“MANUFACTURING DESIGN AND ALLINGMENT WITH REGULATORY REQUIREMENT AS PER NEW REGULATION AMENDED BY CDSCO”

A Thesis Submitted to

NIRMA UNIVERSITY

in Partial Fulfillment for the Award of the Degree of

MASTER OF PHARMACY

IN

REGULATORY AFFAIRS

BY

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We wish her better achievements in her the future endeavours.

Thanking You.

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ACKNOWLEDGEMENTS

History of all great works into witness that no great work was ever done without either active or passive support if the person.

I will like to take the opportunity to express my heartily thanks to all those who are related to my thesis in some or the other way and have been a part to frame it.

First of all I am thankful to my project guide Dr. Nrupesh Patel for his guidance, suggestions and for constant support remarks to complete my thesis .I also express my thanks to all HOD and faculty who has been always been a source of inspiration. I would like to thank my industrial guide Mr. Piyush Patel for the guidance

Most importantly I am thankful to my family and friend who always support me and provide me with all my needs. They always appreciate my work with positive words which helps me a lot. I am grateful to have my seniors who always assist me in my thesis.

Finally I am thankful to all my friends for making my college day's wonderful memory. Thanks are even due to Microsoft word, all new technologies and library.

SONI KRISHA H.

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ABSTRACT

Pharmaceutical part incorporates different divisions, for example, plan, API, excipients, clinical gadget, beautifiers, and biologics. Every division has its own administrative necessities. Administrative specialists are worry about wellbeing of the items. In this way revisions in the administrative prerequisites have been seen radically. Great Manufacturing Practice (GMP) is a framework for guaranteeing that items are reliably delivered and controlled by quality measures. It is intended to limit the dangers engaged with any pharmaceutical creation that can't be disposed of through testing the last product.GMP covers all parts of creation from the beginning materials, premises, and gear to the preparation and individual cleanliness of staff. Point by point composed strategies are basic for each procedure that could influence the nature of the completed item. There must be frameworks to give reported verification that right systems are reliably followed at each progression in the assembling procedure - each time an item is made. Appropriate direction identified with administrative necessities ought to be accommodated the procedure from the concoction element to the market. Pharmaceutical items incorporate different administrative strides for creation of pharmaceutical item according to explicit measures. Great Manufacturing Practice (GMP) is a framework for guaranteeing that items are reliably created and controlled by quality principles. It is intended to limit the dangers engaged with any pharmaceutical creation that can't be disposed of through testing the last product.GMP covers all parts of creation from the beginning materials, premises, and hardware to the preparation and individual cleanliness of staff. Point by point composed strategies are fundamental for each procedure that could influence the nature of the completed item. There must be frameworks to give reported evidence that right methods are reliably followed at each progression in the assembling procedure - each time an item is made. Assembling of pharmaceutical items incorporates different advances including land search, land securing, limit building, natural elements, arranging, structure, and development. Pharmaceutical part incorporates different divisions, for example, detailing, API, excipients, clinical gadget, beautifying agents, and biologics. Every division has its own administrative prerequisites. Administrative specialists are worry about security of the items. The USFDA's Office of Manufacturing Quality (OMQ)

at the Center for Drug Evaluation Research (CDER) assesses consistence with cGMP for drugs dependent on examination reports and proof assembled by USFDA specialists Therefore revisions in the administrative necessities have been seen radically. Great Manufacturing Practice (GMP) is a framework for guaranteeing that items are reliably delivered and controlled by quality norms. It is intended to limit the dangers engaged with any pharmaceutical creation that can't be dispensed with through testing the last product.GMP covers all parts of creation from the beginning materials, premises, and hardware to the preparation and individual cleanliness of staff. Nitty gritty composed methodology are fundamental for each procedure that could influence the nature of the completed item. There must be frameworks to give archived evidence that right systems are reliably followed at each progression in the assembling procedure - each time an item is made. Appropriate direction identified with administrative prerequisites ought to be accommodated the procedure from the synthetic element to the market. Pharmaceutical items incorporate different administrative strides for creation of pharmaceutical item according to explicit norms. Great Manufacturing Practice (GMP) is a framework for guaranteeing that items are reliably created and controlled by quality guidelines. It is intended to limit the dangers associated with any pharmaceutical creation that can't be wiped out through testing the last product.GMP covers all parts of creation from the beginning materials, premises, and gear to the preparation and individual cleanliness of staff. Point by point composed methodology are basic for each procedure that could influence the nature of the completed item. There must be frameworks to give reported evidence that right methods are reliably followed at each progression in the assembling procedure - each time an item is made. Assembling of pharmaceutical items incorporates different advances including land search, land procurement, limit building, ecological variables, arranging, structure, and development. The Indian pharmaceutical organizations have gotten 19 admonition letters, out of the 41 (46 percent) gave by the Office of Manufacturing Quality of the US Food and Drug Administration (USFDA) in 2019, the most in four years. This turned around the ongoing pattern wherein Indian organizations had been progressively consenting to the principles and settling their assembling quality issues rapidly that had sprung up in the course of the last four-five years.If the Indian medication producers represented almost 50 percent of the

present great assembling rehearses (cGMP)- related admonition letters in 2015, it diminished to under 30 percent in 2016. This number additionally decreased to 24 percent in 2017. In 2018, none of the best ten residential firms were in the cGMP notice letter list, however numerous organizations were attempting to escape the trouble.Out of 68 notice letters gave by the USFDA in 2018, 10 were identified with India. In 2017, a lot of caution letters was 17 out of 79. As per an examination by the Indian Pharmaceutical Alliance (IPA) and consultancy firm McKinsey, a few years back, the quantity of FDA reviews in India declined from 272 of every 2017 to 192 out of 2015, however the portion of plants getting a leeway without antagonistic perceptions expanded from 32 percent to 51 for each cent.The USFDA's Office of Manufacturing Quality (OMQ) at the Center for Drug Evaluation Research (CDER) assesses consistence with cGMP for drugs dependent on assessment reports and proof accumulated by USFDA specialists. Failing firms are given notification with Form-483 perceptions specifying the mistakes and are offered time to react and amend the issues. Cautioning letters are given if the organizations despite everything neglect to consent to the standards after the rehashed assessments. Most admonition letters gave in 2019 were essentially founded on investigations held a year back and dissecting the advancement of remediation.

CHAPTER-1

INTRODUCTION

Highlights of New Clinical Trials Rules 2019:

- **INTRODUCTION**
  - Ministry of Health and Family Welfare [MoHFW] has notified the "New Drugs and Clinical Trials Rules, 2019" on 25th March 2019 [Ref Ministry of Health GSR Notification #227 dated 19 March 2019]. The new rules aim to promote clinical research in the country and will change the regulatory landscape for the approval of new drugs and conduct of clinical trials in the country.
- **EFFECTIVE DATE**
- 25 March 2019 [date of publication on eGazette website]. Chapter IV which includes provision for 'Ethics committee for biomedical and health research' will be effective after 180 days i.e. 21 Sep 2019.

- **APPLICABILITY**

- The principles will apply to every new medication, investigational new medications for human use, clinical preliminary, bioequivalence study, bioavailability study and Ethics Committee. The new guidelines will override Part XA and Schedule Y of Drugs and Cosmetics Rules, with prompt impact. In the event that there is any irregularity between these guidelines and some other standard made under the Drugs and Cosmetics Act, the arrangements of these principles will beat such different standards. Activities taken by the current guidelines [Drugs and Cosmetics Rules, 1945] will keep on being as a result and legitimate. This implies existing licenses, orders, bearings will keep on staying legitimate.

- **FEES & FORMS**

- A hiked fee structure has been implemented. Key ones being :
- 3 lakh INR (aprox 3800 Euro/4500 USD) for Phase I
- 2 lakh INR (aprox 2500 Euro/2900 USD) for Phase II, III, IV & BA/BE study
- 5 lakh INR (aprox 6500 Euro/7200 USD) for pre submission meeting
- 50,000 INR (aprox 650 Euro/720 USD) for post submission meeting
- 5 lakh INR (aprox 6500 Euro/7200 USD) for registration of BA / BE study centre
- 5 lakh INR (aprox 6500 Euro/7200 USD) for new drug permission / Finished formulation or API [import]

- Administratively, all the application and approval formats have undergone a change. Some of them are:
- Form CT04 – Clinical Trial Application Form (Replaces Form 44)
- Form CT 04 A- Automatic Approval Information to CDSCO
- Form CT 06 - Permission to Conduct CTs by CDSCO
- Form CT 16- Application to grant of License to Import of New Drug for Clinical Trials (Replaces Form 12)

- **SALIENT FEATURES**

- Definitions of numerous beforehand vague terms have been incorporated. New medication definition has been widened, covers fresher helpful alternatives like SR/MR, NDDS, Living changed life forms, monoclonal antibodies, immature microorganisms determined items, quality restorative items, xenografts and so forth.

  2/4 first May 2019

- Defines orphan drug in the regulation as drug used to treat condition which affects not more than 5 lac persons in India

- **Provision of waiver of local ph III clinical trials**

➢ if drug is approved and marketed in certain countries [as notified from time to time] subject to certain conditions and confirming conduct of Phase IV study. The Ph IV study requirement could be reduced in case of drugs of special relevance, in case of unmet need, for rare disease for which drugs are not available or available at a high cost or orphan drugs

➢ Animal toxicology, reproduction studies, teratogenic studies, perinatal studies, mutagenicity and carcinogenicity studies may be modified and relaxed in case of imported products if new drug is available for more than 2 years in certain countries. In case of locally manufactured product, this relaxation may be allowed if the drug is marketed in other countries for several years.

- **Provision of Pre-submission meetings included** –

- Applicants can discuss their projects with the regulators and subject experts by paying a certain fee, before making actual submission to the regulator, for seeking guidance about the requirements of law and procedure applicable for their projects.

- **Provision of Post-submission meetings included**:

- If the applicant desires to seek clarification in person in respect of pending application and queries related thereto, the applicant may make an application for a post-submission meeting with the officer designated by the Central Licencing Authority within a period of fifteen days from the date the query was received for seeking guidance with regards to the queries concerning pending application.

- **Provision of Post-Trial Access**

- If the drug is beneficial, and there is no alternative therapy, Investigator can recommend post trial access for the patient
- EC approval and Patient/legal heir's consent is required
- No liability on sponsor for post-trial use by patient

- **Validity of clinical trial permissions**

- The permission to initiate Clinical Trial will be valid till 2 years from the date of issue, unless extended by licensing authority
- New provisions to be followed during trial
- Enrolment status should be submitted on quarterly basis to licensing authority
- Six monthly status reports on the trial should be submitted in SUGAM portal
- Early termination of clinical trial should be reported to licencing authority within 30 working days
- In case of study related injury or death, compensation should be provided within 30 calendar days of receipt of orders from licencing authority [previously this was 30 days].
- If a drug is found to be useful in clinical development, firm should submit application for import or manufacture of the drug for sale in India, unless otherwise justified.

3/4 1st May 2019

- SAE reporting timeline for sponsor changed to 14 calendar days from "awareness of SAE/Death" and not "Occurrence/onset of SAE"

- **Compensation for injury or death**

- No change in regulation;
- Central licensing Authority at their discretion may or may not constitute the Expert Committee to review reports of SAE submitted. In case they don't decided to formulate the committee, then the Central Licensing Authority shall review the report and convey the decision

- **Provisions for BA / BE studies are more clearly defined**

- Provisions like application process, inspection process, suspension or cancellation of permission etc are defined clearly in the new regulations.
- Requirements of BA / BE centers registrations have been defined in the new rules
- BE Permission will remain valid for a period of one year from the date of its issue, unless suspended or cancelled by the Central Licensing Authority
- Requirements for Clinical Trial labels are defined under "Manner of labelling" and in addition to routine contents, name of institute where clinical trial is proposed to be conducted is required to be added

- **Differentiation of Phase IV and Post marketing studies is described.**

- Phase IV (Post marketing trial) is expected to be conducted approved protocol with definite scientific objectives, inclusion/ exclusion criteria, safety/ efficacy assessment in approved indication in approved patient population. All ethical guidelines including Compensation rule needs to be followed and drug may be given free of cost.
- Post Marketing Surveillance or observational or non-interventional study for active surveillance is expected to be conducted with approved protocol with scientific objective, Inclusion/ exclusion as per approved pack insert and regulatory provisions or guidelines of clinical trial are not applicable.

- **TIMELINES**

- Time bound approvals:
- Decision to grant of permission to conduct clinical trial of new drug or investigational new drug will be taken within 90 days.
- For clinical trial of drugs discovered in India / research and development done in India and the drug is proposed to be manufactured and marketed in India, application shall be processed within 30 working days. If no response from Licensing Authority is received in 30 working days then this application is deemed as approved.
- The applicant who has taken deemed approval shall before initiating the clinical trial, inform the Central Licensing Authority in Form CT-4A and the Central Licensing Authority shall on the basis of the said information, take on record the Form CT-4A which shall become part of the official record and shall be called automatic approval of the Central Licensing Authority 4/4 1st May 2019
- For clinical trials of drugs already approved outside India, application will be processed within 90 working days. There is no provision of deemed approval.
- New drug approval in 90 working days [import as well as local manufacturing]

- **ETHICS COMMITTEE**

- Composition : 50 percent of its members who are not affiliated with the institute or organization in which such committee is constituted.
- EC registration certificate shall be granted in Form CT-02 with in a period of 45 working days.
- Validity will be for a period of five years from the date of its issue, unless suspended or cancelled by the Central Licensing Authority
- Renewal of EC Registration: Ethics Committee may make an application for renewal of registration 90 days prior to the date of the expiry of the registration to ensure deemed continuity.
- Where a clinical trial site does not have its own Ethics Committee, clinical trial at that site may be initiated after obtaining approval of the protocol from the Institutional Ethics Committee of another trial site; or an independent Ethics Committee. The approving

Ethics Committee shall be responsible for the study at the trial site which should be located within the same city or within a radius of 50 km of the clinical trial site.

- **REJECTION & APPEAL**

- In case of rejection, the applicant may request the Central Licensing Authority, to reconsider the application within a period of sixty working days from the date of rejection of the application on payment of fee and submission of required documents.
- An applicant who is aggrieved by the decision of the Central Licensing Authority under the Ministry of Health and Family Welfare, may file an appeal before the Central Government within forty-five days from the date of receipt of such decision and the Government, may, after such enquiry, and after giving an opportunity of being heard to the appellant, dispose of the appeal within a period of sixty days.

- **SUSPENSION / REVOCATION**

- Provision of putting order of suspension or revocation in public domain:
- In case, the Central Licencing Authority issue any order of suspension or revocation or cancellation of any permission or licence or registration granted under these rules, such order shall be made available in the public domain immediately by uploading it in the website of Central Drugs Standard Control Organisation."

- **INDIA'S GOOD MANUFACTURING PRACTICE (GMP) STANDARDS**

- India's GMP standards for medical devices and drugs are covered in Schedule M and Schedule M III of the Drugs and Cosmetics Act (DCA):
- Schedule M describes the quality assurance, self-inspection and/or quality audit, and quality control system requirements for medical devices and pharmaceuticals; it also lists the requirements for the factory premises, materials, plant, and equipment.
- These requirements are based on World Health Organization guidelines.

- For drugs, there are also additional specific requirements for small volume injectables, large volume parenterals, APIs, tablets, capsules, etc.
- India's GMP regulations are now more aligned with ISO 13485. Standardizing quality requirements will help manufacturers in India register their medical devices more effectively.

- **REGULATORY AUTHORITIES**

- **CDSCO:** The Central Drugs Standard Control Organization (CDSCO) is the national administrative body for Indian pharmaceuticals and clinical. Makers who manage the authority are required to name an Authorized Indian Representative (AIR) to speak to them in all dealings with the CDSCO in India

  DCGI: Directs pharmaceutical and clinical gadgets, under the extent of Ministry of Health and Family Welfare .The DCGI is exhorted by the Drug Technical Advisory Board (DTAB) and the Drug Consultative Committee (DCC). It is partitioned into zonal workplaces which do pre-permitting and post-authorizing examinations, post-advertise reconnaissance, and reviews when require

CHAPTER-2

AIM AND OBJECTIVE

AIM:

Pharmaceutical sector includes various divisions and each division has its own regulatory requirements. Production of pharmaceutical products should be done in accordance with safety standards to obtain products which are safe. Good manufacturing practice ensures that the pharmaceutical products are according to the standards.

OBJECTIVE:

Manufacturing includes various steps form land search to production of trial batches. Each stage has its own regulatory requirements. Importance of regulatory requirements, approvals from the authorities, time frame and additional documents.

CHAPTER-3

LITERATURE REVIEW

1 DRUGS AND COSMETICS ACT 1945

- Drugs and cosmetics act 1945 regulates the guidances for the manufacturing, distribution and import of drugs in india.
- Drugs and Cosmetics sold in india are as per specific safety standards .

2 NEW CLINICAL TRIAL RULES 2019

- Ministry of Health and Family Welfare [MoHFW] has informed the "New Drugs and Clinical Trials Rules, 2019" on 25th March 2019 [Ref Ministry of Health GSR Notification #227 dated 19 March 2019]. The new principles intend to advance clinical research in the nation and will change the administrative scene for the endorsement of new medications and direct of clinical preliminaries in the nation.

- G.S.R.227(E) .— WHEREAS the draft of the New Drugs and Clinical Trials Rules, 2018 was distributed, in exercise of the forces gave by sub-area (1) of segment 12 and sub-segment (1) of segment 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940), in the Gazette of India, Extraordinary, Part II, segment 3, sub-segment (I) vide notice number G.S.R. 104(E), dated the first February, 2018, by the Central Government, after interview with the Drugs Technical Advisory Board, welcoming complaints and proposals from all people liable to be influenced in this way, before the expiry of a time of forty-five days from the date on which duplicates of the Official Gazette containing the said warning were made accessible to general society.

3 GOOD MANUFACTRUING PRACTICE GUIDELILNE FOR PHARMACEUTICAL PRODUCT

- The fi rst WHO draft message on great assembling rehearses (GMP) was set up in 1967 by a gathering of specialists in line with the Twentieth World Health Assembly (goals WHA20.34). It was in this way submitted to the Twenty-fi rst World Health Assembly under the title "Draft necessities for good assembling practice in the production and quality control of meds and pharmaceutical specialities" and was acknowledged.

- In 1969, when the World Health Assembly suggested the fi rst rendition of the WHO Certifi cation Scheme on the Quality of Pharmaceutical Products Moving in International Commerce in goals WHA22.50, it acknowledged simultaneously the GMP message as a necessary piece of the Scheme. Modified renditions of both the Certifi cation Scheme and the GMP content were received in 1975 by goals WHA28.65. From that point forward, the Certifi cation Scheme has been stretched out to incorporate the certifi cation of: veterinary items managed to food-creating creatures;
- beginning materials for use in measurements structures, when they are liable to control by enactment in both the sending out Member State and the bringing in Member State;
- data on wellbeing and effi cacy (goals WHA41.18, 1988).
- Creation of Pharmaceutical Product ought to be as per the Good Manufactruing rehearses with the goal that items are according to explicit norms

.

4 WHO GOOD MANUFACTRUING PRACTICES FOR PHARMACEUTICAL PRODUCTS CONTAINING HAZARDOUS SUBSTANCES

- These rules set out great practices relevant to offices dealing with pharmaceutical items (counting dynamic pharmaceutical fixings (APIs)) that contain risky substances, for example, certain hormones, steroids or cytotoxins. They don't trade national enactment for security of nature and staff. Other WHO advisers for good assembling rehearses (GMP) and guidelines should be seen notwithstanding the laborers' security measures

CHAPTER-4

PLAN FOR PROJECT

A. **STEPS For Project Planning**

STEP -1 : R & D – Formulation design ⟹ DSIR : 1) REQUIREMENTS

2) BENEFITS

STEP 2: test licenses , import licenses / NOC form 29 (CT-10) form 11 or form 16 / NDA

STEP 3: Plan design approval

STEP 4: Manufacturing license in various forms of "Schedule M" and product approvals

STEP 5 : State GMP

STEP 6 : WHO GMP certificate

STEP 7: Non conviction certificate

- Performance certificate
- Free sale certificate

B. **PROJECT**:

1) Project planning :

- Project planning is primary step for development of manufacturing facility design. Quality of the pharmaceutical products is prime requirements for the pharmaceutical companies.
- Quality of pharmaceutical projects is attained if pharmaceutical facility is well designed as per proper regulatory guidelines.
- Project planning includes various parameters. Each parameter is very important for the facility design. Regulations need to be followed properly. In India Schedule M for good manufacturing practices are followed.
- Proper land search, search related to market needs to be done. Environmental policies various environmental factors need to be taken in controlled. Project planning needs to be done very precisely because the pharmaceutical unit is dependent on the basis of project planning.
- Project planning differs from each and every formulation such as for FDC, biopharmaceutical products. Project planning needs to done on the basis of formulation

2) Market search :

- Market search is very important for the pharmaceutical companies' dealings with the new products which are use for animals and human. Multi billaniore industries does there search to meet the demand of the market. Project depends on the research which is done on the basis of the market perspective.
- If proper market search is not done pharmaceutical company loss their money their time if no one need the product. Proper market search plays an important role for the easy of the public demand. Customer satisfaction is prime requirement for the pharmaceutical company because to provide quality medicine is task. Each parameter needs to be followed properly. For each product there would be many stakeholders in the market, it must taken into account to have knowledge about the competition.
- Parameters:

- Customer satisfaction
- Market strategy
- Market analysis
- Stakeholders
- Current scenario
-

3) Land search :

- Land is basic for establishment of pharmaceutical company. There are different types of land, needs to see which land suits for pharmaceutical manufacturing unit. According to Drugs and Cosmetics act 1940 there are different parameters for selection of land. Details will discussed in individual points

4) Plan approval process:

- Plan approval process has become mandatory for establishment of new drugs under Drugs and Cosmetics act 1940. Detailed process for plan approval is shown in individual chapter.

5) Test license:

- Test license obtained by the authority for manufacturing of the batches which are for the examination, test and analysis purpose.

6) Manufacturing license:

- Manufacturing license (Form-25) obtained for permission to start production.

7) State GMP :

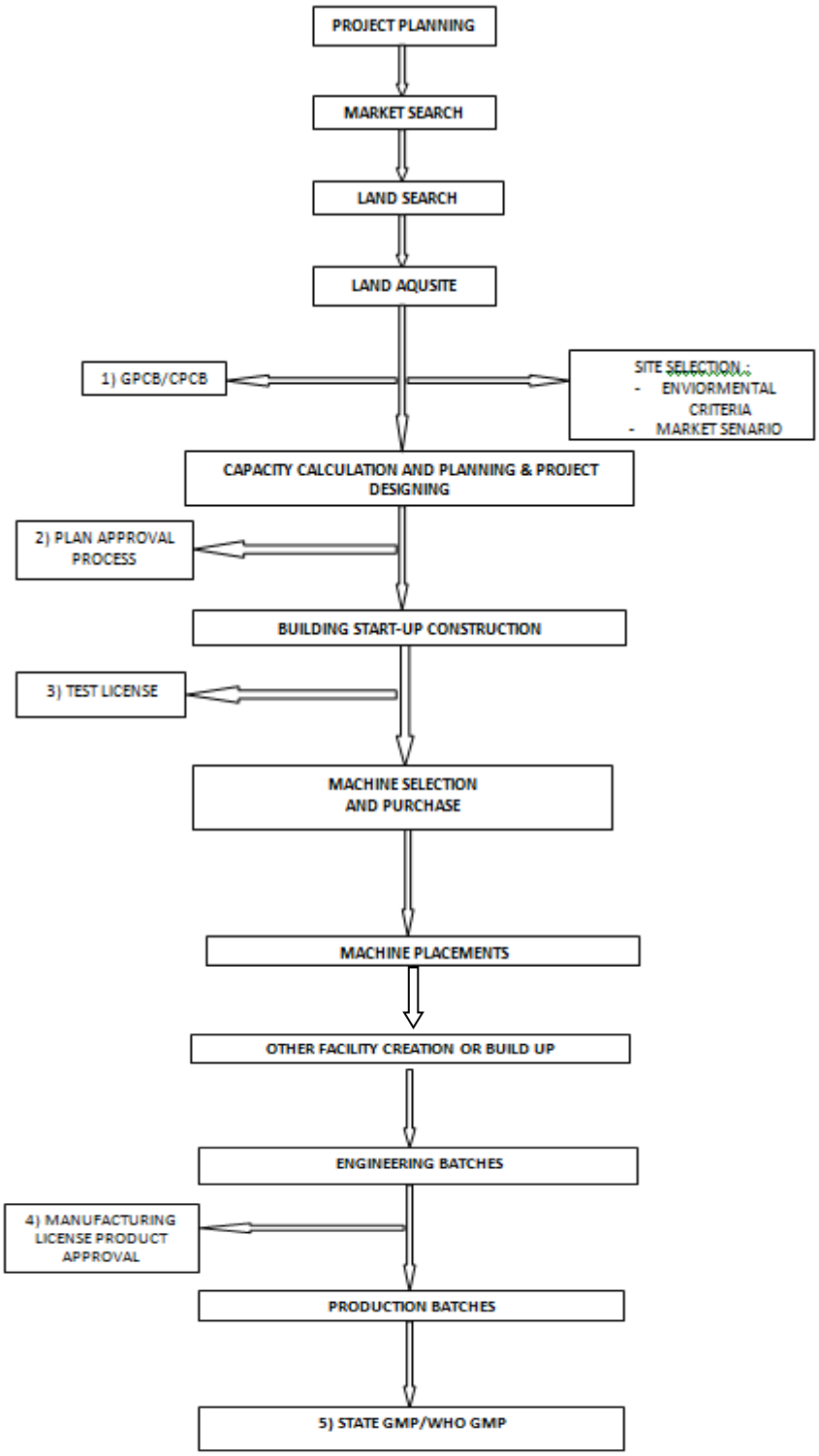
- Quality for standard pharmaceutical product is an important aspect for the companies.
- State authorities give permission for GMP certification. Premises should be in accordance with the guidelines for standard drugs.

8) WHO GMP:

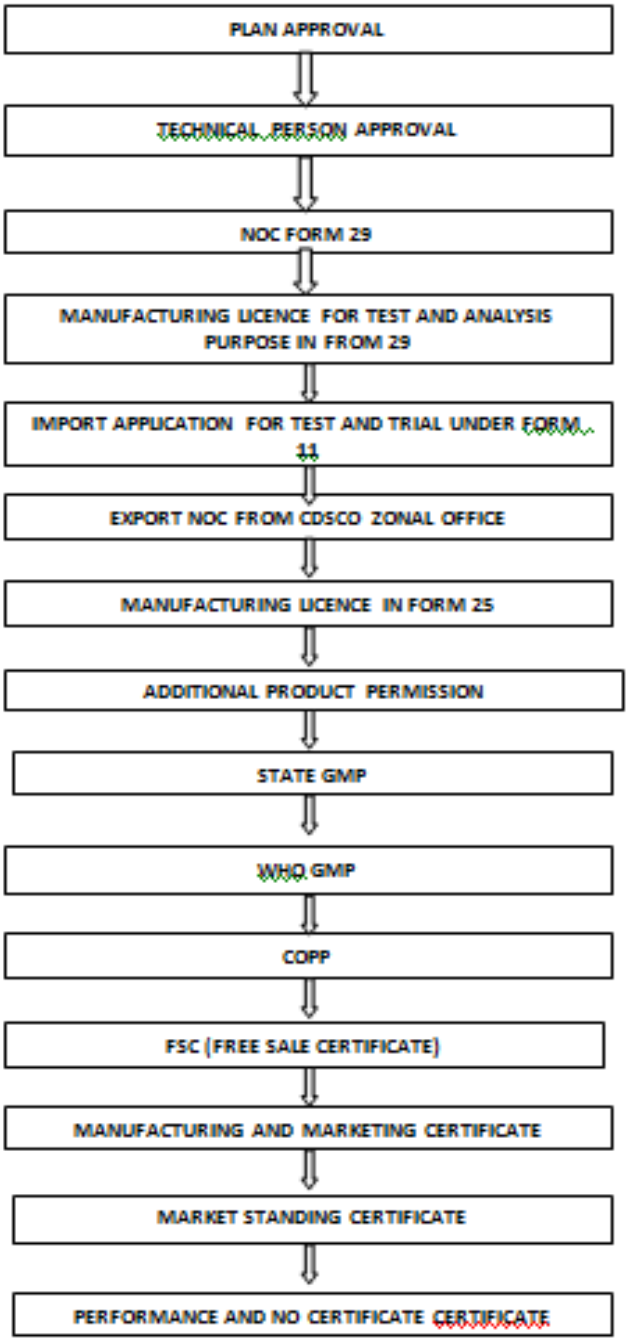
- In 1968 first WHO draft on GMP was accepted. WHO Certification was first introduced by the World Health Assembly in 1969 for the quality of pharmaceutical products. WHO GMP Certification for standard medicines has been adopted by more than 100 countries. WHO GMP Certification for standard quality of medicines and process are under controlled condition.

CHAPTER-5

FLOWCHARTS



Project Planning



Certification Steps

CHAPTER-6

LAND SEARCH & LAND ACQUISITION

1 Introduction:

Land search for pharmaceutical building facility must be selected on the basis of certain criteria. For proper guidance schedule M (Good Manufactruing practices)must be followed from drugs and cosmetics act 1940.

2 Regulatory perspective:

- **Land search and land acquisition is an important perspective concern to be plant design porper land selection according to the rules and regulation mentioned in Drugs and Cosmetics act 1940.**
- **Pollution control board**
  - **NOC for Consent to Establish (CTE)**
  - **NOC for Consent to Operate (CTO)**

3 TYPES OF LAND:

Mainly there are four types of land:

- **Private Industrial Estate**
- **Non-Agricultural Private**
- **GIDC**
- **Agricultural Land : Agricultural Land needs to be converted to non-agricultural land for building facility.**
-

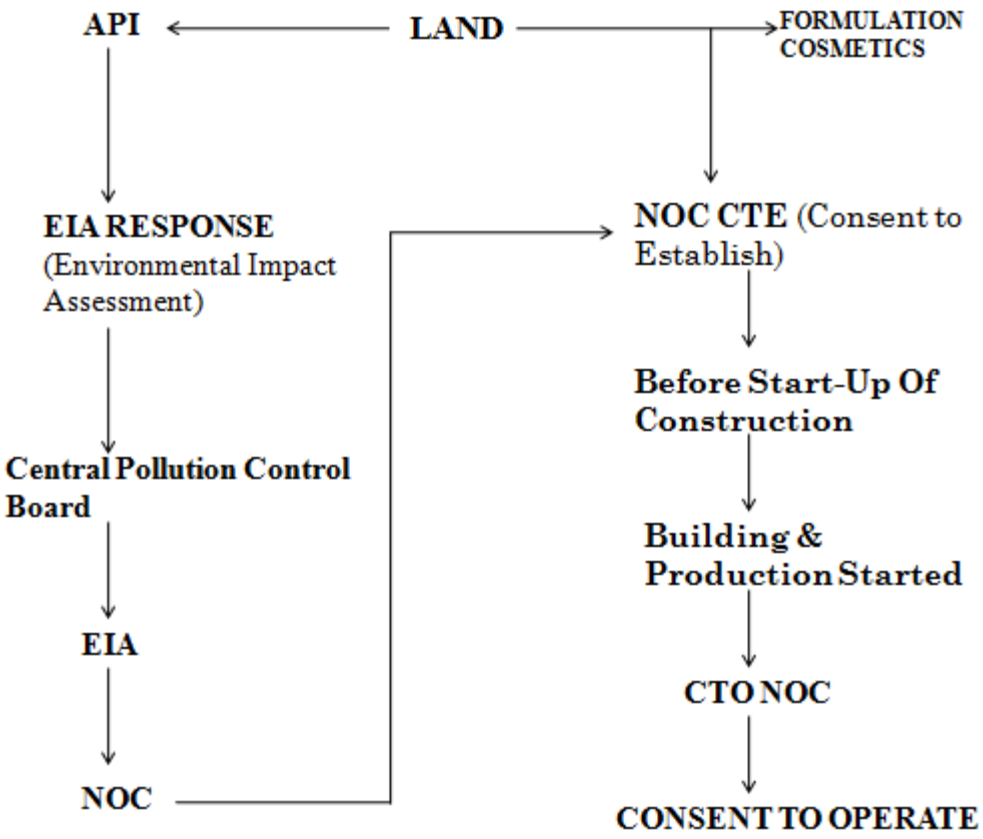
4 Factors for the Selection of pharmaceutical Plant:

- **Availability of Raw Materials:**
  - Raw materials should be available in proposed quantity.
- **Nearness of the Market**
- **Constant Power Supply:**
  - Power supply should be easily available , continuous , use of generators should be avoided so that company cost to spend on electricity is comparatively less.

- **Supply of Labour :**
  - Labour is an important aspect in the company for the supply of the raw material. Skilled labours and unskilled labours both are available.
- **Transportation Network;**
  - Good network is very important because transport cost may increase burden on the company.
  - Railway roads , water , air transportation, good roads are very important.
- **Communication:**
  - Communication between each and every section included in the company is necessary to avoid any misconception.
- **Water Supply:**
  - Water standards are important for the company . use of water of proper standard and have adequate supply of water.
- **Suitability of Land and Climate:**
  - Proper land should be selected for the pharmaceutical company to avoid any harm to the materials , surroundings ,environment
- **Integration with other group of companies:**
  - Relation with other companies must be maintained properly.
- **Availability of housing , other alilmenities and services:**
  - Labours', staff members, company employers required housing facility with is suitable and maintained under proper condition.
- **Local building and Planning Regulation:**
- **Environmental Impact , Waste Disposal and Safety Requirements:**
- Location of land must be selected on the basis on different parameters such as
  - Away from residential area (approx 50km)
  - Risk of contamination must be avoided from external environment such as open sewage, drain, public lavatory or any factory which produce disagreeable or obnoxious odour or fumes, excessive soot, dust, smoke, chemical or biological emission.

- Toxins from manufacturing plant shouldn't be harmful for external environment.
- Pharmaceutical waste management

- After selection of Land, permission from pollution control Board is needed.
  - Centrally it is done by CPCB (Central Pollution Control Board)
  - In Gujarat , it is done by GPCB (Gujarat Pollution Control Board)



Land Certification

CHAPTER-7

PLAN APPROVAL PROCESS

PLAN APPROVAL PROCESS

1 Introduction:

- Plan approval process is the prime stage for pharmaceutical building development. Plan approval is not a mandatory process; it depends on the state policy. In India, Gujarat and Maharashtra plan approval is the mandatory process because of the state policy and permission is taken by the state authorities.
- Plan approval is an important perspective because it is the base for pharmaceutical manufacturing facility. Process which is not governed or directed by D & C act. Building should not be constructed before plan is approved by the state authorities.
- Some state authorities (Food & Drugs) are doing plan approval process for ease of doing business to prevent after build-up changes. Different factors are important for plan approval process. Factors such as planning, market search, land search, land acquisition, capacity calculation and project designing.
- Plan approval process is done on the basis of the site at which manufacturing process will be executed. Environmental criteria are taken into consideration. Project planning and Designing are important points before plan approval process.

2 Regulatory perspective:

- Plan approval process is compulsory for companies to take permission according to the state commissioning. Plan approval process is followed by Drugs and Cosmetics Act 1940 .
- According to the rules of the D & C act companies needs to take permission before manufacturing of new drugs from state authorities . Plan approval is regardless very important step for the pharmaceutical companies for the manufacturing of the new drugs.

3 Explanation:

- After obtaining permission from pollution control board next step is capacity calculation & planning & project designing.

- Capacity calculation for every section needed for the manufacturing operations are calculated.
- There are different areas in manufacturing unit such as :
  - Warehousing area
  - Production area
  - Ancillary area
  - Quality control area
  - Personnel
  - Health , clothing and sanitization of workers
  - Manufacturing Operations and Control
  - Raw materials
  - Equipment
  - Documentation and Records
  - Labels and Printed Materials

4 **Planning building and premises is next step after capacity calculation.**

- Manufacturing plant should be designed, constructed , adapted and maintained properly for to conduct each and every manufacturing operations.
- Manufacturing operations should be done under proper hygienic conditions.
- Same manufacturing operations must be done in same area or adjacent area.
- For equipment, materials , intermediates proper space must be allocated so that to avoid risk of contamination.
- Should be properly designed / well maintained so that insects, pests, birds must be prevented.
- Interior surface such as walls, floors, ceilings build such that free from cracks it should be smooth.
- Properly air conditioned for manufacturing unit, air handling units must be provided to maintain temperature, humidity for specific products.
- Proper drainage system must be provided.

- Purified water is used for the unit operations. Water drawn from any other source must be in accordance with Bureau of Indian Standards or Local Municipality.
- Biomedical waste needs to be destroyed as per provisions of Biomedical Waste (Management and Handling) Rules, 1996.
- Disposal of waste.

5 **Project planning:**

- After planning of building capacity is completed building start-up for R & D (Research & Development) facility is done

Specifications for Areas				
SR NO	DESCRIPTION	AREA(SQ MT)	SEGREGATION	
1.0	Raw Materials Store	1) Up to 2 category 10 sq mt 2) for each additional category	Receiving Bay	
			Approved	Inflammable
				Hazard
				AC
				Non AC
			Under Test	
			Sampling dispensing	RLAF Separate for B lactum , General Cytotoxic & Sex Hormones
2.0	Finished Product Store	.....do.....	AC	
			No AC	
3.0	Packing Material Store	i) ....do.... ii) For LVP 100 sq mt	Foil AC	
			Vial/Ampoule	
			Carton	

			Label (Lock & Key)	
4.0	Empty Bottle Store	10		
5.0	Bottle Washing &Drying	15		
6.0	Quarantine	10		
7.0	Primary Labelling & packing	10 *	(AC/5 Micron) If parenteral AC 0.3 Micron	Separate for B Lectum , Anticancer , Sex Hormone and Vaccine
8.0	Secondary Packng	10 *		
9.0	Visual inspection or Online visual Inspection	10 *		
		.....NA.....		
10.0	Decartoning (Amp/Vial)	10 *		
11.0	Tube Cleaning or On Line Tube Cleaning	10 *		
12.0	Office	10 *		
13.0	Male Worker Change Room	8 to 10 *		
	Female worker Change Room	8 to 10 *		
14.0	Toilet	Adequate		Not directly attached to

				manufacturing sector
15.0	Retain Sample Room	10 *	AC & Non AC	
16.0	Recall/ Rejection Room	10 *		
17.0	Tools Maintanance Room	10 *		
18.0	Scrap Yard	10 *		
19.0	Water Treatment Plant	Adequate		
20.0	AHU – Area – Streaming			
21.0	General Washing	10 *		
22.0	Main passage	1.85 Meter Width *		
23	Physico Chem Testing	15 *		
	Instrumentation Room	8 to 10 *	AC	
	Media Preparation	10 *		
	Microbiological Testing	10 including Airlock of 2.5 Sq meter *	AC , LAF	
	Sterility Testing Room	10 including Airlock of 2.5 Sq meter *	AC , LAF	

	Toxicity Testing Room	10 *	AC	
	Mice Room	10 *	AC	
	Animal House	30 *	Isolated from mfg. Area (Separate Block)	
	1. Kitchen			
	2. Wash			
	3. Hold			
	Pyrogen Testing Room	10 *	AC	

CONDITIONS:

(1) Types of Operations to be Carried Out in the Various Grades for Aseptic Preparation:

Grade	Types of Operations of aspectic Preparation
A	Aseptic preparation and filling
B	Background room conditions for activities requiring Grade A
C	Preparation of solution to be filtered
D	Handling of components after washing

(2) Air Borne Particulate Classification for Manufacture of Sterile Products

Grade	At rest (b)			In Operation (a)
	Maximum number of permitted particles per cubic meter equal to or above			
	0.5 µm	5 µm	0.5 µm	5 µm
A	3250	29	3500	29
B(a)	35,200	293	3,52,000	2,930
C(a)	3,52,000	2,930	35,20,000	29,300
D(a)	35,20,000	29,300	Not defined (c)	Not defined (c)

NOTES:

- In order to reach the B, C and D air grades, the number of air changes shall be related to the size of the room and the equipment and personnel present in the room. The air system shall be provided with the appropriate filters such as HEPA for Grade A, B and C. the maximum permitted number of particles in the "at rest" condition shall approximately be as under: Grade A corresponds with Class 100 or M 3.5 or ISO Class 5; Grade B with Class 1000 or M 4.5 ISO Class 6; Grade C with Class 10,000 or M 5.5 or ISO Class 7; Grade D with Class 100,000 or M 6.5 or ISO Class 8.
- The requirement and limit for the area shall depend on the nature of the operation carried out.
- Type of operations to be carried out in the various grades are given in Table II and Table III as under.

Where:

- Gujarat Government plan approval process is governed by State FDCA.(FOOD AND DRUG CONTROL ADMINISTRATION)
- Commissioner of FDCA Gujarat: Dr**. Hemant Gordhanbhai Koshia**

Checklist:

1. Challan (Applicable Fee)
2. Cover letter
3. Layout Drawings (4 copies of each sheet of drawings) as
   (i) Site Plan
   (ii) Elevation Plan
   (iii) Main Floor Plan (including AHU/HVAC Zoning)
4. Comparative Statement of applicable changes if apply for Revision
5. Existing approved plan if apply for Revision

Application For Approval Of Plan Layout :

Sr. No.	Documents	No. of copies
1	Covering letter	1 copy
2	Self Assesed check list of documents	1 copy
3	List of Directors with address	1 copy
4	Copy of Power of attorney to sign the documents.	1 copy
5	Copy of Plan approval	1 copy
6	Noc/Consent from SSI, Pollution.	1 copy
7	Copy of Memorandum of Articles	1 copy

Fees:

Fresh plan: 250 Rs

Revised plan: 100 Rs.

CHAPTER-8

TEST LICENSE & IMPORT LICENSE

1. AIM:

- Test license ontained for the manufacture of the new drugs or investigational new drugs to conduct clinical trial for test,examination or analysis purpose must be in accordance with Drugs and Cosmetics Act 1940.

2. Objective:

- Proper knowledge about the Rules and regulations as per drugs and cosmetics act 1940 for the manufacture of the new drugs investigational new drugs to conduct clinical trial for test,examination or analysis.

3. Regulatory perspective :

- Test license and Import License according to the New Clinical Trials Rules 2019.
- Manufacturing of new drugs or investigational drugs for the purpose of test or analysis permission given in the Form 29 .
- Form 29 issued by State FDCA .
- Before approval of test license (Form 29) NOC form 29 (CT-10) (see Appendix) is issued which is valid for 4 years governed by Central Licensing Authority. NOC Form 29 is granted under CT-11. (see Appendix)

4. Checklist:

- Covering Letter
- Challan
- Form 30
- List of Products
- Draft Label
- Copy of Manufacturing license / Wholesale license
- Copy of NOC Form 29 & Copy of DSIR approval Letter
- Additional Information Form
- Auhorization Letter

CHAPTER-9

MANUFACTRUING

LICENSE

Manufactring licence :

1 Introduction:

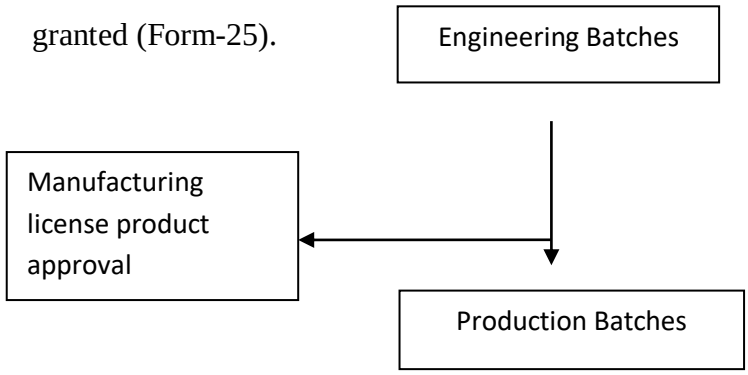
- Manufacturing license obtained at the time of facility build-up and for the formation of engineering batches. According to Drugs and cosmetics act 1940 after obtaining test license Form 29 for Research and Development facility build-up , machine placements , other facilities creation is done after proper check on all the procedure manufacturing license can be obtained.

2 Aim:

- Company formation starts after obtaining manufacturing license (Form -25).

3 Regulatory perspective:

- After commission of the facility by the authorities on the basis of the building construction , machine placement , other facility build-up manufacturing license is granted (Form-25).



4 Where to submit:

- FDCA

5 Checklist :

- Cover letter
- Cover letter includes all the information regarding form.
- Original form 24- 2 sets (with list of Board of Directors)
- Challan (Rs 7500) Up to 10 products

- List of Director (Latest Position with MCA site screen shot)
- Additional information Form- General Information
- Additional Information Form Product Wise
- Memorandum & Article of Association
- List of technical person –Production Department
- List of Technical person - QA/QC Department
- Site Master File
- Equipment list with information date (production)
- List of employee with experience and qualification
- List of Instrument with Installation Date (QC)
- List of products for domestic –Annexure I
- List of products In form 25 (Addition of product In Form-25 For Domestic – o5 copies)
- List of products for Export Annexure-II
- List of Products (Addition of Products In Form-25 For Export – 05 Copies)
- Manufactruing flow chart
- Brief manufacturing process
- Batch Packing Details – Pack Size & Packing Material (Product Wise)
- Copy of Pharmacopiea As Per IP Product Wise (For Domestic)
- Copy of Pharmacopiea As per BP/EP/USP-NF Product Wise (Export)
- List of products – Draft Label As Per IP (For Domestic)
- List of Products - Draft As per BP/EP/USP-NF (Export)
- List SOP's with effective Date
- Copy of General Power Power of Attorney To Signatory Authority(if any)
- Board Resolution – Signatory Authorization To Director (or any one)
- Copy of approved plan of product facility
- Permissions from prohibition & excise / CCOF
- Enviorment Noc GPCB
- Pest Control Aggrement Copy
- GIDC Possession Letter of company

- Medical Status of Key Employee
- Area measurement As per Plan v/s Actually Provided (Area Wise and AHU Wise Details)
- Enviormental,Health and Safety Policy
- Waste Disposal With Agreement (State Goverment Agency)
- List of Fire Safety Equipment
- List of PPE's used for Products
- Health Facility Photograph
- QC Laboratory – Chemical Reagents List
- List of Laboratory Glassware
- SOP for Process Validation
- SOP for Cleaning Validation
- Sop for Medical Checkup

6 DOCUMENTS TO BE SUBMITTED FOR THE GRANT OF DRUGS MANUFACTURING LICENSES:

- Application Form-24/24-A and 27/27-A
- Challam Form for 7500/- per application and fees for the additional 300/- per item excluding first 10 items per section proposed to be manufactured to be separately in government account as per the:-
- Affidavit on behalf of the applicant (Ptoprietor / Partner / Managing Director /General Power of Attorney Holder) duly attested by the Oath Commissioner / Notary (as per the Prescribed Language).
- List of the Plant & Machinery installed.
- List of the Laboratory Equipments provided.(Attested photocopy)
- Valid NOC from the Pollution Control Board (Attested photocopy)
- Registration Papers of the Land in case of owner (Attested photocopy with recent copy of 'Farad' from the Revenue Department. Or In case the Premises are Rented ,rent /Lease Agreement Deed (Attested Photocopy)

- Constitution of the Firm (Attested photocopy)
- Competent Person Responsible ForManufacturing:
  - Medical fitness certificate indicating complete investigation.
  - Apppointment letter of the employee-attested photocopy.
  - Joining / acceptance letter of the employee-attested photocopy.
  - Affidavit on behalf of the appointed competent person responsible for manufacturing (as per the prescribed language)
  - Qualification certificate-degree / diploma / matriculation-attested photocopy.
  - Experience certificate on the letter pad bearing license Nos. of the issuing firm-original copy.
  - Passport size Photographs-1 (attested) and 4 (unattested).
- Competent Person Responsible For Testing:
  - Medical fitness certificate indicating complete investigation.
  - Appointment letter of the employee-attested photocopy.
  - Joining / acceptance letter of the employee-attested photocopy.
  - Affidavit on behalf of the appointed competent person responsible for manufacturing (as prescribed language).
  - Qualification certificate – degree / diploma/matriculation – attested photocopy.
  - Certificate of approval as Analytical chemist by the competent drug authority-attested photocopy.
  - Experience certificate on the letter pad bearing license Nos. of the issuing firm-original copy.
  - Passport size Photographs-1 (attested) and 4 (unattested)
- List of the items proposed to be manufactured section wise category wise (Biological and Non-Biological) indicating the following details:

- Refrence thereof
- Ingredients , Specification and quantity per unit dose
- Brief of the manufacturing including critical steps ,if any
- Testing method-in case of non-pharmacopoeia drugs and ingredients
- Proposed packing presentation and packing material proposed to be used.

- Site Plan (to the scale),Location and Layout of the proposed premises clearly indicating size and defination of the area and details of the furniture and fixtures provided therein,Drawn and certified by the competent authority-Blue Print (2-copies)

DOCUMENTS AS PROPOSED TO BE KEPT READY AT THE TIME OF INSPECTION AS PRESCRIBED IN SCHEDULE 'M' PART 1 OF THE DRUGS AND COSMETICS ACT , 1940.

- Master Formula Record for every product proposed to be manufactured
- Site Master File (SMF)
- Record showing routine sanitation programme drawn up for:
  - Specific area
  - Equipment
  - Material of cleaning
  - Interval
  - Person responsible
- Raw material testing record
- Packaging Record and Batch Packing Records
- Batch Processing Record (BPR)
- Record pertaining to Quality Control
- Distribution Records
- SOP's both for every function and operation to be carried out in the premises
- Others as prescribed under Schedule M

7 Fees:

- Form – 25 – per license 7500 (see Appendix)

  Per product 300

- Form – 28 – per license 7500

Per product 300

Types of manufacturing licenses		
For drugs other than those specified in Schedules C & C (1) & X	Form 25	Form 24
For loan licence for drugs other than those specified in Schedules C & C (1) & X	Form 25A	Form 24 A
For Repacking licence for drugs other than those specified in Schedules C & C (1) excluding those specified in Schedule X	Form 25B	Form 24B
For Homeopathic Medicines	Form 25C	Form 24C
For drugs specified in Schedule X and not specified in Schedules C & C(1)	Form 25F	Form 24F
For drugs specified in Schedules C & C (1) excluding those specified in Schedule X	Form 28	Form 27
For loan licence for drugs specified in Schedules C & C	Form 28A	Form 27A

(1) excluding those specified in Schedule X		
For drugs specified in Schedules C, C(1) & X	Form 28B	Form 27B
For large volume Parenterals/ Sera and Vaccine/ Recombinant DNA derived drugs specified in Schedule C, C(1) excluding those specified in Schedule X	form 28D	Form 27D
For drugs for manufacture of drugs for the purposes of examination, test or analysis	Form 29	Form 30
For manufacture of Cosmetics	Form 32	Form 31
For Loan licence for manufacture of cosmetics	Form 32A	Form 31A
For approval for carrying out tests on drugs/cosmetics or raw materials used in the manufacture on behalf of licensees for manufacture for sale of drugs/cosmetics	Form 37	From 36

CHAPTER-10

GMP CERTIFICATION

1 INTRODUCTION:

- WHO GMP testament was set up in 1969 and reconsidered in 1975.
- It is proposed that the authentication ought to stay legitimate for a time of 2 years from the date of issue, yet not surpassing 3 years after the review was completed.
- It is suggested that, where conceivable, GMP declarations ought to have, for example security seals, watermarks or visualizations, to help forestall forging, altering and other fake exercises.

2 Main objectives:

- GMP is that piece of value the board which guarantees that items are reliably delivered and controlled by the quality guidelines suitable to their proposed use and as required by the advertising approval, clinical preliminary approval or item determination. GMP is worried about both creation and QC. GMP is pointed principally at overseeing and limiting the dangers natural in pharmaceutical assembling to guarantee the quality, security and adequacy of items.

3 GMP Prespective:

- all assembling forms are obviously characterized, efficiently inspected for related dangers in the light of logical information and experience, and demonstrated to be able to do reliably fabricating pharmaceutical results of the necessary quality that agree to their particulars;
- capability and approval are performed;
- every single vital asset are given, including:
  - adequate and fittingly qualified and prepared work force,
  - sufficient premises and space,
  - appropriate gear and administrations,
  - suitable materials, compartments and names,
  - endorsed strategies and directions,
  - reasonable capacity and transport,
  - satisfactory work force, research facilities and hardware for in-process controls;

- guidelines and strategies are written in clear and unambiguous language, explicitly relevant to the offices gave;
- strategies are done effectively and work force are prepared to do as such;
- records are made (physically and additionally by recording instruments) during assembling to show that all the means required by the characterized techniques and directions have in certainty been taken and that the amount and nature of the item are true to form. Any huge deviations are completely recorded and researched with the goal of deciding the underlying driver and fitting restorative and preventive activity is executed;
- records covering production and conveyance, which empower the total history of a cluster to be followed, are held in an understandable and open structure;
- the correct stockpiling and conveyance of the items limits any hazard to their quality and assesses great circulation rehearses (GDP)
- a framework is accessible to review any group of item from deal or flexibly;
- grumblings about advertised items are analyzed, the reasons for quality imperfections examined and proper estimates taken in regard of the damaged items to forestall repeat.

4 **CHCEKLIST:**

- Challan (Rs.1000)
- Copy Of Mfg. License
- List of Product
- List of Directors
- GMP Certificate
- List of Approved Technical Persons
- List of Production & QC Lab Equipment
- Site Master File
- Validation Master Plan
- Process Flow Charts
- Product Wise Raw Material List

CHAPTER-11

OTHER ADDITIONAL CERTIFICATE

A. COPP CERTIFICATE

1 DEFINATION:

- Authentication of pharmaceutical item. The certificate of pharmaceutical product (abbreviated: CPP) is a certificate issued in the configuration suggested by the World Health Organization (WHO), which sets up the status of the pharmaceutical product and of the candidate for this certificate in the sending out nation."

2 CHECKLIST

- Challan (Applicable Fee Rs. 50/- per product)
- Cover Letter
- AIF (Additional Information Form)
- Copy of Valid Manufacturing License
- Copy of Product Permission
- Proof of Domestic Market (Sale)
- Format of COPP
- Copy of WHO GMP Certificate

3 CERTIFICATION:

This certificate conforms to the format recommended by the World Health Organization

- No. of certificate
- Exporting (certifying country):
- Importing (requesting country):

1. Name and dosage form of the product:

1.1. Active ingredient(s) and amount(s) per unit dose:

For complete composition including excipients, see attached:

1.2. Is this product licensed to be placed on the market for use in the exporting country?(yes/no)

1.3 Is this product actually on the market in the exporting country?

If the answer to 1.2. is yes, continue with section 2A and omit section 2B.

If the answer to 1.2 is no, omit section 2A and continue with section 2B:

2.A.1. Number of product licence and date of issue:

2.A.2. Product licence holder (name and address):

2.A.3. Status of product licence holder[8]: (Key in appropriate category as defined in note 8)

2.A.3.1. For categories b and c the name and address of the manufacturer producing the dosage form is:

2.A.4. Is a summary basis for approval appended? (yes/no)

2.A.5. Is the attached, officially approved product information complete and consonent with the
licence? (yes/no/not provided)

2.A.6. Applicant for certificate, if different from licence holder (name and address):

2.B.1. Applicant for certificate (name and address):

2.B.2. Status of applicant: (Key in appropriate category as defined in footnote 8)

2.B.2.1. For categories (b) and (c) the name and address of the manufacturer producing the dosage form is:[9]

2.B.3. Why is marketing authorization lacking? (not required/not requested/under consideration/refused)

2.B.4. Remarks:

3. Does the certifying authority arrange for periodic inspection of the manufacturing plant in which the
dosage form is produced? (yes/no/not applicable)
If not or not applicable, proceed to question 4.

3.1. Periodicity of routine inspections (years):

3.2. Has the manufacture of this type of dosage form been inspected? (yes/no)

3.3 Do the facilities and operations conform to GMP as recommended by the World Health Organization? (yes/no/not applicable)

4. Does the information submitted by the applicant satisfy the certifying authority on all aspects of the manufacture of the product: (yes/no)
If no, explain:
Address of certifying authority:
Telephone:
Fax:
Name of authorized person:

Signature

Stamp and date

B FREE SALE CERTIFICATE

1 DEFINATION:

- A Free Sale Certificate is an endorsement given by a national authoritative authority of a conveying country reliant on national authorization certifying that the thing is uninhibitedly sold in the country yet with no sign that the thing is evaluated for security and ampleness and is selected for use in the country.

2 INTRODUCTION

- Free deal declaration is fundamentally an archive for specific items like pharmaceuticals required in specific nations. This record especially determines the affirmation that the imported products are regularly and unreservedly sold in the sending out nation's open markets and are endorsed for trade.
- The WHO initiated confirmation for Free deal endorsement plot on the nature of pharmaceutical items with the goal that the imported pharmaceutical items should experience a trust of wellbeing, viability and satisfactory quality.
- Generally WHO affirmation plot remembers great practices for the production and Quality control of medications.
- Free Sale Certificate Scheme ought to select upto date rundown of makers conforming to GMP by the sending out nations.
- Health Authorities of exporting countries must have the issuance of batch certificate.
- There are various WHO type certificate which includes:
  - Certificate of pharmaceuticals WHO (1975)
  - Certificate of pharmaceuticals WHO (1988)
  - Certificate of pharmaceuticals WHO (1992)
- BATCH Certificate etc.

3 PROCEDURE

- Usually FREE SALE CERTIFICATE processes various procedures:
- Model: If any nation needs to send out any thing like any food material so it ought to follow these procedures:
- Rustic installment office should create authentications like is it appropriate for human utilization and creature utilization also.
- Human utilization must give confirmation that the item they are trading ought to be sheltered and affirmed. It ought not give any destructive consequences for the wellbeing.
- For Animal utilization again affirmation must be there so as to give item liberated from radioactive components.

- A few Requirements must be followed so as to accomplish confirmation of Free deal Certificate:-

- Organizations must submit duplicates of solicitations indicating the offer of every item so that if in future any issue emerges because of any conditions there must be a legitimate accommodation of duplicates.
- Producer must given a composed announcement to demonstrate that its item is sheltered, made sure about and endorsed.
- Detail of nation name must be there with the goal that no issue could be brought up in future.

- Records which should be submitted for the FSC are:

- Check or confirmation of installment, except if a credit on account office has been set up with the HPRA.
- Evidence of assembling as a legally approved record.
- Ensuing changes to the item posting don't should be legally approved.
- A duplicate of the current informed body testaments for the applicable gadgets.
- Utilizations of this free deal declaration incorporate a Secretary who can give send out affirmation for merchandise for helpful use in people with the assurance of sheltered and endorsed items.

- Legitimacy for Free Sale declaration must be incorporated as a significant part and it is 5 years from the date of issue.

4 **CHECKLIST** :

- Challan (Applicable Fee Rs. 50/- per product)
- Cover Letter
- AIF (Additional Information Form)
- Copy of Valid Manufacturing License
- Copy of Product Permission
- Proof of Domestic Market (Sale)
- Format of FSC (as per FDCA format)
- Copy of WHO GMP Certificate

C Manufacturing & Marketing Certificate

1 DEFINATION

2 CHECKLIST :

- Challan (Applicable Fee Rs. 50/- per product)
- Cover Letter
- AIF (Additional Information Form)
- Copy of Valid Manufacturing License
- Copy of Product Permission
- Format of Manufacturing and Marketing Certificate
- Chartered Account Certificate
- Copy of WHO GMP Certificate
-

D Market Standing Certificate

1 DEFINATION:

- Market standing cum performance Certificate issued by the Licensing Authority according to design in Annexure Vas a Manufacturer for each medication cited for the last 36months before the date of accommodation of the delicate

2 CHECKLIST :

- Challan (Applicable Fee Rs. 100/- per product)
- Cover Letter
- AIF (Additional Information Form)
- Copy of Valid Manufacturing License
- Copy of Product Permission
- Format of Market Standing Certificate
- Chartered Account Certificate
- Copy of WHO GMP Certificate

E Performance & Non conviction Certificate

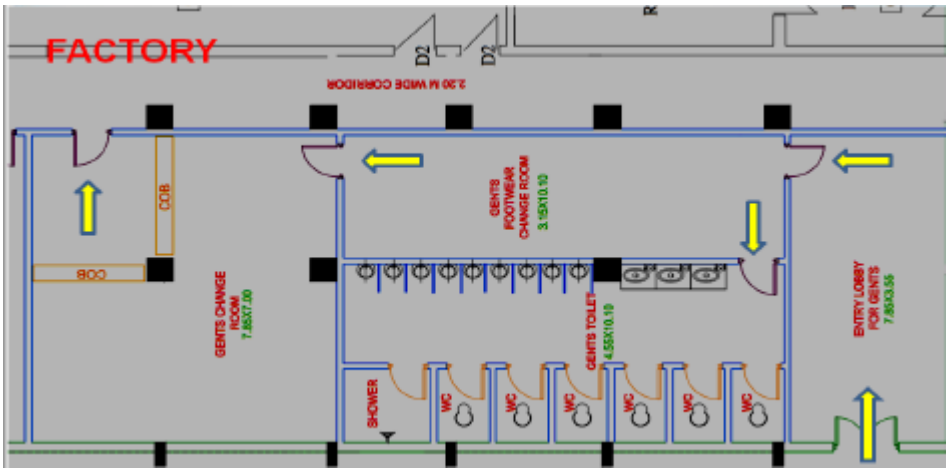
1 DEFINATION:

2 CHECKLIST:

- Challan (Applicable Fee Rs. 50/- per product)
- Cover Letter
- AIF (Additional Information Form)
- Copy of Valid Manufacturing License
- Copy of Product Permission
- Format of Performance Certificate
- Format of Non Conviction Certificate
- Copy of Tender

CHAPTER-12 GMP FACILITY DESIGN (Example)

- PREMISES
- LAYOUT
- CONTAMINATION AREA
- CLEANING AREAS
- PERSONNEL HYGIENE
- SPECIFIC AREA:
- ANCILLARY AREAS
- STORAGE AREAS
- WEIGHTING AREAS
- PRODUCTION AREA
- QUALITY CONTROL AREAS
- ANCILLARY AREAS
- RESTROOMS AND REST AREA
- WASHING AREA
- MAINTENANCE AREA
- CANTEEN AREA


FACTORY
D2
D2
COB
COB
GENTS CHANGE ROOM
GENTS FOOTWEAR CHANGE ROOM
GENTS TOILET
ENTRY LOBBY FOR GENTS
SHOWER
WC
WC
WC
WC
WC
WC


COB

RECIPET AND STORAGE

- Materials are stored under proper condition and free from microbes .
- Materials are kept in proper condition protected from weather.

Requirements of premises: (Airflow)

- Quaratined area
- Separate area for goods
- Separate area for rejected ,recalled and retuned material
- Safe area for radioactive goods , highly active goods.
- Goods are properly monitored and recorded.
- Good storage condition : clean ,dry and appropriate lights (200 to 350 lux)

STORAGE REQUIREMENTS

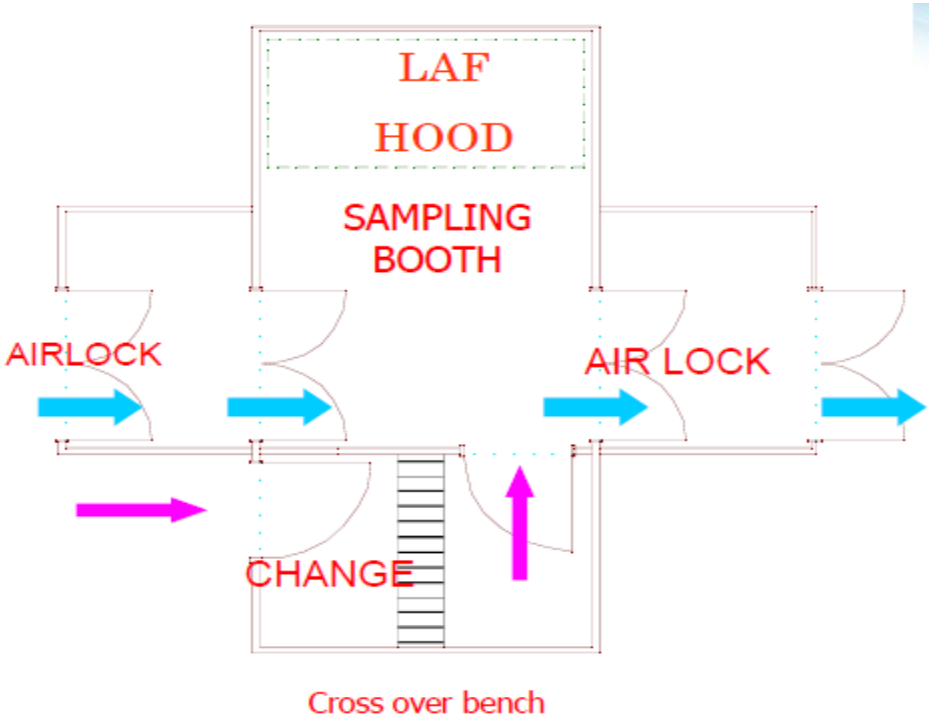
YELLOW: QUARANTINE

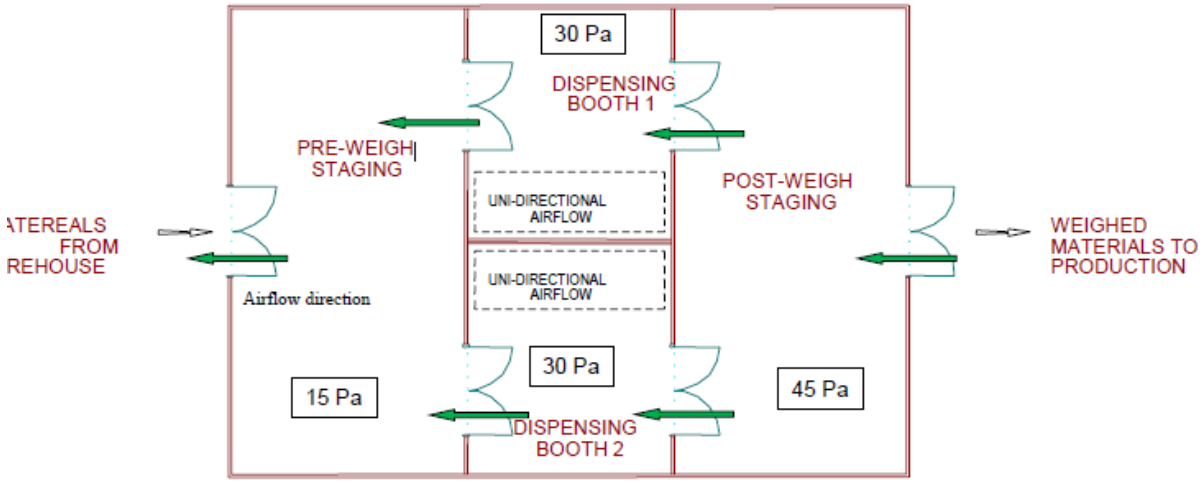
RED: REJECTED

WEIGHING :

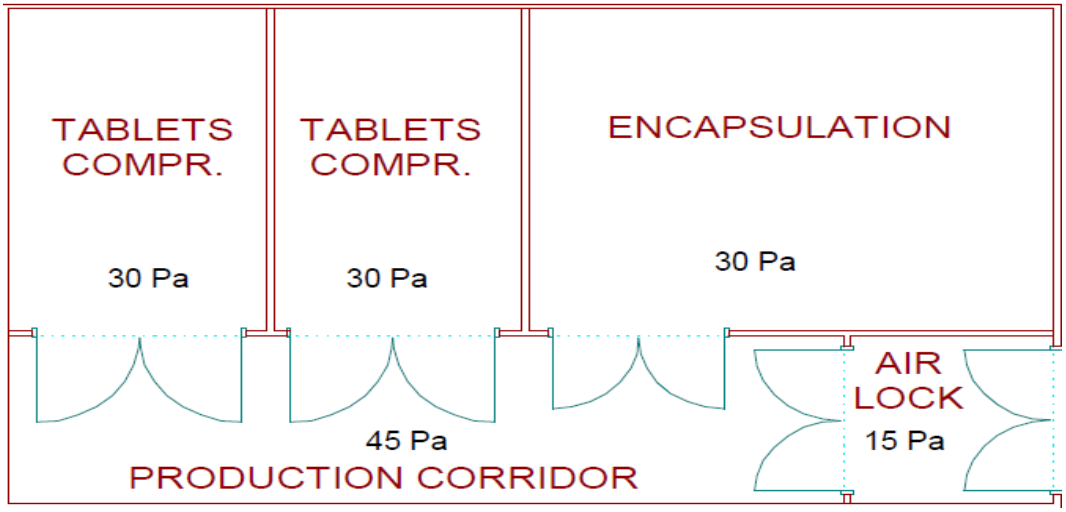
- Separate area
- Dust control
- Cleaning operations
- Documentation done properly;

SAMPLING :





DISPENSING AREA



Requirements on premises: ROOM LAYOUT AND DIFFERENTIAL PRESSURE REQUIREMENT

CHAPTER-13

CONCLUSION

Pharmaceutical industry includes different divisions and each division has its own requirements specialization. Pharmaceutical product must be well designed, planned and safe according to the standards. Good manufacturing practice need to be followed for production of standard pharmaceutical products. Pharmaceutical products need to be developed as per particular guidelines for the safety of the products. Numerous in the Regulatory Affairs Profession accept the New Approach to guideline will in the long run be embraced for all human services items as it speaks to the best model for conveying new medicinal services advances to advertise in a sensible time with adequate wellbeing. Administrative Affairs division is continually advancing and developing and is the one which is least affected during the Acquisition and Merger, and furthermore during downturn. Administrative Affairs offices are developing inside organizations. Because of the changing assets important to satisfy the administrative prerequisites, a few organizations additionally decide to redistribute or out errand administrative undertakings to outside specialist co-ops. In the present serious condition the decrease of the time taken to arrive at the market is basic to an item's and henceforth the organization's prosperity. The best possible lead of its Regulatory Affairs exercises is in this way of extensive financial significance for the organization.

CHAPTER-14

REFRENCES

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11 Naik R, API Contract Research & Manufacturing Services in India, Pharma Times-Vol. 43-No.08 –August2011-p. 29,30

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13 DIPP (2010): "Discussion Paper: Compulsory Licensing" (New Delhi: Department of Industrial Promotion and Policy, Government of India). Gopakumar, K M (2010): "Landscape of Pharma ceutical Patent Applications in India: Implications for Access to Medicines" in Chaudhuri, Park and Gopak

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APPENDIX

FORM CT-10

APPLICATION FOR GRANT OF PERMISSION

TO MANUFACTURE NEW DRUG OR INVESTIGATIONAL NEW DRUG FOR CLINICAL TRIAL OR BIOAVAILABILITY OR BIOEQUIVALENCE STUDY OR FOR EXAMINATION, TEST AND ANALYSIS

I/We, ...

(name and full postal address of the applicant) of ..... hereby apply for grant of

permission to manufacture new drug or investigational new drug for clinical trial or bioavailability or bioequivalence

study or for examination, test and analysis.

The details of the application are as under:

1. Name of applicant:	
2. Nature and constitution of applicant: (proprietorship, partnership including limited liability partnership, company, society, trust, other to be specified)	
3.(i) Corporate or Registered office address, telephone number, mobile number, fax number and e-mail id: (ii) Applicant's address, telephone number, mobile number, fax number and e-mail id: (iii) Address for correspondence:	
4. Details of new drugs and investigational new drugs to be manufactured [As per Annexure].	
5. Particulars of Manufacturer, Manufacturing sites [As per Annexure].	
6. Fee paid on _____Rs_____receipt or challan or transaction ID___.	

7. I hereby state and undertake that: (i) I shall comply with all the provisions of the Drugs and Cosmetics Act, 1940 and the Chapter VIII of New Drugs and Clinical Trials Rules, 2019. (ii) The new drug to be manufactured from M/s..... shall be used exclusively for the purpose of clinical trial and no part of it shall be diverted to the domestic market.

Place: …….. Date:	Digital Signature (Name and designation)

Annexure:

Details of new drug or investigational new drug:

Names of the new drug or investigational new drug:	
Therapeutic class:	
Dosage form:	
Composition:	
Indications:	

Details of manufacturer and manufacturing site:

Name and address of Active Pharmaceutical Ingredient and formulation manufacturer (full address with telephone, fax and e-mail address of the manufacturer).	
Name and address of manufacturing sites of Active Pharmaceutical Ingredient and formulation (full address with telephone, fax and e-mail address of the manufacturing site).	

FORM CT-11

PERMISSION TO MANUFACTURE NEW DRUG OR INVESTIGATIONAL NEW DRUG FOR CLINICAL

TRIAL, BIOAVAILABILITY OR BIOEQUIVALENCE STUDY OR FOR EXAMINATION, TEST AND
ANALYSIS

Licence Number _____

The Central Licencing Authority hereby grant permission _____ (Name and full postal address with contact details of the applicant) to manufacture the new drug or investigational new drug for conduct of clinical trial or bioavailability or bioequivalence study as per protocol number dated in the below mentioned clinical trial sites or bioavailability and bioequivalence study centre [As per Annexure] or for examination, test and analysis.

Serial Number	Name of the new drug or investigational new drug to be manufactured.	Class of new drug or investigational new drug.	Quantity to be manufactured.

2. This licence is subject to the conditions specified in the Chapter VIII of New Drugs and Clinical Trials Rules,2019
under the Drugs and Cosmetics Act, 1940.

3. This licence shall, unless previously suspended or revoked, be in force for a period of three years from the date of its
issuance.

4. Details of manufacturer and manufacturing site under this licence.

Serial Number	Name and address of manufacturer (full address with telephone, fax and e-mail address of the manufacturer).	Name and address of manufacturing site (full address with telephone, fax and e-mail address of the manufacturing site).

Place: …….
Date: .....

Central Licencing Authority
Stamp

FORM 25

(*See* rule 70)

[1]*[Licence to manufacture for sale or for distribution of] drugs other than those specified in* [2][*Schedules C and C(1) and X*]

Number of Licence and date of issue.....

1.....is hereby licensed to manufacture the following categories of drugs being drugs other than those specified in [2][Schedules C and C (1) and X] to the Drugs and Cosmetics Rules, 1945, on the premises situated at.....under the direction and supervision of the following [3][competent technical staff]:

(a) [2][Competent technical staff].(Names)……

(b) Names of Drugs (each item to be separately specified).....….

2. The licence authorises the sale by way of wholesale dealing and storage for sale by the licensee of the drugs manufactured under the licence, subject to the conditions applicable to licence for sale.

3. The licence shall be in force from.....to.....

4. The licence is subject to the conditions stated below and to such other conditions as may be specified in the Rules for the time being in force under the Drugs and Cosmetics Act, 1940.

[4][*Date*.....

Signature.....

Designation.....

*Licensing Authority

*Central Licence Appoving Authority.]

**Delete whichever is not applicable.*

Conditions of Licence

1. This licence and any certificate of renewal in force shall be kept on the approved premises and shall be produced at the request of an Inspector appointed under the Drugs and Cosmetics Act, 1940.

2. Any change in the expert staff named in the licence shall be forthwith reported to the Licensing Authority.

3. If the licensee wants to manufacture for sale additional items of drugs not included above he should apply to the Licensing Authority for the necessary endorsement as provided in Rule 69(5). This licence will be deemed to extend to the categories so endorsed.

4. The licensee shall inform the Licensing Authority in writing in the event of any change in the constitution of the firm operating under the licence. Where any change in the constitution of the firm takes place, the current licence shall be deemed to be valid for a maximum period of three months

from the date on which the change takes place unless, in the meantime, a fresh licence has been taken from the Licensing Authority in the name of the firm with the changed constitution.

FORM 25A

(*See* rule 70A)

Loan [1][*licence to manufacture for sale or for distribution of*] *drugs other than those specified In* [2][*Schedules C and C (1) and X*]

1. Number of licence and date of issue.....

2.....of.....is hereby granted a loan licence to manufacture the following drugs other than those specified in [2][Schedules C and C(1) and X] to the Drugs and Cosmetics Rules, 1945, on the premises situated at C/o under the direction and supervision of the following [2][competent technical staff]:

(a) [2][competent technical staff]. (Names):…….

(c) Names of drugs.....

3. The licence authorises the sale by way of wholesale dealing and storage for sale by the licensee of the drugs manufactured under the licence subject to the conditions applicable to licences for sale.

4. The licence is subject to the conditions stated below and to such other conditions as may be specified in the Rules for the time being in force under the Drugs and Cosmetics Act, 1940.

Date..... Signature.……..

Designation……

Conditions of Licence

1. This licence and any certificate of renewal in force shall be kept on the approved premises and shall be produced at the request of an Inspector appointed under the Drugs and Cosmetics Act, 1940.

2. Any change in the [3][competent technical staff] named in the licence shall be forthwith reported to the Licensing Authority.

3. If the licensee wants to undertake during the currency of the licence the manufacture for of sale additional drugs he should apply to the Licensing Authority for the necessary endorsement to the licence as provided in Rule 69-A. This licence will be deemed to extend to the drugs so endorsed.

4. The licensee shall inform the Licensing Authority in writing in the event of any change in the constitution of the firm operating under the licence. Where any change in the constitution of the firm takes place, the current licence shall be deemed to be valid for a maximum period of three months from the date on which the change takes place unless, in the meantime, a fresh licence has been taken Sfrom the Licensing Authority in the name of the firm with the changed constitution.

[FORM 25B

(*See* rule 70)

Licence to repack for sale or distribution of drugs being drugs other than those specified in Schedules C and C (1) [2]*[excluding those specified in Schedule X]*

Number of licence and date of issue.

1. ……. .....of.....is hereby granted a licence to

repack the following drugs for sale or distribution on the premises situated at.....under the supervision of the following competent staff. *Drugs and Cosmetics Rules, 1945* 207

(a) Names of drugs to be repacked.

(b) Names of competent staff.

2. The licence shall be in force from.....to.....

3. The licence authorises the sale by way of wholesale dealing by the licensee and storage for sale by the licensee of the drugs repacked under the licence subject to conditions applicable to licences for sale.

4. The licence is subject to the conditions stated below and to such other conditions as may be specified in the Rules for the time being in force under the Drugs and Cosmetics Act, 1940.

Date..... Signature……..

Conditions of Licence

1. This licence and any certificate of renewal in force shall be kept on the approved premises and shall be produced at the request of an Inspector appointed under the Drugs and Cosmetics Act, 1940.
2. Any change in the expert staff named in the licence shall be forthwith reported to the Licensing Authority.
3. If the licensee wants to repack for sale or distribution additional items he should apply to the Licensing Authority for the necessary endorsement to this licence. This licence will be deemed to extend to only those items so endorsed.
4. The drugs repacked under this licence shall bear on their label, apart from other particulars required by these Rules, the name and address of the licensee and the number of the licence under which the drug is repacked preceded by the words "Rpg. Lic. No.".
5. The licensee shall inform the Licensing Authority in writing in the event of any change in the constitution of the firm operating under the licence. Where any change in the constitution of the firm takes place, the current licence shall be deemed to be valid for a maximum period of three months from the date on which the change takes place unless, in the meantime, a fresh licence has been taken from the Licensing Authority in the name of the firm with the changed constitution.

FORM 25C

(*See* rule 85-D)

[1][*Licence to manufacture for sale or for distribution of*] *Homoeopathic medicines*

Number of Licence and date of issue.....

[1] [*1. ……. of.....who holds a licence in Form 20-C is hereby licensed to manufacture undermentioned Homoeopathic Mother Tinctures/ potentised and other preparations on the premises situated at....under the direction and supervision of the following technical staff:
Names of the Homoeopathic preparations.
(*Each item to be separately specified*).
Names of the Technical Staff.....]

2. The licence shall be in force from.....to.....

3. The licence is subject to the conditions stated below and to such other conditions as may be specified in the Rules for the time being in force under the Drugs and Cosmetics Act, 1940.

Drugs and Cosmetics Rules, 1945 208

Date..... *Signature……*

Designation….

Conditions of Licence

1. This licence and any certificate of renewal in force shall be kept on the approved premises and shall be produced at the request of an Inspector appointed under the Drugs and Cosmetics Act, 1940.

2. Any change in the expert staff named in the licence shall be forthwith reported to the Licensing Authority.

[3][3. The licensee shall inform the Licensing Authority in writing in the event of any change in the constitution of the firm operating under the licence. Where any change in the constitution of the firm takes place, the current licence shall be deemed to be valid for a maximum period of three months from the date on which the change takes place unless, in the meantime, a fresh licence has been taken from the Licensing Authority in the name of the firm with the changed constitution.]

**Delete* the words "who holds a licence in Form 20C" in case this is not applicable.

---

1. Subs. by.. G.S.R.788(E) , dt. 10.10.1985.
2. Subs. by. G.S.R. 13(E) , dt. 7.1.1983.
3. Added by S.O. 903, dt. 28.2.1976.

[FORM 25D

(*See* rule 154)

Licence to manufacture for sale of Ayurvedic (including Siddha) or Unani drugs

No. of Licence……

1. …. .....is / are hereby licensed to manufacture the following Ayurvedic (including Siddha) or Unani drugs on the premises situated at.....under the direction and supervision of the following technical staff: —

(a) Technical staff (Names)

(b) Names of drugs (each item to be separately specified).

2. The licence shall be in force from.....to.....

3. The licence is subject to the conditions stated below and to such other conditions as may be specified in the Rules for the time being in force under the Drugs and Cosmetics Act, 1940.

Date: …… Signature.....

Designation.....

Conditions of Licence

1. This licence and any certificate of renewal in force shall be kept on the approved premises and shall be produced at the request of an Inspector appointed under the Drugs and Cosmetics Act, 1940.

2. Any change in the expert staff named in the licence shall be forthwith reported to the Licensing Authority.

3. This licence shall be deemed to extend to such additional items as the licensee may intimate to the Licensing Authority from time to time, and as may be endorsed by the Licensing Authority.

4. The licensee shall inform the Licensing Authority in writing in the event of any change in the constitution of the firm operating under the licence. Where any change in the constitution of the firm takes place, the current licence shall be

deemed to be valid for a maximum period of three months from the date on which the change takes place unless, in the meantime, a fresh licence has been taken from the Licensing Authority in the name of the firm with the changed constitution.

---

1. Added by Notfn. No. 1-23/67 -D, dt. 2-2-1970.

[FORM 25E]

(*See* rule 154A)

Loan Licence to manufacture for sale Ayurvedic (including Siddha) or Unani Drugs

1. Number of Licence…….

2.....of.....is hereby granted a

loan licence to manufacture for sale Ayurvedic (including Siddha) or Unani drugs, on the

premises situated at.....C/o.....under

the direction and supervision of the following expert technical staff:

(a) Technical staff (Names)……

(b) Names of drugs (each item to be separately specified)

3. The licence shall be in force from.....to……

4. The licence is subject to the conditions stated below and to such other conditions as may be specified in the Rules for the time being in force under the Drugs and Cosmetics Act, 1940.

Date of Issue.....

Signature.....

Designation.....

Conditions of Licence

1. This licence and any certificate of renewal in force shall be kept on the approved premises and shall be produced at the request of an Inspector appointed under the Drugs and Cosmetics Act, 1940.
2. Any change in the technical staff named in the licence shall be forthwith reported to the Licensing Authority.
3. This licence shall be deemed to extend to such additional items as the licensee may intimate to the Licensing Authority from time to time, and as may be endorsed by the Licensing Authority.
4. The licensee shall inform the Licensing Authority in writing in the event of any change in the constitution of the firm operating under the licence. Where any change in the constitution of the firm takes place, the current licence shall be deemed to be valid for a maximum period of three months from the date on which the change takes place unless, in the meantime, a fresh licence has been taken from the Licensing Authority in the name of the firm with the changed constitution.

---

1. Added by G.S.R. 376 (E), dt. 20.7.1978

[FORM 25F]

(*See* rule 70)

[2][*Licence to manufacture for sale or for distribution of*] *drugs specified in Schedule X and not specified in Schedules C and C(I)*

1. .....of.....is hereby licensed to manufacture at the premises situated at……the following drugs specified in Schedule X to the Drugs and Cosmetics Rules, 1945.

Krisha Soni-02-September-2020

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