EVALUATION OF PHARMACEUTICAL REGULATORY SYSTEM & PRESENT SCENARIO OF INDIAN PHARMACEUTICAL INDUSTRY

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ABSTRACT

Indian pharmaceutical industry evolved in true sense only after independence. India is the fourth largest generic pharmaceutical market in the world. Ranking fourth in terms of volume and thirteenth in terms of value in global pharmaceutical markets and is consistently growing. Proper regulatory system ensures the quality, safety and efficacy and standard of medicinal product for sales, importing and manufacturing. India’s pharmaceutical industry is one of the most highly regulated industries in the country. Understanding the regulatory scenario is extremely crucial due to the rapid and ongoing changes and due to the burden on the regulatory bodies to ensure a healthy supply of quality drugs at affordable prices to the Indian masses.


INTRODUCTION

The pharmaceutical industry is the world’s largest industry due to worldwide revenues of approximately US$2.8 trillion. Pharma industry has seen major changes in the recent years that place new demands on payers, providers and manufacturers. The Regulatory Affairs departments of life-science companies ensure that their companies comply with all of the regulations and laws concerning their business. The Regulatory Affairs department is an important part of the organisational structure of pharmaceutical companies. Internally it
liaises at the interphase of drug development, manufacturing, marketing and clinical research. Externally it is the key interface between the company and the regulatory authorities.\textsuperscript{[1-3]}

REGULATORY ENVIRONMENT
The principal regulatory body involved in the approval of manufacture, drug development and marketing of quality drugs in India is The Central Drug Standards and Control Organization (CDSCO) under Ministry of Health and Family Welfare which works on developing standards and measures for ensuring the safety, efficacy and quality of drugs, cosmetics, diagnostics and devices in the country. It regulates the market authorization of new drugs and clinical trials standards; supervises drug imports and approves licenses to manufacture the products. At the state level, state drug regulatory authority issues licences to manufacture approved drugs and to monitor the quality of drugs along with CDSCO.\textsuperscript{[2-4]}

TABLE -1-INDIAN DRUG REGULATORY SYSTEM

The regulatory bodies involved in the pharmaceutical industry and their functions are as follows\textsuperscript{[5-7]}

- **Drugs Control General of India (DCGI)** – Main authority for clinical trials, ensures standards, registers all imported drugs, new drugs, biologics and medical devices.
- **Indian Council of Medical Research (ICMR)** – main center for biomedical research.
- **Genetic Engineering Approval Committee (GEAC)** – deals with genetic engineering and molecular biology, trials in which biotech products are used will be referred here by DCGI.
- **Department of Biotechnology (DBT)**-oversees the development of modern biology and biotechnology in India.
• Atomic Energy Review Board (AERB) – Has regulatory control over radiation equipment.
• Baba Atomic Research Centre (BARC) –approves all radiation related projects and radio pharmaceuticals in India.
• Drugs Consultative Committee (DCC) – Provides technical guidance to the CDSCO.
• Central Drugs Laboratory (CDL)-Maintains quality control of drugs
• Central License Approving Authority (CLAA)– Provides approval for manufacturing licenses’
• Drugs Technical Advisory Board (DTAB) –Provides technical guidance to the CDSCO
• National Pharmaceutical Pricing Authority (NPPA) – NPPA fixes or revises the prices of decontrolled bulk drugs and formulations and periodically updates the list under price control according to guidelines.

USFDA(USA), MHRA(UK), TGA(Australia), CDSCO(India), HEALTH CANADA(CANADA), MCC(South Africa), ANVISA (Brazil), EMEA (European Union), SFDA(China), NAFDAC(Nigeria), MEDSAFE(Newzeland), MHLW(Japan), MCAZ(Zimbabwe), SWISSMEDIC(Switzerland), KFDA(Korea), MOH (Sri Lanka) are the few regulatory agencies and organizations established in respective countries.

REGULATORY FUNCTIONS[8]

• Regulatory Affairs is actively involved in every stage of development of a new medicine and in the post-marketing activities with authorised medicinal products.
• Regulatory Affairs professionals can play a key role in guiding drug development strategy in an increasingly global environment.
• Regulatory professionals ensure that the information and data to be conveyed and discussed with the regulatory bodies are presented in the right way and form.
• They develop the regulatory strategy, arrange agency meetings, prepare and compile the questions and briefing documents; they attend the meetings and manage all communication with the agencies.
• Since the regulatory environment is constantly changing the regulatory team provides advice on necessary adaptations to development plans and target product profiles.
• Many aspects in India are not regulatory intensive, these may lead to supply of poor quality pharmaceutical agents to the patients. There is no way to check the quality of drugs after 4 years from the date of first introduction in India.
During this 4-year period the drugs will be under “new drug” category and they require bioequivalence and if necessary clinical studies are conducted.

Those drugs which are called “old drugs” after this 4-year period, need not be subjected to bioequivalence studies and they can be permitted to market without these stringent requirements as compared to new drugs.

Evolution of regulatory system changes the industry in any country and encourages people to do more to discover and invent new drugs for emerging diseases. India is rich in biodiversity and plants with high medicinal values.

The USFDA is responsible for giving rise to the most competitive pharmaceutical industry in the world. They set standards so that doctors and patients are not afraid of using new drugs.

India has a federal form of government and medical regulatory structure is divided between national and the state authorities.

The Present Scenario
Pharmaceuticals are considered as the most highly regulated industries worldwide. The regulatory body ensures compliances in various legal and regulatory aspects of a drug. Every country has its own regulatory authority, which is responsible to enforce the rules and regulations and issue the guidelines to regulate drug development process, licensing, registration, manufacturing, marketing and labelling of pharmaceutical products.
Regulatory Approval in India
The drug approval process in India has faced challenges in recent years, some around compulsory licensing of patents, government price control and narrow standards for patentability. Other issues have also occurred in the clinical trials area, which, despite India’s high treatment-naïve population and emerging economy, have reduced pharmaceutical sponsors’ interest in India as a priority area in which to conduct clinical studies. The international regulatory organizations play essential role in all aspects of pharmaceutical regulations related to drug product registration, manufacturing, distribution, price control, marketing, research and development, and intellectual property protection.\(^{[9-11]}\)

A cursory overview of the Indian drug regulatory process is as follows\(^{[12]}\)
Currently, the Drug Controller General of India (DCGI) requires a confirmatory Phase III study that includes a proportion of local patients, although if Indians are included in multinational trials this can be avoided and decided on a case-by-case basis.

The Central Drug Standard Control Organization (CDSCO) handles the approval process. Apart from the CDSCO approval, DCGI has given rights to each state’s drug control authority to regulate the manufacture, sale and distribution of drugs.

The states include North India: Jammu and Kashmir, Himachal Pradesh, Uttaranchal, Haryana, Panjab; South India: Kerala, Tamilnadu, Karnataka, Andhrapradesh; East India: West Bengal, Assam, Arunachal Pradesh, Nagaland, Manipur, Mizoram, Tripura, Jharkhand, Bihar, Orrisa; West India: Gujarat, Rajasthan, Maharashtra; and Middle India: Madhya Pradesh, Chhattisgarh. However, final authority does rest with DCGI. The first occurred when a principal investigator was found to have generated fraudulent data and referring patients from a government hospital where he was working, to his private clinic to gain more income.

Meanwhile, amendments to clinical trial regulations under the Drugs and Cosmetics Rules (Third Amendment) were introduced in February 2013. The objective was to improve patient safety, reporting timeliness of serious adverse events including deaths during clinical trials, and the payment of compensation to patients. The amendment resulted in several concerns for researchers and research organizations around the areas of financial compensation and liability of the trial researchers. Because of these changes to the regulatory framework, many multinationals withdrew their clinical studies from India. This resulted in a standstill for the
entire clinical research industry in India. Regulatory authorities act as a guardian that ensures the safety, efficacy and quality of drugs available to the public, to identify the strengths and weaknesses of drug regulation and to propose strategies to improve drug regulations.\textsuperscript{[13]}

Regulatory Stance to Eliminate the Bottle Neck\textsuperscript{[13]}

The Health Ministry and stakeholders—including sponsors, CROs, investigators, and the regulatory agency—made a concentrated effort to address the concerns and formed a Subject Experts Committee (SEC, formally known as New Drugs Advisory Committee), Technical Committee and Apex Committee to examine applications for clinical trials in India. All of the studies approved by the DCGI were then evaluated and approved by these committees prior to commencement.

The Technical and Apex Committees consist of experts like SEC, however, each acts on the recommendations received from the SECs. The committees review the protocol application and further passes its recommendations to the DCGI. Basically, the SEC acts as a gateway in the clinical trial approval process by advising the DCGI in the following matters:

- To undertake in-depth evaluation of non-clinical data, including pharmacological toxicological data, clinical trial data (Phase I, II, III, and IV) furnished by the applicant for approval of new drug substances of chemical and biological origin, global clinical trials, fixed-dose combinations and those of two or more drugs.
- Defining roadmap for research industry for appropriate development of new drugs relevant to Indian population.
- The Committees formed are Anesthetics and Rheumatology, Antimicrobial-Antiparasitic-Antifungal-Antiviral, Cardiovascular and Renal, Dermatology and Allergy, Gastroenterology and Hepatology, Metabolism and Endocrinology, Neurology and Psychiatry, Oncology and Hematology, Ophthalmology, Pulmonary, Reproductive and Urology and Vaccines.

INDIAN PHARMACEUTICAL INDUSTRY: AN OVER VIEW\textsuperscript{[11-12]}

It is often said that the pharma sector has no cyclical factor attached to it. Irrespective of whether the economy is in a downturn or in an upturn, the general belief is that demand for drugs is likely to grow steadily over the long-term. The Indian pharmaceutical sector has come a long way, being almost non-existent before 1970 to a prominent provider of healthcare products, meeting almost 95 per cent of the Country’s pharmaceuticals needs. The Industry today is in the front rank of India’s science-based industries with wide ranging
Capabilities in the complex field of drug manufacture and technology. It ranks very high in the third world, in terms of technology, quality and range of medicines manufactured. The Indian pharmaceutical industry is the world's fourth-largest by volume and is likely to lead the manufacturing sector of India. The number of purely Indian pharma companies is fairly low. Indian pharma industry is mainly operated as well as controlled by dominant foreign companies having subsidiaries in India due to availability of cheap labour in India at lowest cost. In 2002, over 20,000 registered drug manufacturers in India sold $9 billion worth of formulations and bulk drugs. 85% of these formulations were sold in India while over 60% of the bulk drugs were exported, mostly to the United States and Russia.

Most of the players in the market are small-to-medium enterprises; 250 of the largest companies control 70% of the Indian market. The government started to encourage the growth of drug manufacturing by Indian companies in the early 1960s and with the Patents Act in 1970.

**TABLE-2: INDIAN PHARMACEUTICAL MARKET**

<table>
<thead>
<tr>
<th>INDIAN PHARMACEUTICAL MARKET</th>
<th>$12 Bn - Growth - 12.14% per year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Export</td>
<td>4.2 Bn</td>
</tr>
<tr>
<td>Import</td>
<td>905 m</td>
</tr>
<tr>
<td>13th largest in value</td>
<td>4th largest in volume</td>
</tr>
<tr>
<td>100 US FDA Approved manufacture sites</td>
<td></td>
</tr>
<tr>
<td>MNC contribution to Pharma FOR DOMESTIC USE 20%</td>
<td></td>
</tr>
</tbody>
</table>

**TABLE-3: TOP FIFTY PHARMACEUTICAL COMPANIES**

<table>
<thead>
<tr>
<th>Rank</th>
<th>Company Name In 2009</th>
<th>Company Name In 2014</th>
<th>Rank</th>
<th>Company name in 2009</th>
<th>Company name in 2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pfizer</td>
<td>Novartis</td>
<td>26</td>
<td>Baxter International</td>
<td>Celgene</td>
</tr>
<tr>
<td>2</td>
<td>GlaxoSmithkline</td>
<td>Pfizer</td>
<td>27</td>
<td>Servier</td>
<td>Otsuka Holdings</td>
</tr>
<tr>
<td>3</td>
<td>Sanofi-Aventis</td>
<td>Sanofi-Aventis</td>
<td>28</td>
<td>Gilead Sciences</td>
<td>Allergan</td>
</tr>
<tr>
<td>4</td>
<td>Novartis</td>
<td>Roche</td>
<td>29</td>
<td>Mylan Les</td>
<td>Laboratoires Servier</td>
</tr>
<tr>
<td>5</td>
<td>AstraZeneca</td>
<td>Merck</td>
<td>30</td>
<td>UCB</td>
<td>Shire</td>
</tr>
<tr>
<td>6</td>
<td>Johnson &amp; Johnson</td>
<td>Johnson &amp; Johnson</td>
<td>31</td>
<td>Genzyme</td>
<td>Abbott Laboratories</td>
</tr>
<tr>
<td>7</td>
<td>Merck</td>
<td>Glaxo Smithkline</td>
<td>32</td>
<td>Shionogi</td>
<td>Sun Pharmaceutical</td>
</tr>
<tr>
<td>8</td>
<td>Roche</td>
<td>AstraZeneca</td>
<td>33</td>
<td>Ratiopharm Ulm</td>
<td>Industries</td>
</tr>
<tr>
<td>9</td>
<td>Eli Lilly</td>
<td>Gilead Sciences</td>
<td>34</td>
<td>Mitsubishi Tanbe</td>
<td>Valeant Pharmaceuticals</td>
</tr>
<tr>
<td>10</td>
<td>AbbVie</td>
<td>AbbVie</td>
<td>35</td>
<td>Chugai</td>
<td>International</td>
</tr>
<tr>
<td>11</td>
<td>Bristol-Myer Squibb</td>
<td>Amgen</td>
<td>36</td>
<td>Allergan</td>
<td>CSL</td>
</tr>
<tr>
<td>12</td>
<td>Abbott</td>
<td>Teva</td>
<td>37</td>
<td>Forest</td>
<td>Eisai</td>
</tr>
<tr>
<td>13</td>
<td>Bayer</td>
<td>Bayer</td>
<td>38</td>
<td>CSL</td>
<td>UCB</td>
</tr>
<tr>
<td>14</td>
<td>Amgen</td>
<td>Eli Lilly</td>
<td>39</td>
<td>Apotex</td>
<td>Fresenius</td>
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<tr>
<td>15</td>
<td>Meda Novo</td>
<td>Nordisk</td>
<td>40</td>
<td>Nycomed</td>
<td>Chugai</td>
</tr>
<tr>
<td>16</td>
<td>Boehringer Ingelheim</td>
<td>Boehringer Ingelheim</td>
<td>41</td>
<td>Menarini</td>
<td>Menarini</td>
</tr>
<tr>
<td>17</td>
<td>Takeda</td>
<td>Takeda</td>
<td>42</td>
<td>Biogen</td>
<td>Grifols</td>
</tr>
</tbody>
</table>
Indian Pharmaceutical Industry[^10]

**Increasing investments in the sector**

- The Indian pharmaceuticals market increased at a CAGR of 17.46 per cent during 2005-16 with the market increasing from US$ 6 billion in 2005 to US$ 36.7 billion in 2016 and is expected to expand at a CAGR of 15.92 per cent to US$ 55 billion by 2020.

- By 2020, India is likely to be among the top three pharmaceutical markets by incremental.

- India’s cost of production is significantly lower than that of the US and almost half of that of Europe. It gives a competitive edge to India over others.

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**FIGURE-3: Revenue of Indian pharmaceutical sector**

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[^10]: World Journal of Pharmaceutical Research
Generic drugs form the largest segment\textsuperscript{[13-15]}

- With 70 per cent of market share (in terms of revenues), generic drugs form the largest segment of the Indian pharmaceutical sector. India supply 20 per cent of global generic medicines market exports in terms of volume, making the country the largest provider of generic medicines globally and expected to expand even further in coming years.
- Over the Counter (OTC) medicines and patented drugs constitute 21 per cent and 9 per cent, respectively, of total market revenues of US$ 20 billion.

\begin{figure}
\centering
\includegraphics[width=0.5\textwidth]{figure4.png}
\caption{Revenue share of Indian pharmaceutical sub-segments in 2015 (%)}
\end{figure}


\textbf{FIGURE-4-Revenue share of Indian pharma sub segments}

Types of Pharmaceutical Management

\begin{figure}
\centering
\includegraphics[width=0.5\textwidth]{figure5.png}
\caption{PHARMA MANAGEMENT}
\end{figure}
Functions of Pharmaceutical Management

FIGURE- 6 FUNCTION OF PHARMA MANAGEMENT

Functions of Pharmaceutical Marketing

FIGURE- 7 PHARMA MARKETING FUNCTIONS

Process of Pharmaceutical Marketing

FIGURE- 8 PHARMA MARKETING PROCESS
CONCLUSION
This integration is opening up tremendous new opportunities for Indian Pharma across all segments including generics, research and development of New Chemical Entities (NCE) & New Biological Entities (NBE) and Contract Research and Manufacturing Services (CRAMS). Indian companies are now well positioned to explore these opportunities as they adopt effective and efficient business models that are spread across one or more of each of these segments. Regulatory agencies and organizations around the world need to ensure the safety, quality and efficacy of medicines and medical devices, harmonization of legal procedures related to drug development, monitoring and ensuring compliance with statutory obligations. The major challenges of these regulatory bodies are to promote public health and protect the public from harmful and dubious drugs.

To establish proper legalization covering all products with a medicinal claim and all relevant pharmaceutical activities, whether carried out by the public or the private sector. To increase worldwide regulatory growth to ensure safety of people.

REFERENCES


