCOBEX FORTE	Antioxidants with Vitamins & Zinc	10X2X15 Cap.

- Synokem **Divisions: Soft gels**

S. No.	PRODUCT NAME	PRODUCTS COMPOSITION	PACKING
266	IVORIN-20 Soft Gelatin Capsules	Isotretinoin 20 mg. Soft Gelatin Capsules	10X3X10
267	KLINDEX-M Soft Gel Suppository	Clindamycin 100 mg. + Miconazole 200 mg. Soft Gelatin Vaginal Suppository	10X1X7 VS
268	NANCE®-200 Soft Gel Capsules	Natural Progesterone 200 mg.	10X1X10 C.
269	SINEX-DMR Soft Gels	Chlorpheniramine Maleate 2 mg.+ Dextromethorphan Hydrobromide 10 mg. + Phenylephrine Hcl 5 mg.	10X10 C.
270	SNEZEE BREATH	Camphor 25 mg. Chlorothymol 5 mg. + Eucalyptus 130 mg. + Menthol 55 mg. + Terpineol 110 mg.	20x10
271	ZELID-D Soft Gel Cpasules	Nimesulide 100 mg, + Diclofenac Sodium 50 mg.	10X10 C.

- Synokem **Division :: Dry Syrups -Oral Powders**

S. No.	PRODUCT NAME	PRODUCTS COMPOSITION	PACKING
272	CECEL®	Cefaclor Dry Syrup 125mg./5ml.	15gm./30ml.
273	CEFZIM DRY SYRUP	Cefuroxime Axetil Dry Syrup	15gm./30 ml.
274	COLILIFE	Collagen Peptide 10 gm. + Glucosamine 1 gm. + Calcium Carbonate 1 gm.	1 Sachet
275	DEEZEE 3	Cholecalcioferol Sachet	25X1 gm.
276	DEWIN Sachet	Cholecalciferol 60000 I.U. per sachet	25X1gm. Sachet
277	DIACOWIN Sachet	A powerful combination of Prebiotic &	25X1gm. Sachet

S. No.	PRODUCT NAME	PRODUCTS COMPOSITION	PACKING
		Probiotic	
278	ELYTE ORS POWDER	Oral Rehydration Salts - A	21.8 gm.
279	MONACEF	Cephalexin 125 mg./5ml..	15gm./30ml.
280	MONAMOX®	Amoxycillin 125 mg./5ml.	15gm./30ml.
281	MONAMOX®-CL B.D.	Amoxycillin 200 mg. + Clavulanic Acid 28.5 mg. per 5 ml.	3.6gm./30ml.
282	NINETY NINE	L-Arginine + Proanthocyanidin Granules	25x5 gm..
283	RACEX SACHET	Racecadotril 15 mg. Sachet	25 Sachets
284	RUXOWEL	Cefuroxime Axetil (Dry Syp)	Glass Bottle 30ml & Carton
285	SEFXIM®	Cefixime 50 mg./5ml. Dry Sup.	15gm./30ml.
286	SEFXIM® Drops	Cefixime 25mg./ml. Powder for Oral Paediatric Drops	6gm./10 ml.
287	SEFXIM-CL Dry Syrup	Cefixime 50 mg. + Clavulanic acid 31.125 mg. per 5 ml. after reconstitution	30 ml./15 gm.
288	ZEXTIL®	Cefpodoxime Proxetil 50 mg./5ml. Dry Syp.	30ml./15gm.
289	ZEXTIL® Drops	Cefpodoxime Proxetil 25mg./ml. Powder for Oral Paediatric Drops	6gm./10 ml.
290	ZEXTIL-CL Dry syrup	Cefpodoxime 50 mg. + Clavulanic Acid 31.25 mg.	30ml

- Synokem **Division :: Liquid Orals**

S. No.	PRODUCT NAME	PRODUCTS COMPOSITION	PACKING
291	ACCENT	A Mouth Wash	100 ml.
292	AFRESHO® MOUTH WASH	Chlorhexidine Gluconate Solution 2%	100 ml.
293	ALCEE	Calcitriol + Calcium Carbonate + Zinc + L-Lysine Syrup.	200 ml.
294	ALTEC	Albendazole Susp.	10 ml.

S. No.	PRODUCT NAME	PRODUCTS COMPOSITION	PACKING
295	ASMAWEL	Ambroxol 30 mg. + Levosalbutamol 1 mg + Guaiphenesin 50 mg per 5 ml. Syrup	100 ml.
296	ASONAC® PLUS	Aceclofenac 50 mg. + Paracetamol 125 mg. per 5ml.	60 ml.
297	AXID	Sucralfate 1000mg./5ml.	200ml.
298	AXID-O	Sucralfate 1000mg. + Oxetacaine 20mg.	100ml.
299	AXZE®	Ambroxol 15 mg. + Guaiphenesin 50 mg. + Phenylepherine 2.5 mg. + CPM 2 mg. per 5 ml. Sup	60 ml.
300	AXZE®	Ambroxol 15 mg. + Guaiphenesin 50 mg. + Phenylepherine 2.5 mg. + CPM 2 mg. per 5 ml. Sup	100 ml.
301	AZITH LIQUID	Azithromycin Suspension	30 ml.
302	BETNEVIN	Betamethasone Sodium Phosphate oral Drops	15 ml.
303	BREETEX	Bromhexine 4 mg. + Guiaphenesin 50 mg. + Terbutaline 1.5 mg. per 5 ml.	100 ml.
304	BREXIWIN	Salbutamol, Bromhexine, Guaiphenesin & menthol Syrup	100 ml.
305	CALZY	Calcium Carbonate + Vit. D3 Syp.	200 ml.
306	CEDEL	Cyproheptadine Syp.	200 ml.
307	CETZY	Cetirizine Susp.	60 ml.
308	CORTRIK	Deflazacort 6 mg. Suspension	30 ml.
309	COSO Laxative	Sodium Picosulphate Solution	100 ml.
310	CREMAX	Milk of Magnesia 11.25 ml. + Liquid Paraffin 3.72 ml. per 15 ml.	170 ml.
311	CROZY® PLUS	Phenylephrine + C.P.M. + Para Susp	60 ml.
312	ELBUGESIC PLUS	Ibuprofen 100 mg + Paracetamol 125 mg per 5 ml.	60 ml.

Synokem **Division :: Injections**

S. No.	PRODUCT NAME	PRODUCTS COMPOSITION	PACKING
444	ARTFIN	Artesunate 60 mg. Injection	Vial

S. No.	PRODUCT NAME	PRODUCTS COMPOSITION	PACKING
445	BETNEVIN	Betamethasone Injection 4mg/ml.	1 ml.
446	ELMETIL	Prochlorperazine 12.5 mg. Injection	1 ml.
447	HYTORIX	Hyscine Butylbromide Injection 20mg/ml.	1 ml.
448	HICORT 10	Triamcinolone 10 mg. per ml. Injection	1 ml. Vial
449	HICORT 40	Triamcinolone 40 mg./ml. Injection	1 ml. Vial
450	MYSOLONE	Methylpredinolone 40 mg./ml.	1 ml. Vial
451	PREE®-M	Methyl Prednisolone 40 mg./ml. Injection	1 ml. Vial
452	ALESE® -250	Hydroxyprogesterone 250mg. Inj.	1 ml.Amp & Dispo
453	MONAMOX®-CL1200	Amoxycillin + Potassium Clavulanate 1200 mg Inj.	10 ml. Vial
454	ZENTIVIN	Gentamicin Sulphate 40 mg/ml. Inj.	10ml. Vial
455	KETZY®	Ketorolac Tromethamine Inj.	10X10X1 ml. Amp.
456	DICLOZEE	Diclofenac Sodium Inj.	10X10X3ml. Amp.
457	DICLOZEE	Diclofenac 75mg./ml. Injection	10X1ml. Amp.
458	ZONDE®-4	Ondansetron Injection 2mg./ml.	10X2 ml.
459	WIROX®	Piroxicam Inj.	10X2 ml. Amp.
460	TRAZAC	Tramadol Inj	10X2ml. Amp.
461	ZINCOBEX	Vitamin B-Comp with B12.	10X3ml. Amp.
462	DEWIN 6L	Vitamin D3 Injection 600000 Lacs IU (15mg.)	10X5X1 ml.
463	NEXI	Tranexamic acid	10X5X5 ml. Amp
464	ZEBOL®-25	Nandrolone Decanoate 25 mg. Inj.	1ml.Amp.&Dispo
465	ZEBOL®-50	Nandrolone Decanoate 50 mg. Inj.	1ml.Amp.&Dispo
466	ZEDEX	Dexamethasone Inejction	2 ml.
467	ELWIGAN	Promtehazine 25mg/ml. Injection	2 ml.
468	FRUSIZEX	Frusemide Injection 10mg/ml.	2 ml.

Synokem **Division :: Topical Range**

S. No.	PRODUCT NAME	PRODUCTS COMPOSITION	PACKING
386	ACNEFIN Face Wash	Anti Acne Face Wash with Tea Tree Oil, Allantion & Vitamin E	60 g.
387	ACCENT PASTE	Potassium Nitrate Medicated Tooth Paste	50 gm.
388	ALE CREAM	Aloe Vera with Vitamin E Cream	50 gm.
389	ALESIA Cream	Squalene, Aloe Vera & Vitamin E Cream	60 gm.
390	ASONAC® GEL	Aceclofenac 1.5% + Methyl Salicylate 10% + Linseed Oil 3% + Menthol 5% + Capsaicin 0.01%	30 g.
391	BANCE® DUSTING POWDER	Salicylic Acid, Benzoic Acid & menthol	100 gm.
392	BARBIE Baby Massage Oil	Baby Massage Oil	100 ml.
393	BARBIE BABY POWDER	A gentel & soft talcum powder for babies.	100 gm.
394	BECZE®-N CREAM	Beclomethasone + Neomycin Cream	15 gm.
395	BENCHEK	Ketoconazole 2% + ZPTO 1% Lotion	60 ml.
396	BREXELANT® Long Stay Gel	Lidocaine 2.5% & Prilocaine 2.5% Gel	10 gm.
397	BURNOCHILL	Acriflavine 0.12% + Thymol 5 mg + Cetirimide 0.5 gm	30 gm.
398	CAPTAIN KAVIN Body Massage Oil	Body Massage Oil	100 ml.
399	CHARMIN	KOJIC ACID & VITAMIN C CREAM	15gms
400	CHIFFON HERBAL HAIR TONIC	An Ayurvedic Hair Vitaliser	100 ml.
401	CLOB-MG CREAM	Clobetasole + Miconazole + Gentamicin + Zinc Cream	15 gm.
402	CLOZE-BG CREAM	Clotrimazole + Beclomethasone + Neomicin Cream	10 gm.
403	DBS Cream	Calcium Dobesilate 0.25% + Hydrocortisone 0.25% + Lignocaine + Zinc 5% Cream	30 gm.
404	DENON Shampoo	Ketoconazole 2% Shampoo	100 ml.

S. No.	PRODUCT NAME	PRODUCTS COMPOSITION	PACKING
405	DENON Shampoo	Ketoconazole 2% Shampoo	50 ml.
406	DICLOZEE GEL	Diclofenac Diethylammonium gel	30 gm.
407	DICZONE® GEL	Diclofenac+ Methyl Salicylate +Oleum Linn+ Menthol Gel	30 gm.
408	DICZONE® SPRAY	Diclofenac, Oleum Linn, Methylsalicylate & Menthol Spray	55 gm.

PRODUCTION

The action of making or manufacturing from raw materials to the pharmaceutical product.

Pharmaceutical Industries must comply **with Schedule M of Drugs and Cosmetics Act, 1940 & Rules, 1945**. According to GMP i.e, Schedule M

Pharmaceutical Industries must have some prescribed manner for it follow that requirement accordingly to a certain extent.

General Requirements for the pharmaceutical Plant;

1. **Location & Surrounding**

- Avoid risk of Contamination from external environment
- Away from Sewage, drain, Public lavatory.

♦ Buildings & Premises
It should be designed, constructed, adapted and maintained to suit the manufacturing operations
It must possess all requirements for the production of particular pharmaceutical product.

- Water system
- Disposal of waste

➢ **Clean Room:**
Clean rooms & zones are typically classified according to their use (the main activity within each room or zone) & confirmed by the cleanliness of the air by the measurement of particles**.**

✓**Clean room classification:**

1) GRADE A (should be less than 100 particles/cubic feet-class 100)
2) GRADE B (should be less than 1000 particles feet-class 1000)
3) GRADE C (should be less than 10000 particles feet-class 10000)
4) GRADE D (class 100000)

- The Manufacturing Room and Filling Room are Grade B in Synokem Pharmaceutical The area under LAF Grade A.

2. **Warehousing Area**
3. **Production Area**
4. **Quality Control Areas**
5. **Personnel**
6. **Health, clothing and sanitation of workers**
7. **Manufacturing operations and controls**
8. **Precautions against Mix-up and cross contamination**

- Proper Air Handling System
- Differential Pressure
- Status Labeling
- Cleaning

9. **Sanitation In the Manufacturing Premises**
10. **Raw Material**
11. **Equipment**
12. **Documentation & Records**

    - Labels & other printed Materials
    - Quality Assurance
    - Self-Inspection & Quality Audit
    - Q.C System
    - Master Formula Record
    - Packaging Records
    - Batch Processing Record
    - SOPs & Records regarding
    - Sampling
    - Batch Numbering/ Lot Number
    - Testing
    - Record of Analysis
    - Reference Samples
    - Reprocessing & Recoveries
    - Distribution Records

- Validation & Process Validation
- Product Recalls
- Complaints & ADRs
- Site Master File

- **Production area** can be divided into;

i. Manufacturing area/Production area
ii. Filling area
iii. Packaging area
iv. Dispatch area

1. <u>Manufacturing area:</u>

In order to commence the production of a formulation, it needs many things. Production consists of many of the activities from the De-cartoning to dispatch.

- The main provisions under Production are:

a) De-cartoning Area
b) Raw Material Quarantine Area
c) Raw Material store
d) Rejection area
e) Weighing of Raw Materials
f) Sterile Entry Room
g) Air Lock Room
h) Manufacturing of the Particular product
i) Air Handling Unit (AHU)
j) Water Management System.

- **Equipment's used in the Manufacturing Area;**

1. Double Door Autoclave:

- Supplied by: New Tech Equipment's, Mumbai
- Tested by: Unique Testing Solutions, Kochi

- It is fixed between two adjacent rooms.
- One end of the autoclave is in the Manufacturing room.
- They are mainly works by Steam sterilization at 121°C for 30 minutes.
- In order to kill the microorganisms to attain sterility.
- The materials are covered by either Barrier paper or BOPP pouch
- BOPP means **'Biaxially Oriented Poly Propelyne'**, it consists an indicator which helps to mark the sterilization process.

2. **UV-Hatch:**

   - Mainly for the transfer of materials from one room to the adjacent room with the assistance of UV radiation.

3. **Autoclaves:**

   - 2 normal autoclaves are there for sterilize the solutions and others.
   - Model: Ketan fully automatic autoclave (without vacuum).

4. **Poly round vacuum desiccator:**

   - Used for the vacuum leak test, one of the In-process Q.C test.

5. **Washing Machine:**

   - Used to wash the gowns, masks, gloves & other cloths.

6. **Vacuum Cleaner**
7. **Laminar Air Flow**:

   - For the Aseptic Techniques
   - Manufactured By : Air tech system & services.

8. **Weighing Balance**
9. **PH Meter**
10. **Scale Balance**
11. **Mechanical Stirrer**

12.Manufacturing Vessels by Pharma Lab, Ravikiran.
13.Pressure vessels
14.Filling vessels
15.Membrane Filtration Unit
16.Water storage vessel
17.Spatulas
18.Scoops etc.

❖ **Washing Area:**

- This area meant for the Cleansing purpose.
- Mainly for the Vessels that are used for the Manufacturing.
- Manufacturing vessel, pressure vessel, filling vessels, scoops, filtration unit, syringes for filling, connecting taps all are washed here and subjected to Autoclaving.
- For washing mainly used for the RO Water.
- And the wash water is collected for the Wash water analysis of Q.C.
- After washing the tag of the vessels must be changed.
- Here one Washing Machine is used for the washing of the clothes that are used for the Manufacturing & filling area after washing it undergoes autoclave.

➢ **Documents:**

1. Cleaning & Setting log books.

    - Syringe log book
    - Filling vessel log book
    - Filter log book.

2. Records for Autoclaves

    - Autoclave 1
    - Autoclave 2
    - Autoclave 3

3. Filling Machine Log Book

4. **Batch Processing Record (BPR):**

- ✓ BPR is step-wise procedure that production operators follow to manufacture of a drug product.
- ✓ It shall include complete information relating to the production and control of each Batch.
- ✓ Each BPR is a controlled document from the time it is issued until it can eventually be destroyed.
- ✓ It consist of;

  - Dates & times
  - Identity of major equipment's
  - Specific identification of each batch, including weights, measures and batch number.
  - Actual results recorded for critical process parameters sampling details
  - Signatures of the persons performing and directly supervising or checking each critical step in the operation.
  - In-process results
  - Actual yield details
  - Description of packaging materials and label
  - Representative label of Product
  - Any deviation noted, its evaluation & investigation, etc.

  ✓ BPR is checked by Q.A personnel.

5. **Cleaning Records**
6. **AHU log book.**
7. **Batch Manufacturing Records (BMR):**

- ➢ BMR is the necessary documentation for tracing the complete cycle of manufacturing batch or lot.
- ➢ It should be prepared for each product and include complete information relating to the manufacturing and control of each batch.
- ➢ These records should be numbered with a unique batch or identification number and dated and signed when issued.

- **Contents:**

Manufacturing records relating to manufacture of sterile products shall contains:

1) Serial Number of the BMR
2) Name of the product
3) Reference to Master Formula Record
4) Batch/lot Number
5) Batch/lot size
6) Date of commencement of manufacture & date of completion of manufacture
7) Date of Manufacture & assigned date of expiry
8) Date of each step in manufacturing
9) Names of all ingredients with the grade given by the Q.C department
10) Quantity of all ingredients
11) Control reference numbers for all ingredients
12) Time and duration of blending, mixing etc.
13) PH of solution
14) Filter Integrity Testing Records
15) Temperature & Humidity records
16) Records of Plate count
17) Records of volume of drug filled in containers
18) Leak test Records
19) Inspection Records.
20) Sterilization Records including autoclave, pressure etc.
21) Container washing record
22) Total number of containers filled
23) Total number of containers rejected at each stage
24) Theoretical yield, permissible yield, actual yield & variation thereof.
25) Reference number of relevant analytical reports
26) Details of reprocessing if any
27) Name of all operators carrying out different activities

28) Environmental monitoring records
29) Specimens of printed packaging materials
30) Records of destruction of rejected containers & printed packaging materials
31) Signature of the competent technical staff responsible for manufacture & testing.

8. Master Formula Record:

- Master document for any Pharmaceutical product. It contains all information about the manufacturing process for the product.
- MFR is used as reference standard for preparing Batch Manufacturing Record (BMR) by manufacturing units.

2) Filling Area:

Filling area is next to the Air lock room. It consists of Filling Machine at part which is assisted by the LAF.

- Filling Machine:
- The area under LAF is Grade A & its surroundings are Grade B.
- The solution is aseptically transferred from the Manufacturing room to the Filling room through the air lock.
- Then the filling vessel is connected to the Syringes of the Machine. Syringes are there for this machine.
- Set the required volume and fill the bottles accordingly.
- Nitrogen Blanketing is a process of introducing an inert gas, such as Nitrogen (the most cost effective), to the bottle to counter the effects of oxygen on storage. Mainly LDPE bottles are used for filling.
- Low Density Poly Ethylene Bottle (LDPE): Less toxic than other plastics & relatively safe for use.
- Bottles are sterilized by Ethylene oxide & Gamma radiation. Bottles are manufactured by Thermador, Dr. Pack.
- Bottles are placed on the Turret. Nozzles & caps are on the hoppers and through the conveyers the bottles first fill the solution from the syringes and fix the nozzles and cap. Finally seal the cap properly.

- And collect the filled bottles at the end to a box.
- Take around 1000 filled bottles for the In-Process checking, it has an In-process card to identify.
- During the filling, volume checking is carried out each 30 minutes. Then the filled bottles transfers outside through a hot air oven.
- Then in it is goes for IPQC checking. After checking, the passed products are stored in the 'Semi finished goods storage area.'
- Failed products are keeps it in the rejected area.'

❖ **IPQC:**

- In-Process Quality Control is the test between the production. For this there is a particular area, specially for the optical inspection of the bottles and leakage checking.

❖ **Product Development Area:**

- This area is mainly used for the formulation and development of the products.

❖ **Fumigation:**

- At the end of the day, the manufacturing room & filling room should be fumigated by using Potassium Permanganate & Formaldehyde to keep the controlled area from being contaminated.

3) **<u>Labeling Area:</u>** The filled bottles from the semi-finished products storage area transfer to the Labeling area by Hoist. Then the filled bottles are placed on the turret of the Labeling machine.

- **Labeling Machine:** Automatic self-adhesive labeling machine.

  - Model Number: NKSAL-120
  - Manufacturing year: 2010
  - Manufacturer: N.K Industries, Ahmedabad.

- Previously printed label roll placed on the conveyor, the sensor that sense the bottles and print on it. The properly labeled bottles are packed in the respective cartons.

4) Packing Area:

- Then the labeled bottles are packed in the cartons. They are printed by another machine.
- Carton Printing Machine: Ramatech machine.
- Then the printed cartons are put into the 20s, which is a box consists of 20 cartons.
- Then these 20s are weighed and check properly. And stick the label on the outside of the latter box.
- Keep one of the 20s as Control & pack these 20s into the Master cartons. Outside of that box also properly stick the label for the identification of the product.
- Tie the box or tape it properly.

❖ **Documents:**

1) Cleaning Records
2) Line Clearance
3) Packing Slip
4) Issue Slip.

5) Dispatch Area

- From this area only the final packed product transferred into the distribution area along with invoice.
- The Dispatch record must contain product name, batch number, manufacturing date, expiry date, checked by whom dispatching date etc.

QUALITY ASSURANCE (QA)

- Quality assurance (QA) and Good manufacturing practices (GMP) are the prime consideration for the manufacturing, distribution and marketing of Pharmaceutical products for the ensuring of its identity, strength, purity, pharmacological safety and efficacy and effectivity.
- The quality of a product of a pharmaceutical manufacturer depends on the fact that up to which at the satisfactory level of QA, GMP system has been adopted in the process of manufacturing, distribution and marketing of products during its total shelf life.
- Quality Assurance is a wide ranging concept covering all matter that individually or collectively influences the quality of a product.
- It is the sum total of the organized arrangements made with the objects of ensuring that Pharmaceutical products are of the expected quality required for their intended use.
- Quality Assurance therefore incorporates GMP, GLP, QC and Product Design & Development.
- **QA= GMP + QC + Product Design & Development + Quality Goal Activities.**

▪ **Activities done by Q.A:**

✓ In order to achieve the quality objective a wide range of activities are involved. Some of them are:

1. Ensuring fulfillment of **regulatory requirements**.
2. Establishing specifications and control procedures for all starting material, intermediate and finished products.
3. Arranging **Quality Audit** visits to suppliers and self- inspection.
4. Monitoring of the systems to ensure implementation of GMP in routine operation.
5. Establishing **manufacturing methods and SOPs** covering entire operations and their regular updating.
6. Communication of every aspects relating to quality to all relevant persons for early positive actions.

7. Identification of those parts of the process where in-process control checks are required and its implementation.
8. Identification of high risk areas of contamination for action towards it.
9. Establishing proper **Batch documentation system**, reviewing data and accessing problems.
10. **Validation of equipment, process, control procedures, critical systems.**
11. Review of **Market complaints** for actions.
12. **Rejection analysis.**
13. Identifying problems and positive actions for error cause removal.
14. Establishing a system of measuring the cost of rejection & identifying what measures can reduce such costs.
15. Solving of production and testing difficulties.
16. Coordination of packaging development and process improvement.
17. Ensuring product stability
18. Ensuring proper complaint, recall and other relevant QA system.
19. Ensuring a suitable product quality review system.
20. Ensuring adequate **Training Program.**
21. Ensuring complete **medical check up** to the workers once in a year.
22. Proper Documentation of each and every thing from the de-cartoning to dispatch and also include the post marketing analysis also.
23. Implement quality improvement plans according to the need.

- Quality Assurance Department (QA) of 'SYNOKEM PHARMACEUTICAL .' has a great & inevitable role throughout the process.
- It imparts a significant role in each and every step of the product development. According to the guidance of Q.A only QC, production carried out.
- QA maintained all the related records of the Manufacturing and properly store them. Internal Quality Audit also done by QA Personnel
- Thus, QA evaluate and guide the entire process according to the prescribed manner, GMP and other quality control systems.

❖ **<u>Documents prepared by QA Department:</u>**

1. **Annual Product Report Quality Report (APQR):**

APQR is an estimation prepared according to the current GMP requirements of different regulatory authorities. Normally annually or yearly performed. Previous reviews should be taken into account.

- **Contents:**
  1) Product Description
  2) Time period covered for APQR
  3) Manufacturing & Testing procedures followed
  4) Batch summary
  5) Raw material (API) review
  6) Environmental condition during manufacturing operation
  7) In-process results
  8) Critical equipment process result
  9) Finished product review
  10) Packing material review
  11) Process deviation & change controls
  12) Out of specification/ out of trend
  13) Non-conformance Report
  14) Product complaints
  15) Returned goods / Recalled products
  16) Yield reconciliation
  17) Adverse Drug Reactions (ADR)
  18) API Data
  19) Trend Analysis
  20) Conclusion & Recommendation.

2. Master Validation Plan:

A document that provides information on the respective company's validation work program. It should define details of and timescales for the validation work to be performed.

• **Validation**; Action of proving and documenting that any process, procedure or method actually and consistently leads to the expected results.

3. Process Validation:

The collection and evaluation of data, from the process design stage through. Commercial production, which establishes scientific evidence that a process is capable of consistently delivering quality products. Synokem pharmaceutical . carried out **Retrospective validation.**

• In case of Retrospective Validation,

- ✓ Protocol does not need to be submitted
- ✓ Prepare product quality review report on already manufactured batches
- ✓ Ten batches of same product subjected to analysis in this validation

- **Process Validation Phases:**

Fig. 2: Phases in Process Validation

4. Master Formula Record (MFR):

Master document for any Pharmaceutical product. MFR contains all information about the manufacturing process for the product. MFR is used as reference

standard for preparing Batch Manufacturing Record (BMR) by manufacturing units. MFR is keeps both Production & Q.A Department.

5. Site Master File:

• Document in the pharmaceutical industry which provides information about the production and control of manufacturing operations.

- Contents:
  1. General Information
  2. Personnel
  3. Premises
  4. Equipment
  5. Sanitation
  6. Documentation
  7. Production
  8. Q.C
  9. Loan license manufacture & Licensee
  10. Distribution, complaints & product recall
  11. Self- Inspection
  12. Export of Drugs.

Quality Control is an important part of Quality Assurance. Q.C mainly handles the product's quality. Analytically they ensure the product safety, purity and quality. Production is dependent on Q.A & Q.C.

QUALITY CONTROL

- According to WHO, QC is the part of GMP concerned with sampling, specifications and testing and with the organization, documentation and release procedures which ensure that the necessary and relevant tests are actually carried out and the materials are neither released for use, nor products are used for supply & sale until their quality has been satisfactory.
- QC head should have appropriate qualification and experience, which has control over one or several labs.

- Adequate facilities, trained personnel and approved procedures must be available for sampling, inspecting and testing of starting materials, packaging materials and intermediate bulk and finished products and where appropriate of monitoring environmental conditions for GMP purpose.

❖ COMPONENTS OF QC

Quality Control (QC) department of Synokem Pharmaceutical is well occupied and sufficient. They ensures the quality aspects related to each and every stage of the product development. The four main responsibility of quality control department of synokem pharmaceutical :

- Efficacy
- Safety
- Quality
- Compliance.

❖ Main Provisions of QC:

1. Chemical Testing Lab

2. Instrumental Analysis Lab
3. Microbiology & Toxicology Lab
4. Provision for retained samples and stability samples
5. Documentation Room
6. Relevant Books
7. SOPS
8. Trained Personnel.

❖ **Objectives of QC:**

- Establishment of quality standard: Economical production of a high quality product at the quality level the customer wants.
- Locating quality deviations: It is necessary to analyse the trend and extent of quality deviations in a manufacturing process, which should be explained by statistical techniques.
- Evaluating methods and processes of production: It is a corrective measure to maintain the quality.
- Sale of quality goods: QC accelerates the sale of the goods by supplying only the quality goods.
- Production of standard Quality goods: QC aims at manufacturing standardquality products and avoids producing inferior quality goods.
- Improvement in Quality: Aims at creating quality consciousness at all levels in the organization.

Main Functions Of Quality Control

1. **Raw Material Analysis**
2. **Instrumental Analysis**
3. **Water Analysis**
4. **Manufacturing Area Analysis**
5. **In-Process Quality Control**
6. **Microbiological Analysis**
7. **Finished products Analysis**
8. **Returned products Analysis**
9. **Documentation.**

1. RAW MATERIAL ANALYSIS:

- All materials that used into the manufacturing of a finished bulk (even though it may not be present in final product) eg; certain solvents etc, and which are consumed by person using it are called as raw materials.
- Starting materials can be either active drug or inactive substances. Raw material testing ensures that the raw materials used in pharmaceutical products are suitable for their intended use.
- This analysis using appropriate test methods & successfully meeting the challenges of such testing can prevent costly production problems and delays.
- Before finished pharmaceutical dosage forms are produced, the identity, purity & quality of raw materials must be established with the use of suitable test methods.
- This requires a wide range of analytical chemistry expertise.

- **Some of the important Raw Materials used in Industrty:**

1) Carboxy Methyl Cellulose Sodium IP
2) Chloramphenicol IP
3) Ciprofloxacin Hydrochloride IP
4) Dexamethasone Sodium Phosphate
5) Gentamicin Sulphate IP
6) Hydroxy Propyl Methyl Cellulose IP
7) Ketorolac Tromethamine IP
8) Moxifloxacin Hydrochloride IP
9) Olopatadine Hydrochloride IP
10) Oxymetazoline Hydrochloride IP

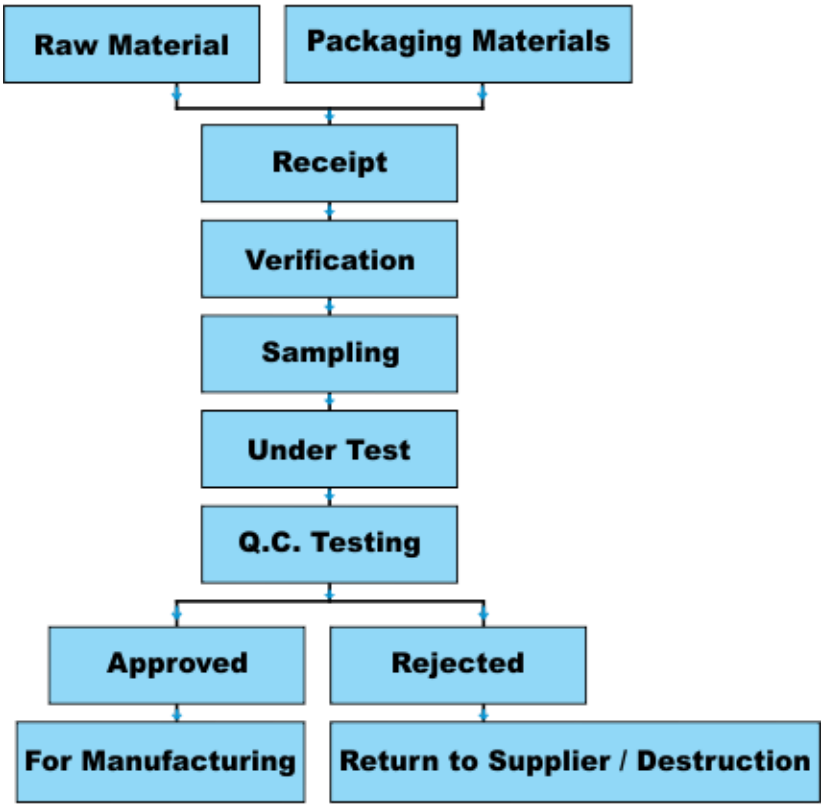
- **The most Commonly used instruments for Raw Material Analysis include;**
  - Weighing Balance
  - PH Meter
  - UV-Visible Spectrophotometer
  - General Titration Apparatus

- Ovens
- Melting Point Apparatus
- Polarimeter
- Flame Photometer
- Conductivity Meter.

- Quality Control shall receive "Goods Receipt Notes" (GRN) from Warehouse as an intimation for raw material sampling.
- Upon receipt, sampling personnel shall verify the details on the GRN and Supplier Certificate Of Analysis (COA).
- Sampling personnel shall enter the details in the Raw Materials Inward Record as per the GRN and assigns an Analytical Reference Number as per SOP.
- QC personnel should prepare the required number of labels i.e., "**Sample for Analysis" and "Sampled".**
- QC personnel shall carry self-sealed polyethylene bags, glass bottles, cleaned sampling devices, prepared labels and sampling record to proceed for sampling.
- Sampling personnel should verify the physical condition, consignment details and "Under Quarantine" label of the containers against GRN.
- In case of discrepancy the same shall be recorded and immediately informed to warehouse in charge for rectification.
- QC Personnel randomly select the containers for sampling and instruct the warehouse personnel to shift the same containers to sampling booth.
- QC Personnel should wear the safety devices and proceeds for sampling of selected containers one by one in the sampling booth.
- Sampling Personnel/ Executive should check the physical appearance of the material and mix the contents thoroughly within the container by sampling devices and collects the sample in self-sealed bags (for solids) and glass bottles (for liquids).
- Post sampling container shall be sealed or closed immediately and "Sampled" labels shall be affix on the containers adjacent to "**Under Quarantine" Labels.**
- Sampling Executive shall take equal quantity from each container and collect composite sample.

- If the physical appearance of the material is varying from container to container and specification as well, sampling activity shall be discontinued and informed to Head of the QC.
- In such cases Head-QC & QC representative shall approach warehouse and verifies the physical appearance of the materials.
- If the material is confirmed failing in physical appearance, consignment shall be rejected without OOS (Out Of Specification) investigation.
- If the physical appearance of the material in all the containers is similar and complying, all the samples shall be collected.
- All observations of sampling shall be recorded in "Raw Material Sampling Record".
- Sampled containers shall be shifted to their original place immediately. Details of sampling shall be entered into the sampling booth usage and cleaning record of warehouse.
- Collected composite sample shall be brought to QC and divided into 3 parts in sample distribution area.
- One part shall be preserved as retention sample (for starting raw material only) and other two parts shall be used for complete analysis.
- The QC Analyst shall test all the samples as per respective standard test procedures.
- Some of the common things tested for Raw Material Analysis are;
  - PH
  - Assay
  - Description
  - Physical Appearance
  - Other chemical tests
- If the sample meets the prescribed specification, material shall be approved and retention sample shall be logged.
- In case sample does not meet the specifications, repeat the test then also it fails, OOS shall be raised and investigation shall be carried out.

- **Flow Chart For Raw Materials Inspection:**



2. INSTRUMENTAL ANALYSIS:

Instruments are one of the essential thing in the Quality Control Department. By the help of those instruments only the analysis of various items are carried out.

Some of the Important Instruments In The QC Department of Synokem Pharmaceutical are

1. Weighing Balance
2. Magnetic Stirrer
3. Desiccator
4. Flame Photometer
5. Conductivity Meter
6. Heating Mantle
7. Hot Air Oven
8. UV-Visible Spectrophotometer
9. Polarimeter.
10. PH Meter
11. Water Bath

12. Melting Point Apparatus
13. HPLC
14. Refrigerator
15. Bunsen Burner.

1. Weighing Balance:

- This is mainly used for the determination of weight.
- Helps to weigh the materials more accurate and précised.
- Manufactured By: Mettler Toledo, Columbus.
- Capacity: Maximum: 220 Grams, Minimum: 0.1 Milligrams.
- Model No: ML201/01.

➢ **Calibration:**

Operate the instrument as per respective SOP. Switch 'ON' the instrument. The display will blink and wait for some time to a stable display. Place 10 gram on the weighing pan. Note the weight. Calculate the difference between the weight in the specification and observed weight. Repeat the above two steps using 50 gram and 100 gram. Record the reading and check the accuracy. Note it down in the Calibration record of Weighing balance.

2. Magnetic Stirrer:

It is a device widely used in laboratories and consists of a rotating magnet or a stationary electromagnet that creates a rotating magnetic field. Used to make a stir bar, immerse in a liquid, quickly spin, or stirring or mixing a solution.

3. Desiccator:

They are sealable enclosures containing desiccants used for preserving moisture sensitive items such as cobalt chloride paper for another use. Mainly used to protect chemicals which are hygroscopic or which react with water from humidity.

4. Flame Photometer:

It is a device used in inorganic chemical analysis to determine the concentration of certain metal ions, among them sodium, potassium, lithium, and calcium. Group 1 and Group 2 metals are quite sensitive to Flame Photometry due to their low concentration energies.

5. Conductivity Meter:

It measures the exact and accurate conductance of solutions. A calibrated Conductivity meter has the efficiency to measure the TDS or Total Dissolved Solids in any solution.

- **Calibration**

Put the Knob into 200 ppt and a solution of 0.1 N KCl dipped by the electrode. Then weigh until it shows 14.2.After that reset the knob into 20 ppt. Wash properly several times by water.

6. Heating Mentle:

A heating mantle, or isomantle, is a piece of laboratory equipment used to apply heat to containers, as an alternative to other forms of heated bath. Used to heat or temper certain media in glass vessels.

7. Hot Air Oven:

These are electrical devices which use dry heat to sterilize. They were originally developed by Pasteur. They use a thermostat to control the temperature. Their double walled insulation keeps the heat in and conserves energy, the inner layer being a poor conductor and outer layer being metallic.

8. UV-Visible Spectrophotometer:

Routinely used in analytical chemistry for the quantitative determination of different analytes, such as metal ions, highly conjugated organic compound, and biological macromolecule. Solvent polarity and PH can affect the absorption spectrum of an organic compound. The principle of UV-Visible Spectroscopy is based on the absorption of monochromatic radiations by solutions of chemical substances, in the range of 185 nm to 380 nm & 380 nm to 780 nm of the spectrum respectively.

- **Calibration**
    a) Control of Wavelength
    b) Control of Absorbance
    c) Limit of stray light
    d) Resolution Power.

a) Control of wavelength:

Weigh accurately 1.0g of Holmium Oxide & dissolve it in 1.4 M Perchloric acid solution. Makeup to 25 ml with the same solvent. Select the method file of CONTROL of WAVELENGTH in the instrument. After selecting the file press Reference button for baseline correction. Then fill the cuvette with 1.4 M Perchloric acid and put in the sample cubicle and press referenced to zero. After auto Zero put the Holmium Perchlorate solution in sample cubicle then press start key. Scan it & verify the wavelength using absorption maxima of Holmium Perchlorate solution.

b) Control of Absorbance:

Dry a quantity of the Potassium dichromate by heating to constant weight at 130° C. Weight accurately about 60 mg of dried potassium dichromate & dissolve it in 0.005 M Sulphuric acid solution. Make up to 1000ml with the same solvent. Make the solution as (A). Weigh accurately about 60 mg of dried potassium dichromate & dissolve it in 0.005 M Sulphuric acid solution. Make up to 100 ml with the same solvent. Make the solution as (B).Select the method file of CONTROL OF ABSORBANCE in the instrument. After selecting the file press reference button for baseline correction. Then fill the cuvette with 0.005 M H_2SO4 for blank and put in both sample cubicle & press reference to zero. After auto zero put the Potassium dichromate solution labeled as solution 'A' in sample cubicle then press start key taking absorbance individually for first four wavelengths. Now take the absorbance at 430 nm for solution 'B'. Note the absorption maxima of potassium dichromate solution at a different wavelength and calculate the absorbance, tolerance.

c) Limit of Light stray:

Dry a quantity of the Potassium Chloride by heating to constant weight at 130° C. Weigh accurately 1.20g of dried KCI & dissolve it in 50 ml distilled water. Make up to 100 ml with the same solvent. Select the method file of LIMIT OF STRAY LIGHT in the instrument. After selecting the file press Reference button for baseline correction. Check the absorbance of above solution using water as a blank at 200 nm. Absorbance should be greater than 2.0.

d) Resolution Power:

Prepare 0.02% v/v solution of Toluene in Hexane UV. Select the method file of RESOLUTION power in the instrument. After selecting the file press Reference button for baseline correction. Measure the absorbance of above solution at 266 nm & 269 nm using Hexane UV as blank solution. The ratio of absorbance maxima at 269 nm to that of 266 nm minima should be more than 15. Note down the report in the internal calibration certificate & in instrument log book.

9. Polarimetry:

A Polarimeter is a scientific instrument used to measure the angle of rotation caused by passing polarized light through an optically active substances. It is used to analyze chiral substances and determine their concentration in solutions. It is applied in quality control, laboratory analytics, as well as in R & D in the pharmaceutical, cosmetics, chemical, food and medical industries.

10. PH Meter:

It is an electrical device that determines the acidity or basicity of aqueous solutions, one of the most commonly monitored parameters.

- **Calibration:**

Calibrated by three point method. Switch 'ON' power switch at the rear panel. Press the CAL button. Rinse the electrode with deionized water and blot dry using a piece of tissue. Place the electrode in the solution of PH 9.2 buffer, allow the display to stabilize. Bring the standby/ Read switch to

'standby.' Remove the electrode from PH 9.2 buffer. Wash thoroughly and place PH 7.00 buffer and wait for 30 secs. Press standby/ Read switch to 'Read'. Check back PH 4.00 and note the value. Repeat 7.00, 4.00 & 9.2 buffers to get correct values. Rinse the electrode with purified water and place it in sample and wait for 30 seconds and read the PH of the sample. Switch 'OFF' the instrument when not in use for a long period.

11. Water Bath:

One of the laboratory equipment made from a container filled with heated water. It is used to incubate samples in water at a constant temperature over a long period of time..

12. Melting Point Apparatus:

Used to determine the melting point of a substance. Some types of Melting point apparatus include the Thiele tube, Fisher- johns apparatus & automatic melting point apparatus.

13. HPLC:

High Performance Liquid Chromatography (HPLC) is a form of column chromatography that pumps a sample mixture or analyte in a solvent (Mobile Phase) at high pressure through a column with chromatographic packing material (Stationary Phase).

3. WATER ANALYSIS:

Products licensed to manufacture at Chethana pharmaceuticals are liquid formulations.

- All the products uses sterile purified water I.P is used as vehicle.
- **Reverse Osmosis (RO)** Water is used for the production of all formulations. Q.C Personnel conduct both raw water & Purified water analysis.
    - Methods used by Chethana Pharmaceuticals:
    - Microbial Limit Test (MLT)
    - Membrane Filtration
    - Plate Count Method.

- **Types of Water Analysis:**

a) Raw Water Analysis:

Raw water samples are collected directly from the well into clean glass containers for chemical, physical & microbiological analysis. The complete analysis of raw water is performed once in a year as per Bureau of Indian Standards (BIS) specification. Microbiological analysis of raw water is conducted in every 3rd month to monitor the bio-load of the sample. Test for the presence of 'E.coli, salmonella, pseudomonas are performed in raw water & the observations are recorded. Pour plate method using plate count agar is used for microbiological analysis.

b) Purified Water Analysis:

The purified water produced by 'Reverse Osmosis' system is further allowed to run through the 'Loop system' at 80°C to avoid contamination of the water used for the production of sterile products. Total microbial count of water, presence of pathogenic organisms is monitored or tested in every sample intended for manufacturing process. Samples of Purified water is taken from sterile manufacturing area, washing area and send it to Q.C lab for analysis. Analysis is carried out as per the requirements of the Pharmacopoeia. Results are recorded. 'Pour plate' method is used for the microbiological analysis. Test for the presence of E.coli, salmonella, pseudomonas' are performed in purified water & the observations are recorded. Also tested for chlorides and sulphates by AgNO, & BaCl, respectively. By adding the above reagents, if any opalescence or turbidity may occurs means the water fails the test. Q.C Personnel should inform the result to Production unit and accordingly the production unit done the production by changing the water or taking any other measures to rectify it.

TEST	LIMIT
Description	Clear, colourless solution
Acidity or Alkanity	Resulting solution is not coloured
Heavy Metals	Less than 0.1 ppm

Nitrates	Blue colour is not inense than std.
Oxidizable Substance	Solution Remain faintly Pink
Conductivity	<5 u seimens/cm
pH	5.50-6.50
Pathogens organism	Nill
(TDS)	<1 ppm

c) Wash Water Analysis:

Wash water is any water used to clean or wash materials or equipments. Industrial wash water is waste water that may contain hydrocarbon residue, solids, sludge, various ions and water. This water is mainly subjected to test for chlorides and sulphates by AgNO3 & BaCl, respectively. By adding the above reagents, if any opalescence or turbidity may occurs means the water fails the test.

4. MANUFACTURE AREA ANALYSIS:

In order to control the contamination & entry of unwanted foreign particles and keeping them out of the product is a challenge. It is essential to check the Microbial count of the Manufacturing area by 'Settle plate Method'.

- **Settle plate Method:**

✓Ensure the room is sterilized.

✓ On the next day perform the settle plate method.

✓ Prepare the agar plates.

✓ Before performing the work place the agar plates under UV lights for 30 minutes.

✓ Open the agar plates and keep 2 numbers in manufacturing area & 3 numbers in filling area including inside the Laminar flow bench for detection of bacterial colony forming units.

✓ One of the prepared agar plates taken to the aseptic area should not be opened & maintained as a -ve control.

✓ Record all observations.

✓ If any microbial growth found in the agar plates means that area is not sterilized properly.

✓ Take proper measures to rectify it.

- **Swab Test:**

Surface monitoring using cotton swabs method is best to evaluate the effectiveness of hygiene procedures on uneven surfaces. Swab or wipe sampling can be used to detect organic and inorganic contaminants. This method is most effective on smooth surfaces such as glass, metal, painted surfaces.

5. IN-PROCESS QUALITY CONTROL (IPQC):

IPQC is the controlling procedures involved in manufacturing of dosage forms starting from raw material purchase to dispatch in final packaging. It prevents errors during processing. Human errors during process can be minimized.

It is a planned system to enforce the flow of manufacturing and packaging operations according to the established rules & practices. IPQC procedures are usually rapid and simple tests or inspection that are performed when the manufacturing of the product batch is in process.

IPQC Tests:

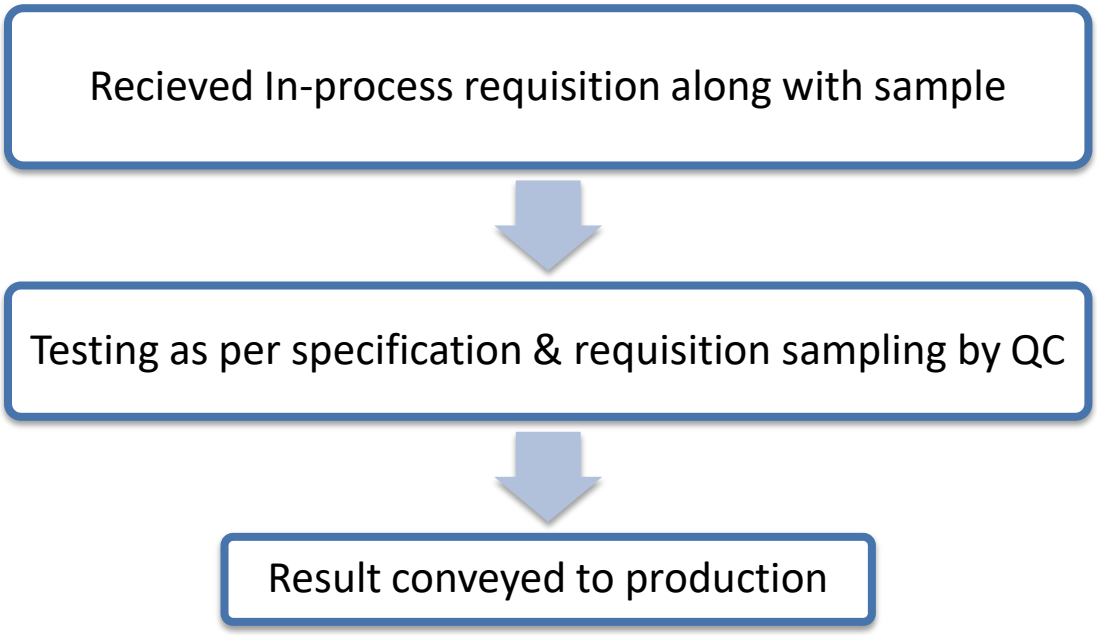
I. **Vaccum Leak Test:** 20 bottles are taken and put it in the Vaccum desiccator, switch 'ON' the equipment and check the leakage after sometime.

II. **Volume:**Check the volume of all filled bottles. The volume withdraws should not less than the label claim. Volume should be measured at the start of filling & after every two hours by using a calibrated measuring cylinder.

III. **Clarity of Solution:** Clarity should be checked on the every cover.

IV. **Test seal integrity and leakage test**.

- **Flow chart In-Process Check:**



6. MICROBIOLOGICAL ANALYSIS:

Microbiology is the study of microscopic organisms. Microorganisms are ubiquitous diverse occupying almost all environment & habitats including the air, sea, land, on the human skin & inside the human body. The primary objective of pharmaceutical microbiology is "contamination control."

- Some of the important areas are;

A. <u>STERILITY TEST:</u>

a) Direct Inoculation Method:

Prepare both Soyabean casein digest media and fluid thioglycollate media in two different conical flask, and cover the mouth with aluminium foil paper. Autoclave the above medias at 121°C for 30 minutes. Under the assistance of LAF, add the particular drops into the two media. Incubate for 14 days and after that observe the media and record the result.

b) Membrane Filtration Method:

Autoclave all the requirements that needed for this test, i.e, Membrane filtration unit + Fluid thioglycollate media + NaCl + Soyabean casein digest media at 121°C for 30 minutes. Under LAF, put 10 bottles of prepared drops to the sterile flask or Membrane filtration unit. Then add NaCl solution. Then cut the 0.2/ 0.45µ membrane filter that present inside the membrane filtration unit. And put into casein digest media & fluid thioglycollate media and incubate for 14 days.

B. MICROBIAL ENUMERATION METHOD:

- **Plate Method:**

I. Pour Plate Method: Purified water sample is collected aseptically in clean sterilized containers from manufacturing area.Pour plate method, using plate count agar is used for microbiological analysis. Plates are incubated at 35°C for 48 hours. Number of CFU is checked after incubation period. CFU/100 ml of sample is calculated. Test for the presence of E.Coli, Salmonella and Pseudomonas are performed in Purified water and the observations are recorded.

II. Settle Plate Method:

- Mainly used to for the Environmental monitoring.

C. METHODS & LIMITS FOR THE TESTING OF PHARMACEUTICAL GRADE WATER:

- Total Dissolved Solids
- Conductivity
- PH
- Microbial Limit Test
- Pathogenic Organisms.

D. ENVIRONMENTAL MONITORING:

▪ It is the key part of the assessment of pharmaceutical manufacturing facilities.

▪ This data indicates if clean rooms are operating correctly, the effectiveness of cleaning and of personnel activities.

- Assessment of contamination control.
- HVAC; Heating, Ventilation & Air Conditioning.
- These Parameters include:
- Temperature
- Humidity
- Pressure
- Room air changes
- Air flow pattern
- Contamination analysis
- Particles count.

Types Of Environmental Monitoring:

1. **Viable**
2. **Non-Viable**

Viable Environmental Monitoring:

Examination of microorganisms (bacteria & fungi) located with the manufacturing area. For this:

1. Air sampling
2. Settle Plates
3. Active (volumetric) air samplers.

Non-viable Environmental Monitoring:

For airborne particles.

E. In case of Products containing Antibiotic + Dexamethasone combination, Microbiological assay carried out for the assay (Well Diffusion Method).

- Particulate Monitoring in Air- 6 Months
- HEPA Filter Integrity Testing (Smoke Testing) – Yearly
- Air changes rates - 6 Monthly
- Air Pressure differentials – Daily
- Temperature & Humidity – Daily

- Microbiological Monitoring by Settle Plate & Swabs in aseptic areas- Daily.

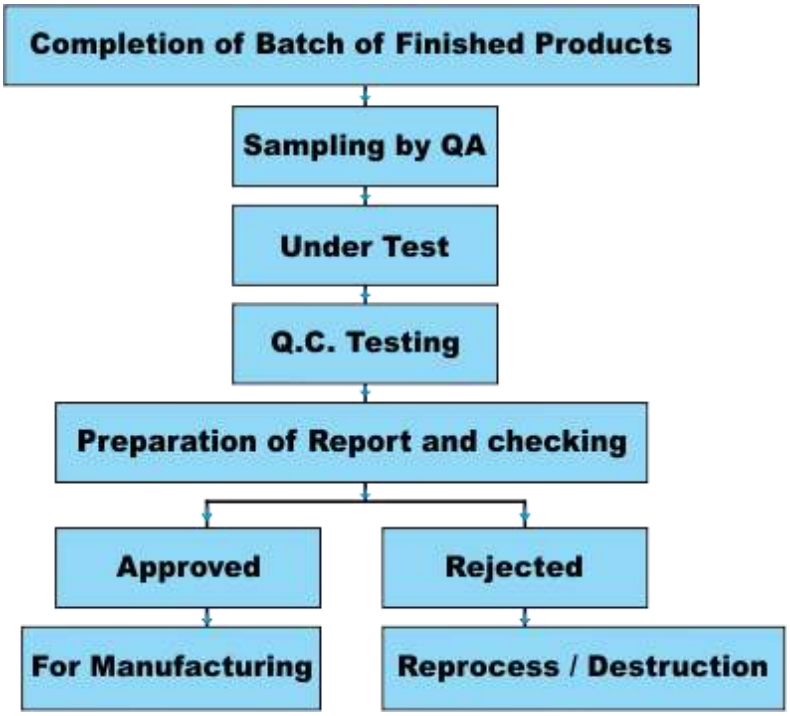
7. FINISHED PRODUCTS ANALYSIS:

Finished product analysis is different for each product. Each product have its' own tests according to the composition in it. Some products requires microbiological assay, products containing Antibiotics and Dexamethasone.

- Some of the common things that are analyze in this area are;

  - Identification
  - PH
  - Assay of the components
  - Sterility Test
  - Clarity Test
  - Leakage Test.

❖ **Flow chart of Finished Product Inspection:**



8. RETURNED PRODUCT ANALYSIS:

Returned products are either fails to meet the established specification or returned on the basis of breakage or expiry date or damaged packaging, commercial or administrative aspects, or on the basis of customer complaint investigation and action thereof. Warehouse personnel shall receive the returned goods from the market or any other location. Store the materials on separate place as per the appropriate storage condition of the respective products in the designed area of return goods. After receipt of the material, the warehouse shall verify the returned consignment for the following points against receipt documents received.

- Identify the product/ authenticity of labels.
- Batch Number
- The number of containers
- Condition of containers and seal integrity.
- Weight and the total quantity of returned goods containers.
- Warehouse personnel shall check the physical condition of returned goods and record the details in the "Returned Goods Verification Report".
- In case of discrepancy in the receipt documents, Warehouse shall not confirm the "Goods Returned Settlement Memo" and intimate to concern person/ customer/ marketing department for its rectification.
- Warehouse personnel shall send the "Returned Goods Verification Report" to the QC for verification.
- QC shall verify the goods consignment and shall recommend for decision according to the nature of the returned goods.
- After completion of physical verification of return goods by warehouse and QC, Warehouse personnel shall ensure cleaning/ de-cartooning of the return goods as per the condition required.
- The final disposition of the returned goods shall have to be finalized within 60 days of receipt.
- It should dispose properly without cause any harmful effect to the environment and surroundings.

9. DOCUMENTATION:

There are many Records that are strictly maintained by the Q.C department, they are;

1. Purified Water Report
2. Environmental Monitoring Register
3. Sterility Register
4. Finished Good Product Register
5. Raw Material Analysis Register
6. Packing Material Register
    - Primary Packing Material Analysis
    - Secondary Packing Material Analysis
7. Raw Water Analysis Register
8. Microbial Limit Test (MLT)
9. Reagent Preparation Register
10. Sampling Register
11. Water Testing Register
12. Conductivity & General Packing Material Test Register
13. Conductivity Meter Log Book
14. PH Meter Log Book
15. In-Process Analysis Register
16. Calibration Register - Weighing Balance
17. Calibration Register - Conductivity Meter
18. Calibration Register - PH Meter
19. Fumigation Register
20. Sub-culturing Register
21. Sterility test Register for primary packing material
22. Environmental Monitoring Test Register.

CONCLUSION

Through this Industrial Training I gained lots of knowledge about Pharmaceutical Industry and its' inevitable role in the society.

This one month helps me to understand the provisions to manufacture the sterile ophthalmic preparations, its analysis and all about the production to a certain extent within this short period.

Also helps me to understand the GMP requirements that should comply by the pharmaceutical Industry and its significance for the maintenance of quality of the formulations.

These 30 days gave me lots of field work experiences in the Industry.

THANK YOU.....

GOVIND GUPTA

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