2.0 RESEARCH METHODOLOGY

2.1 Study Rationale

U.S. has a lion’s share in the global pharmaceutical market. The Federal government policy is to take care of the total health care cost of the U.S. citizens as well as permanent residents. Due to this clause and downward trend of U.S. economy, the federal government encourages less expensive drugs. This opened the gates for generic market thus emerging as an important destination for India’s pharmaceutical exports.

Rationale in Selecting U.S. Market

1. Demographically USA is the third largest country in the world behind China and India.
2. U.S. is the densely populated behind China and India.
3. U.S. has a noticeable rise in the aged (65 years) population.
4. U.S. is the world’s largest and wealthiest pharmaceutical market accounting for 48% of the world total.
5. Per capita expenditure on drugs is double the level found with ROW.
6. Generic Product Registration in U.S. Federal government is free of cost unlike ROW where charges are very high.

In view of overwhelming importance of USA in global pharmaceutical markets, the emergence of India’s pharmaceutical industry as flag ship industry is of strategic importance due to the large share of USA in India’s exports of pharmaceutical products. The research study aims at studying
India’s presence in U.S. pharmaceutical market by focusing various strengths.

In case of pharmaceutical markets such a study can be undertaken by studying drug registration patterns which is a prerequisite for marketing in all regulated markets such as USA. Typically in pharmaceutical markets enhancement comes through exploiting various opportunities such as acquiring NDAs, foraying into value added products/segments/therapies. There are alternative routes for acquiring all important NDAs such as 505(b)(2), or niche product opportunities. Such opportunities, competitive situation that can be easily studied through a study of drug substance (DMFs) and product registration (ANDAs) patterns.

It is observed that there is a lack of consolidated and comparable published information is available in the following aspects to identify India’s potential in U.S. pharmaceutical market for growth and exports.

1. Concise U.S. market research analysis.
2. India’s strengths in bulk drug registrations (DMFs) in terms of molecules, therapeutic categories, their market shares and high value segments.
3. India’s strengths in formulation (generic) approvals by drug molecules, therapeutic categories, country and company competition.
Considering the above facts, an attempt is made to study India’s strengths in product registrations and approvals with U.S.FDA.

Currently, though a few Indian companies have direct subsidiaries in U.S. markets these subsidiaries act merely as agents of their principals in India for marketing & drug product registrations and therefore majority of Indian company’s presence in U.S. market is through direct exports. The study therefore aims to analyze trends in pharmaceutical exports from India/imports of pharmaceuticals into USA from India.

2.2 Objectives

The main objectives of the research are therefore laid down as follows:

1. To study India’s strengths in Drug substance registrations/filings by India in USA in terms of number of registrations, yearly growth rate, company and country competition, molecules and therapeutic categories to identify India’s potential for growth and exports.

2. To study India’s strengths in formulation product approvals by number of approvals, yearly growth rates, country wise approvals, company and country competition, therapeutic categories, molecules and dosage forms. The study also aims to analyze emerging opportunities for India arising from patent expiries with reference to opportunities awaited in various therapeutic categories.
3. To study trends in India’s exports of pharmaceutical products to USA, to identify countries strengths and statistically establish if India would continue to grow or not. This is done by testing hypothesis which is defined as follows.

**Hypothesis Testing**

Null hypothesis (Ho) therefore is: “India’s pharmaceutical market presence in USA would remain stagnant or decline in the coming 5 years.”

Alternate hypothesis (Ha) is: “India’s pharmaceutical market presence in USA would continue to grow in the coming 5 years.”

### 2.3 Study Plan

Due to dominant share of U.S. in the world pharmaceutical market and the large share of USA in India’s pharmaceutical exports, analysis of U.S.FDA was comprehensively carried out by studying drug registration patterns, both bulk drug registrations [Drug Master Files (DMFs)] and formulation registrations [Abbreviated New Drug Application (ANDAs), NDA (New Drug Application), NME (New Molecular Entity), and BLA (Biological Licensing Application)]. A schematic representation of the study plan is shown in Figure 2.1

The study plan involves the following steps

I. **Parameters Studied**
1. India’s Bulk drug registrations, DMFs (Drug Master File) with U.S.FDA for the data available as on 24 October 2011 has been extensively studied in various aspects such as

- Number of DMF registrations
- Yearly growth rate (1999 to 24 October 2011)
- Molecule wise DMFs
- Therapeutic segments and
- Country wise company analysis to derive India’s position globally in DMFs registrations with U.S.FDA.

2. India’s pharmaceutical product approvals (BLA, NDA, ANDA and NME) granted by U.S.FDA as on 28 December 2010 are studied in terms of

- Number of product approvals
- Molecules
- Therapeutic categories
- Country wise product approvals
- Country and company competition

All the above mentioned parameters for product approvals are individually studied for prescription and OTC products. Products that are tentatively approved and discontinued products are also studied.
3. India’s bilateral trade as on 31 Mar 2011 is studied for drugs, pharmaceuticals and fine chemicals with respect to

- Country wise (Imports and Exports)
- Region wise (Imports and Exports) and
- Category wise (Imports and Exports)
Figure 2.1: Study Plan

![Study Plan Diagram]

**Study Parameters**
- Product Registrations
- Bulk Drug Registration (DMFs)
- Formulations Registration (NDA, ANDA, NME, BLAs)
- India's Bilateral Trade
- Number of DMFs
- Molecules
- Therapeutic Categories
- Number of Companies
- Number of Product Approvals
- Company Competition
- Country Competition
- Prescription Approvals
- OTC Approvals
- Tentative Approvals
- Discontinued ANDAs
- Country-wise
- Region-wise
- Category-wise
- Imports
- Exports

**Data Source**
- Primary Source: Electronic Databases, Data Files & Soft Copies Provided by Regulatory Bodies
  - For DMFs: DMF Database
  - For ANDAs, NDAs, NMEs, BLAs: Regulatory electronic data bases (Drugs@FDA, Orange Book, National Drug Code Directory, For ANDAs: Patent office and Regulatory websites of UK MHRA, Ethiopia, Tanzania, Azerbaijan, EQM, and CDSCO)
  - For India's Bilateral Trade: Data from DGCI&IE
  - US Trade Database "TradeStat Export"; CMIE Package "India Traders"

- Secondary Source: National & International Journals, Country Websites and Data from Official Agencies

**Analytical Tool/Statistical Tool**
- Scenario Analysis; Sensitivity Analysis

**Interpretation**
- Forecast of India's Product Registrations and Exports to US Market for the next five years (2011-2015)
DATA SOURCE
Primary Source: The primary source of research is the data provided by U.S.FDA and DGCI&S (Director General of Commercial Intelligence and Statistics). U.S.FDA with the purpose and intention of encouraging generic competition and thus enabling lowering healthcare costs, making available all the drug substance and product registrations through its website. Complete and comprehensive information is provided by Center for Drug Evaluation and Research (CDER) in the form of electronic data files, excel sheets and online databases.

The data is comprehensive as it provides particulars of all the drug substance (API/bulk drug) and product (generic) registrations by various companies filed or approved by U.S.FDA. These data files were analyzed by identifying therapeutic categories, countries of holder companies.

i) To study bulk drug registrations (DMFs), softcopy of Type-II active DMFs (DMF Database) provided in U.S.FDA is used. This data is used to identify India’s bulk drug registration status by studying company wise and country wise Type II Active DMFs filed with U.S.FDA.

ii) Formulation registrations namely NDAs (New Drug Application), ANDAs (Abbreviated New Drug Application), NME (New Molecule Entity), and BLAs (Biologic Licensing Application) are studied from electronic database files of Drugs@FDA, Orange book and National Drug Code (NDC) Directory. Further, to identify India’s product
approval status, NDAs, ANDAs, NMEs, and BLAs for prescription and Over the Counter (OTC) formulation products granted by U.S.FDA were studied. [Products which have been discontinued or tentatively approved were not considered for the final forecast analysis].

**Orange Book**

Orange Book is commonly known as Approved Drug Products with Therapeutic Equivalence Evaluation. It is compiled by FDA and lists all approved drugs along with their official and proprietary names. When patent information is submitted for a new drug application in accordance with C.F.R. section 314.53 the patent information is included in the orange book. The orange book identifies drug products approved on the basis of safety and effectiveness by the FDA under FD&C Act.

The orange book stores

- Prescription drugs (Human)
- OTC drugs (Human)
- Discontinued drugs (Human)

The patent and exclusivity listing can be found in this online book which is updated periodically. It can be obtained by searching a drug product by the active ingredient, applicant holder, the application number, proprietary name and patent number.
ii) India’s bilateral trade of drugs, pharmaceuticals and fine chemicals were studied using the data provided by Director General of Commercial Intelligence and Statistics (DGCI&S). The data provided by the agency was extracted through the package ‘India Trades’ provided by a private agency, Center for Monitoring Indian Economy (CMIE). By making use of the HS codes, this data is further used to study country wise, region wise and category wise imports and exports of Indian pharmaceuticals.

**Study of India’s Bilateral Trade using Harmonised Codes (HS Codes)**

Towards research on India’s pharmaceutical exports using official basket for Drugs, pharmaceuticals & fine chemicals, at 8 digit HS codes it was noticed that the basket consists of the below mentioned besides formulations and bulk drugs. They are several intermediates, fine chemicals, excipients, medical & diagnostic equipment, surgicals, medical devices, diagnostic reagents, a few herbals and products under Alternate Systems of Medicine (medicants and medicaments of Ayurveda, Siddha, Unani and Homeopathy are commonly referred to as AYUSH products). However, the official basket is not an exhaustive one and does not comprehensively cover under each of the categories. All the HS codes available are at eight digit level (Table 2.1). An attempt was therefore made to exhaustively identify all the available HS codes falling under different categories under Pharmaceutical sector.
Table 2.1: Sample list of HS codes & their descriptions which are not included in India’s Official basket of HS codes for Drugs, Pharmaceuticals & fine chemicals

*Data Source: DGCI&S Data, Merck Index*

<table>
<thead>
<tr>
<th>SL. No.</th>
<th>Commodity Code</th>
<th>Commodity Name</th>
<th>Category</th>
<th>Merck Index+ code</th>
<th>Application</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>29182200</td>
<td>0-acetylsalicylic acid its salts and esters</td>
<td>API</td>
<td>851</td>
<td>Analgesic</td>
</tr>
<tr>
<td>2</td>
<td>29333300</td>
<td>Alfentanil, anileridine, propiram &amp; trimeperidine, etc., salts thereof</td>
<td>API</td>
<td>236</td>
<td>Analgesic</td>
</tr>
<tr>
<td>3</td>
<td>29335300</td>
<td>Allobarbital and other barbital compounds and its salts</td>
<td>API</td>
<td>263</td>
<td>Sedative ,Hypnotic</td>
</tr>
<tr>
<td>4</td>
<td>29339100</td>
<td>Alprazolam, camazepam &amp;</td>
<td>API</td>
<td>312</td>
<td>Anxiolytic</td>
</tr>
<tr>
<td></td>
<td></td>
<td>other compounds of zepam, salts thereof</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>----------------------------------------</td>
<td>---</td>
<td>---</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>29223100</td>
<td>Amfepranone(inn), methdone &amp; mormethadone salts</td>
<td>API</td>
<td>3127</td>
<td>Anorexic</td>
</tr>
<tr>
<td>6</td>
<td>29349100</td>
<td>Aminorex, brotizolam and other like compounds, salts thereof</td>
<td>API</td>
<td>476</td>
<td>Anxiolytic</td>
</tr>
<tr>
<td>7</td>
<td>29337200</td>
<td>Clobazam (inn)</td>
<td>Indian Pharmacopoeia</td>
<td>Sedative &amp; Hypnotics</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>29389020</td>
<td>Digitalis Glycoside</td>
<td>Indian Pharmacopoeia</td>
<td>Cardiotonics (Congestive Heart Failure)</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>29225024</td>
<td>Domperidone</td>
<td>API</td>
<td>3418</td>
<td>Antiemetic</td>
</tr>
<tr>
<td></td>
<td></td>
<td>29362400</td>
<td>D-or dl-pantothenic acid (vitamin B3 or vitamin B5) and its derivatives</td>
<td>API</td>
<td>Indian Pharmacopoeia</td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>10</td>
<td></td>
<td>29396210</td>
<td>Ergotamine Tartarate</td>
<td>API</td>
<td>Indian Pharmacopoeia</td>
</tr>
<tr>
<td>11</td>
<td></td>
<td>29280010</td>
<td>Isoniazide</td>
<td>API</td>
<td>5186</td>
</tr>
<tr>
<td>12</td>
<td></td>
<td>28369100</td>
<td>Lithium carbonates</td>
<td>API</td>
<td>Indian Pharmacopoeia</td>
</tr>
<tr>
<td>13</td>
<td></td>
<td>29335500</td>
<td>Loprazolam, mecloqualone, methaqualone, salts thereof</td>
<td>API</td>
<td>5579</td>
</tr>
<tr>
<td>14</td>
<td></td>
<td>29241100</td>
<td>Meprobamate</td>
<td>API</td>
<td>5862</td>
</tr>
<tr>
<td>15</td>
<td></td>
<td>30042097</td>
<td>Polymyxin b and colistin</td>
<td>Formulations</td>
<td>Indian Pharmacopoeia</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
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<td>---</td>
<td></td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>29394200</td>
<td>Pseudoephedrine (inn) and its salts</td>
<td>API</td>
<td>7916</td>
<td>Nasal Decongestant</td>
</tr>
<tr>
<td>18</td>
<td>28372050</td>
<td>Sodium nitroprusside (sodium nitroferricyanide)</td>
<td>API</td>
<td>Indian Pharmacopoeia</td>
<td>Vasodialators</td>
</tr>
<tr>
<td>19</td>
<td>29124930</td>
<td>Thiacetazone</td>
<td>API</td>
<td>9290</td>
<td>Antitubercular</td>
</tr>
<tr>
<td>20</td>
<td>29362940</td>
<td>Vitamin D</td>
<td>API</td>
<td>Indian Pharmacopoeia</td>
<td>Vitamins</td>
</tr>
</tbody>
</table>

**Accuracy Verification**

*To ensure accuracy, verification of the commodity description was carried out with Merck Index and various pharmacopoeias. HS codes pertaining to herbals were identified into the basket, if over 50% of the commodity under the HS code is utilized in pharmaceuticals based on the judgmental approach. Currently though many countries have HS Codes identifying medicinal grade fine chemicals and HS*
codes at 10 digit levels, India does not have such separate classification. Therefore, all the HS codes pertaining to fine chemicals used for pharmaceutical purposes were included based on their description.

The research yielded 1,150 HS codes under 10 categories whose break up is given Table 2.2. Using these HS codes analysis, country wise, region wise and category wise exports and imports of Indian pharmaceutical sector was carried out on data provided by DGCI&S. The data available for last 20 years (1991 to March 2011) was studied during the research.

**Table 2.2: Comparison of Identified HS Codes with Existing Official Basket of India**

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Category</th>
<th>Codes Identified</th>
<th>Existing Codes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Formulations</td>
<td>164</td>
<td>148</td>
</tr>
<tr>
<td>2</td>
<td>Bulk Drugs &amp; Intermediates</td>
<td>211</td>
<td>175</td>
</tr>
<tr>
<td>3</td>
<td>Biologicales</td>
<td>63</td>
<td>52</td>
</tr>
<tr>
<td>4</td>
<td>Excipients</td>
<td>34</td>
<td>29</td>
</tr>
<tr>
<td>5</td>
<td>Herbals</td>
<td>106</td>
<td>28</td>
</tr>
<tr>
<td>6</td>
<td>Fine Chemicals</td>
<td>464</td>
<td>6</td>
</tr>
<tr>
<td>7</td>
<td>Medical &amp; Diagnostic</td>
<td>62</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Equipment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Surgical &amp; dressings</td>
<td>32</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>Medical Devices</td>
<td></td>
<td>Diagnostic Reagents</td>
</tr>
<tr>
<td>-------</td>
<td>-----------------</td>
<td>-------</td>
<td>---------------------</td>
</tr>
<tr>
<td>9</td>
<td></td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td><strong>1,150</strong></td>
<td><strong>457</strong></td>
</tr>
</tbody>
</table>

**Data Source for studying India’s Pharmaceutical exports to U.S.**

While this data was used to study India’s exports, due to several lacunae such as non-classification of fine chemicals into ‘medicinal grade’, etc., statistics provided by US Trade Department database ‘Tradestat Express’ on country’s imports of pharmaceutical and country wise imports was considered to analyze India’s exports to USA. All the trade data available for the last 21 years beginning with 1990 was analyzed.

**Source of Secondary Research**

Further secondary research was carried out through various articles published in national and international journals, company websites, data from official agencies, etc. All data was gathered and analyzed for 21 years from 1990 to 2010.

**Data Validation**

During the research, several validation and data checking steps were undertaken while collecting and post collection of data to ensure its accuracy. Data was analyzed using spreadsheets. Results were then cross checked and a data validation was performed.
2.4 ANALYTICAL TOOLS

- While conclusions on India’s strengths were drawn through growth rates, % share etc., the main statistical tool used for validating hypothesis is ‘Scenario Analysis’.

- Deterministic models such as Multiple Linear Regression models, are too simplistic for accommodating unpredictability associated with business situations such as market presence. On the other hand, stochastic models such as Montel-calro Method, Markov Chain analysis85 were used in some of the not so easily statistically amenable parameters.

A ‘Scenario analysis’ of exports was therefore carried out based on Multiple Linear Regression equation fitted for bulk drug registrations, generic drug approvals and pharmaceutical exports to U.S. from India using MS Office application ‘Excel’.86 The same data is validated using statistical analysis software (SAS), (version 9.2) provided by SAS Institute, India.

Data Interpretation

Based on growth rates of India’s DMF registrations and ANDA approvals for the past 10 years and considering all the associated factors, sensitivity analysis was carried out to predict range bound export values by taking three scenarios namely

- Optimistic,
● Normal (Most likely) and

● Pessimistic conditions

Thus scenario analysis based on assumptions is carried out on the data obtained from SAS to forecast the DMF registrations and ANDA approvals for the next five years (2011 to 2015). Finally using these predictions and regression equation, forecast of India’s Pharmaceutical exports (both bulk drugs and formulation) to U.S. market is provided for the next five years (2011 to 2015).

2.5 LIMITATIONS

While the study attempted to accurately, and comprehensively analyze the information due to enormous depth and complexities involved, certain kinds of analytical study is beyond the scope of the present investigation. Some of the limitations are listed below:

a) The study comprehensively covers only human medicines as under the purview of CDER, U.S.FDA. Several drug products which are not under it such as biologicals, veterinary, herbal based products and nutraceuticals, radioactive medicine which are not under CDER were not studied.

b) Analysis of several complex issues such as alternate drug registration pathways [such as 505(b)(2)], molecular chemistry, patents and other issues for which data is not available in public domain such as market size of molecules, therapies, companies,
technology and chemistry capabilities of Indian companies, etc., are beyond the scope of the study.