REGISTRATION OF INDIAN DRUG PRODUCTION IN OVERSEAS MARKET

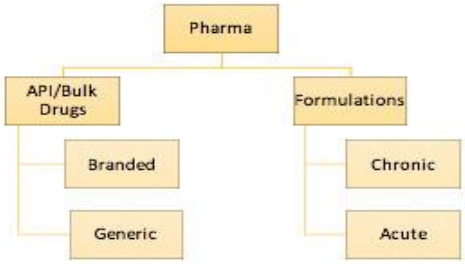
Introduction:

1. Indian pharmaceutical market:

The Indian pharmaceutical industry has acquired a noteworthy position in the global pharmacy sector and has been achieving significant growth in the recent years. India is among the top six global pharmaceutical producers in the world. Presently there are 10500 manufacturing units and 3000 pharmacy companies in India, growing at an exceptional rate. India has about 1400 who GMP manufacturing units. India has been accredited with approximately 1105 ceps (certificate of suitability) more than 950 TGA approvals and 584 sites approved by USFDA.

2. Structure of Indian pharmaceutical sector:

Indian pharmaceutical sector can be divided into two major segments namely, active pharmaceutical ingredients (API) or bulk drugs and formulations. The API can be branded or generic and these ingredients will be a part of formulations, which will be used to treat acute or chronic disease. The structure of Indian pharmaceutical industry is detail in the figure below:



3. Export of pharmaceuticals from India:

administrative requirements of documents and procedure for export of drug from India. Explains export process of pharmaceutical products, government rules to export pharmaceutical products, export documentation to export pharmaceutical products:

A. Introduction.

B. Purpose.

C. Scope.

D. Procedure.

The following documents are required to be submitted in the following manner and order for issue of the no objection certificate for export of drugs from India:

1. Covering letter:

The covering letter mentioning list of products to be exported clearly indicating name of the drug, dosage form, composition and strength back size along with quantity and country to be exported Duly signed and stamp by the authorised signatory, indicating the name and designation of authorised signatory along

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with the name and address of the firm.

2. Import export code number (IEC) given by DGFT.

3. Purchase order:

(a) order from the foreign buyer either in the name of manufacturer or in the name of trader mentioning list of products to be exported clearly indicating name of the drug, dosage form, composition and strength pack size duly signed by the competent authority with specific destination point of the importing country.

(b) it should be signed by the competent authority/person with a valid purchase order number and recent date not more than 6 months prior to the application made by the firm.

4. Manufacturing licence: licence issued by the state licensing authority should be enclose along with each application for the required location to manufacture the drug for export purpose.

5. Performa invoice.

6. Indent.

7. Custom clearance certificate.

8. Registration certificate.

9. Certificate of analysis (COA)

10. GST.

11. Consignment sample.

12. Pre shipment sample.

13. Department of economic affairs.

- Rules related to export or drugs from India:

Rule 94: labelling and packaging of drugs other than homeopathic medicines

1. Labels on packages are containers of drugs from export shall be adapted to meet the specific requirements of the law of the country to reach the drug is to be exported but the following particular shawl appear in a conspicuous position on the innermost container in which the drug is pact and every other covering in which that container is packed.

2. The provision of rule 96 to 101 inclusive, shall not apply to a medicine made up ready for treatment, whether after or without dilution, which is supplied on the prescription of register practitioner provided.

Rule 95: Prohibition of sale or distribution unless labelled. Subject to the other provisions of these rules, no person shawl sale or distribute any drug unless it is labour in accordance with these rules.

Rule 96: Manner of labelling: subject to the other provisions of these rules, the particulars shall be either printed or written in indelible ink and shall appear in a conspicuous manner on the label of the innermost container of any drug and on every other covering in which container is packed.

Regulatory affairs: The regulatory affairs (RA) department of pharmaceutical company is responsible for obtaining approval for new pharmaceutical products and ensuring that approval is maintained for as long as the company want to keep the product on the market.

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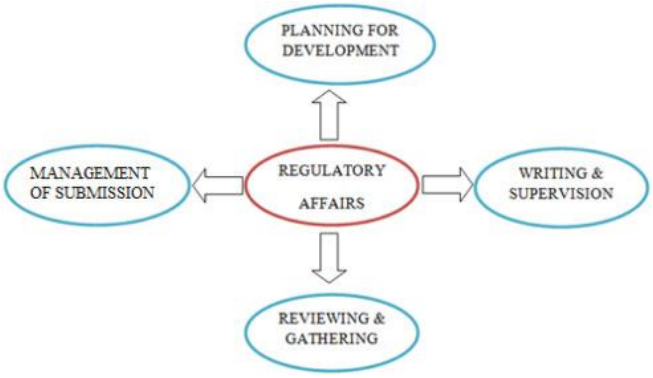

❖ **Rules and act responsible for import and export of pharmaceutical products.**

1. Drugs and cosmetics act 1940 and rules 1945.

2. The drugs (price control) order 1995.

3. Medicinal and toilet preparation act 1956.

4. Narcotic and psychotropic substances act 1985.

5. Drugs and magic remedies act 1954.

❖ **Steps involved in export of pharmaceutical products:**

1. Apply for IEC number.

2. Get the customers mean contact the countries interested in importing the drug.

3. Register the drug product in the country where you are going to export.

4. Get the DCGI approval for exporting.

5. Finalize the shipping method.

6. Receive the purchase order from the country which is important and say invoice with complete product details.

7. Sign the contract with the agency of the importing country.

8. Pre shipment inspection.

9. Export of the product.

- **Technical documentation:**

Documentation is the essential and crucial part in any of the company in Pharma we can say "if it is not documented, it has not done". Documentation is evidence to show or to prove that the things have done accordingly. Quality assurance documents are the heart of the company.

Technical documents are:

1. Master formula record (MFR).

2. Batch manufacturing record (BMR).

3. Batch packaging record (BPR).

4. Certificate of analysis (COA).

5. Certificate of pharmaceutical product (COPP).

6. Product specifications.

- **DRUG MASTER FILE (DMF):**

DMF is a confidential document for API submitted to the regulatory body for the approval process. In fact, there is no regulations to

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file a DMF. It is not reviewed on receipt as like dossier and DMF's are neither approved nor disapproved.

It has divided into two parts;

1. Open part (applicants' part): Contains all the required information related to method of manufacture and brief outline of method of manufacture, potential impurities, manufacturing system etc.

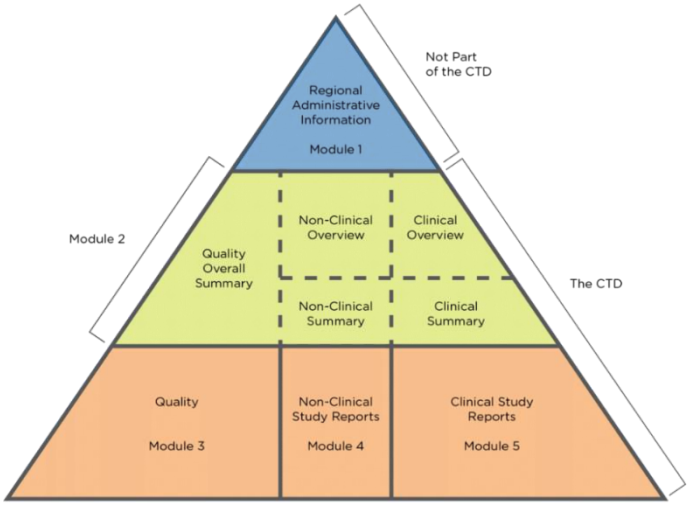
2. Close part (restricted part): Contains confidential information on the manufacture of API like extraction, validation, process, solvents used, reactions, temperature, conditions, critical steps in manufacture etc.

Apart from this DMF is divided into 5 types:

1. Type I: plant information (no more part of DMF)
2. Type II: drug substance, drug products, intermediates and materials used in manufacturing.
3. Type III: packaging materials.
4. Type IV: excipients or additives.
5. Type V: FDA accepted reference information.

- **COMMON TECHNICAL DOCUMENTS (CTD):**

Common technical document is an essential document to be submitted to regulatory body as a supportive list of leaflets attached with the registration applications for pharmaceuticals to get market authorisation. Mainly CTD tells about the format for the data.



Module 1 - Administrative information:

This module contains administrative and legal information about the submission, including the application form, the cover letter, and the regulatory history of the product.

Module 2 - Quality overall summary:

The general introduction to the medicinal product provided in Module 2 section of CTD dossier, which is harmonized for all regions (The International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH)). This module presented by summary documents for each upcoming modules: quality data, non-clinical and clinical study reports.

Module 3 - Quality:

Module 3 was identified by ICH as the

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Quality Module. Thus, "Quality" became the global term for CMC (chemistry, manufacturing and controls). CMC should not be confused with the elements of quality control, quality assurance, sops (standard operating procedures), internal company documents (specifications, batch records, etc.)

Module 3 section also harmonized for all regions with providing information of chemical-pharmaceutical and biological information for chemical active substances and biological medicinal products.

Throughout development and after a product is approved by health authorities, the chemistry, manufacturing and control (CMC) aspects continue to evolve and change.

Pharmaceutical Quality = CMC

Module 4 - Non-Clinical study reports:

The relevant section the appropriate location for individual-animal data is in the study report in the Common Technical Document for applications that will be submitted to Regulatory Authorities. Module 4 is harmonized for US and EU based on ICH principals, and contains all necessary sections and sub-sections for study reports. References to ICH guidelines Common Technical Document (CTD).

Module 5 - Clinical study reports:

Module 5 section this is the structure and content of clinical study reports.

This part of CTD presented human/clinical study reports, other clinical data, and references within a Common Technical Document (CTD) for registration of a pharmaceutical product for human use. These elements should facilitate the preparation and review of a marketing application.

Module 5 is harmonized for US and EU based on ICH principals, and contains all necessary sections and sub-sections for study reports. References to EU guidelines Common Technical Document (CTD).

- **ELECTRONIC COMMON TECHNICAL DOCUMENT (eCTD):**

eCTD is electronic common technical document, an electronic format where the information and document is submitted to regulatory body electronically by using a software. Sum of the eCTD software is pharmed ready, Edios etc. eCTD submission is for applications, amendments, variations, supplementary, reports, master formulae etc. Understanding the eCTD format and applying successfully in submission is the biggest hurdle. While sponsors or the applicant may face problem when the documents does not fit into the format because the application or submission shall be bounced back known as technical rejection.

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Requirements of eCTD:

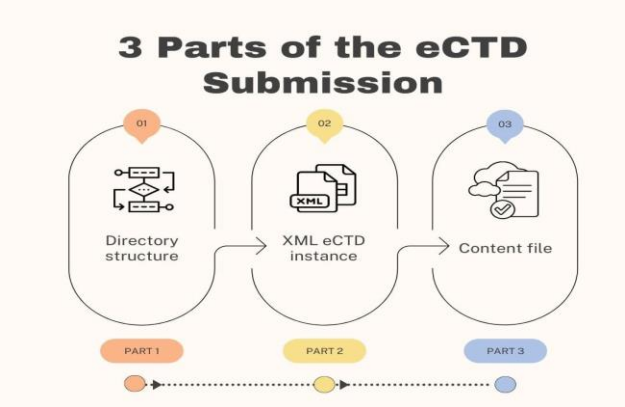
1. Copy and paste.

2. Verifying and printing documents.

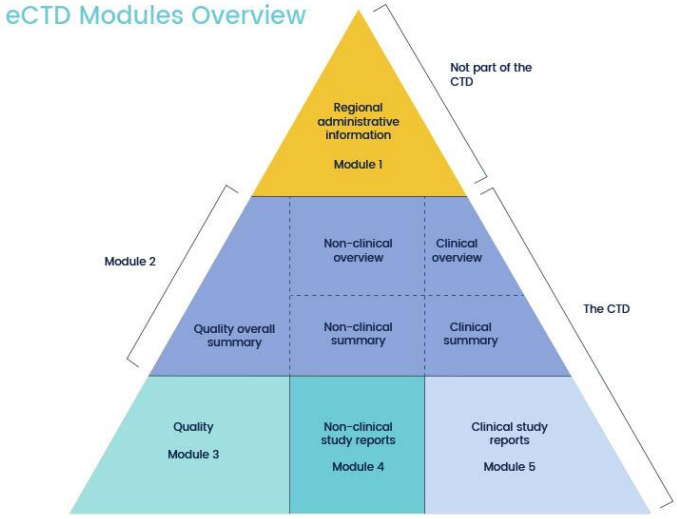
3. Document annotation.

4. Export of information to data bases.

Structure of submission of eCTD:



Modular structure of eCTD:



I. Module 1: Administrative information and pre- scribing information.
II. Module 2: Overviews and Summaries of Modules 3–5.
III. Module 3: Quality (pharmaceutical documentation).
IV. Module 4: Non-clinical reports (pharmacology/ toxicology).
V. Module 5: Clinical trials.

- **ASEAN common technical document (ACTD):**

ASEAN (association of South East Asian nations) common technical document (ACTD) easy structured document for the registration of pharmaceuticals in ASEAN countries.

ASEAN countries and their regulatory bodies:

1. Indonesia - National agency of drug and food control (NADFC).

2. Vietnam- drug administration of Vietnam.

3. Thailand- Thai FDA.

4. Singapore- health science authority (HAS).

5. Malaysia- National pharmaceutical regulatory agency (NPRA).

6. Philippines- food and drug administration (FDA).

7. Brunei- ministry of health.

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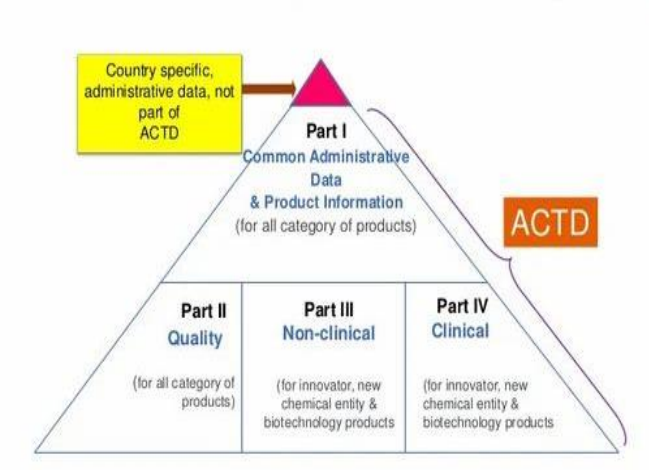
8. Cambodia-department of drugs and food.

9. Myanmar- food and drug administration (FDA).

10. Laos- food and drug department.

ACTD includes for parts:



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