CHAPTER – 5

RESEARCH AND DEVELOPMENT IN
PHARMACEUTICAL INDUSTRIES

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Chapter 5

RESEARCH AND DEVELOPMENT

5.1. Introduction

Having talked about the price policies and regulations relating to pharmaceutical industry in India and at global level we now talk about Research and Development issues in this sector. This chapter presents and analytically based review of the mechanism of development and nature of drug research along with drug discovery process. Research and development of pharmaceutical companies in India comprises collaborative research, basic drug discovery and development and contract services. (B Rajesh Kumar and S M Satish, 2007)

Due to increasing cost of developing a new drug and risks involved in the process, companies are looking to mitigate risks involved. Such R and D expenses in Indian and global scenario its problems and changes have been discussed. This section two deals with area and process of drug discovery and nature of drug research in second section. Section five explains about emerging R and D activities, section six deals with clinical trials in India and seven describes contract manufacturing. Section eight mentions the R and D expenses. In the concluding section nine major challenges in drug development has been described. The status of R and D in India has been highlighted and pharma market as a global perspective in third and fourth section. Factors and trends of development of Indian pharmaceutical industry have also been discussed. Lastly the policy framework has been summarized.
5.2 Area and Process of Research and Development (R and D)

Basic research involves the discovery/invention of a new medically effective chemical. Basic research involves more time and cost compared to process research. Moreover patents to drug formulations and New Drug Approval (NDA) regulations are other typical characteristic features of the pharmaceutical industry. Hundreds of molecules need to be analyzed to determine possible effectiveness of the drugs. (B Rajesh Kumar and S M Satish, 2007)

Following such laboratory testing, actual clinical trials are then carried out to determine the drug's efficacy on patients. The process thus requires around 12-15 years. It was estimated that this and costs USD350-400 million per new chemical entity. Process R&D is the reverse engineering of a molecule effected through process alterations. In India, the Drug controller of India handles new drug approvals. Normally, clinical trial of a drug involves 3 stages: (B Rajesh Kumar and S M Satish, 2007)

- Animal toxicity (testing on animals);
- Trials on a few select volunteers; and
- Trials on a larger scale in hospitals/institutions.

Research companies are involved in discovery research, generic R&D and new drug delivery systems (NDDS). To facilitate research, companies usually concentrate on select therapeutic areas such as anti-ulcer, anti-cancer etc. Major diseases for which new drugs are continuously being researched globally are AIDS, Alzheimer's disease, arthritis (rheumatism), cancer, depression, diabetes, heart disease, osteoporosis and stroke. The drug research in today's context is a multi-disciplinary activity
encompassing design and synthesis of compounds, bioactivity, screening, toxicity study, pharmokinetic studies, bioavailability etc. Thus, it needs expertise in areas such as medicinal chemistry, molecular modeling, biochemistry, microbiology, toxicology and pharmacology etc. (B Rajesh Kumar and S M Satish, 2007)

5.2.1 The Discovery Process

The process of new drug development is knowledge intensive, time consuming and full of uncertainties. The development process can be broadly divided in two major stages viz., pre-clinical and clinical. The objective of pre-clinical studies is to come up with a molecule that is effective against the disease vector and safe in animal testing. This stage is called the Investigational New Drug (IND) stage. This stage of investigation may take anywhere between 3 to 5 years and cost between USD100-150 million overseas or about Rs.400-600 million in India. (B Rajesh Kumar and S M Satish, 2007)

On satisfactory completion of the pre-clinical studies the dossier on the IND is submitted to the regulatory authorities (the Drug Controller General of India) for permission to study its use in human clinical trials, in Phases of I, II, and III with review at each phase, to ensure efficacy and safety. (B Rajesh Kumar and S M Satish, 2007)

If an Investigational New Drug passes through all these clinical studies the compound becomes a drug that could be marketed. The clinical studies take generally 5 to 8 years and it is estimated to cost approximately USD 300-350 million abroad and around Rs.100 crore in India. (B Rajesh Kumar, S M Satish 2007) Clinical trials need Good clinical Practice (GCP) conforming facilities and expertise of clinicians, clinical pharmacologists and toxicologists & analytical chemists.
5.2.2. Drug Development Process

**Fig 5.1**

Target Validation - Genomics, proteomics, and therapeutic identification.
The discovery process begins with screening of thousands of compounds

Lead Identification - Synthetic and combinatorial chemistry, biotechnology, pharmacology profiling compounds that are active are identified

Lead Optimization - Non-GL Ptoxicology, metabolism, pharmacology. Testing compounds for toxicity and metabolism and their activities in the human body

Developing the lead - Pre-clinical studies GLP toxicology, safety pharmacology, and scale up chemistry. Animal studies and development of chemistry process

Human trials: phase 1

Human trials: phase 2

Human trials: phase 3

Commercialization

Source: Business world, January 23rd, 2006
The various stages of the drug discovery process are explained as follows:

The first step involves the identification of people with disease to cure. The aim is to identify patterns in the human genome that are common to these people. (B Rajesh Kumar and S M Satish, 2007) The objective of drug target leads to finding out the biological functions of these patterns and identify the protein that causes the disease. In the lead optimization, the chemical molecules that can inhibit the disease causing protein is identified. Drug testing involve finding out whether the chemical molecules can be druggable. Clinical trials involve testing the drugs for efficacy and side effects on a population. Drugs that clear clinical trials are ready for use in treatment. (B Rajesh Kumar and S M Satish, 2007)

5.2.3. Nature of Drug Research

Pharmaceutical industry has deep roots in science and technology. Discoveries and developments of drugs along with economic considerations are the guiding factors for Pharmaceutical research and development. (B Rajesh Kumar and S M Satish, 2007)

In the past most drugs have been discovered either by isolating active ingredients from traditional remedies or by chance discoveries. Modern bio-technology often focuses on understanding the metabolic pathways related to disease state or pathogen and manipulating the pathways using molecular biology or biochemistry. Great deals of early stage drug discoveries are from traditional knowledge of herbs and other things commonly available. (B Rajesh Kumar and S M Satish, 2007)

Drug development is also required to establish physico chemical properties of the New Chemical Entities (NCE), its chemical make up stability and solubility. These
properties will determine its suitability to be used as capsules, tablets, aerosol, intramuscular or under the skin injections. Those processes are known in preclinical development as CMC (chemical, manufacturing and control). Once an NCE begins human clinical trials for the first time its long term toxicities are determined as well as effects on various systems (fertility, reproduction immune system etc)

If the compound comes out from the tests with an accepted toxicity and safety profile and it can further be demonstrated to have desired effect in clinical trials, then it can be submitted for marketing approval in various countries where it will be sold. Most NCEs however will fail during drug development, because of high level of toxicity or because of unfavorable results during clinical trials. (B Rajesh Kumar and S M Satish, 2007)

5.3. Status of Research and Development in India

Research is increasingly becoming an area of focus for Indian pharma companies. Indian companies started their drug discovery programs in the 1990s with Dr. Reddy's and Ranbaxy leading as pioneers. (B Rajesh Kumar and S M Satish, 2007) In the early period Indian companies were involved in recognizing lead molecules and out licensing several of them at preclinical stage. Now Indian companies are conducting clinical trials of drugs of their own. On account of the near completion of human genome sequencing projects several disciplines like functional and structural genomics, proteomics, population genetics, bioinformatics became relevant to new drug research. (B Rajesh Kumar and S M Satish, 2007)
A report entitled "Pharma New World View" from IBM Global Business services part of IBM group also mentions that research in India costs about 40 percent less than that in US and developing a new drug can cost one tenth of what it does in the West. This represents a huge opportunity for India. The report further states that by 2035, the emerging nations of Brazil, Russia, India and China are expected to represent 25 percent of the global pharmaceutical market. In India, research spending on life threatening disease is abysmally low. The country has to focus on research and development if it has to occupy global leadership position. (B Rajesh Kumar and S M Satish, 2007)

India could emerge as an offshore location for research and development destination. The Confederation of Indian Industry (CII) opines that Indian firm with weak R&D intensity has to out license development work to their multinational counterparts who are well versed with regulatory processes, clinical trials and registration procedures. According to International Strategy and Management Consulting firm, India would soon become a vital hub in the multinational pharmaceutical firms' global R&D network. India ranks among the top nations for R&D spending by MNCs across all industries. Study by global strategy consulting firm Booz, Allen, Hamilton and France based business school instead said that more than three quarters of the R&D sites to be set up over the next three years would be located in India or China. (B Rajesh Kumar and S M Satish, 2007)

On account of India's new patent regime in the mid-1990s, domestic pharma started investing in drug discovery research. On an average, research oriented domestic pharma companies spend about one third of their R&D expenditure on drug discovery
research. The rest is spent on generic R&D and new drug delivery systems. (B Rajesh Kumar and S M Satish, 2007) Companies that involve in R and D do so in specific areas to target based on the strength in market and commercial potential. The various aspects of research can broadly be as follows:

i.) **Basic R and D**: this involves discovering new a molecule from scratch. It is highly capital intensive and relies on great deal of tests and trials to fully understand the potential of the drug. There are handful of Indian companies that are able to conduct some form of basic research (Ranbaxy and DRC). In the drug development process in any pharmaceutical company a typical product take 7-10 yrs and USD 350-500 million. But the statistics varies greatly with diseased type. (B Rajesh Kumar and S M Satish, 2007)

ii.) **Process research or reverse engineering**: this entails studying the process by which a drug is made and making modifications to the process. Here a company copies the molecule of another company and develops a cost effective method of producing that molecule. This is much less expensive to conduct since it does not need to conduct any discovery research or clinical trial. Till 2005 when the new patent law came into effect this has been the focus of the most Indian players. (B Rajesh Kumar and S M Satish, 2007) Analog or discovery research companies modify existing molecule or a new one that has not been commercialized after accessing international patent database to arrive at a new molecule. Biotechnology research: it aims at establishing the link between ones genes and diseases one has and could determine the best drug for a individual based on ones genetic maker.
iii. Bringing out a generic drug: Bringing a generic product to the market requires equivalency tests to the product already in existence in market. It is much cheaper and takes less time. This process is known as ANDA (Abbreviated New Drug Application) process.

iv. NDDS research: NDDS (New Drug Delivery System) is delivering existing drug in a novel method. Indian companies are looking to research NDDS way to new drugs being developed. This takes about 3 yrs at a cost of between USD 10 and 20 million. An NDDS can fetch a patent if it is a new concept and if it is an improvement, it can give market exclusivity for 3 years in US. It has been observed earlier that drug discovery and delivery process require about 40-50% cost than compared with the same in developed countries. In order to make investments in India as R and D destinations more attractive the following measures are being contemplated:

- Attractiveness for Investment in India as R&D Destination
- Hundred percent foreign equity investments is automatic in the drugs and pharma sector and over 74 percent is on case to case basis.
- Fast track clearance route for foreign direct investment.
- Depreciation allowance on plant and machinery set up based on indigenous technology.
- Customs duty exemption on goods imported for use in government funded R&D projects.
- Customs and excise duty exemption to recognized scientific and industrial research organizations (SIROs).
- One hundred and fifty percent weighted tax reduction on R&D expenditure.
- Three years excise duty waiver on patented products.
5.3.1 Pharmaceutical Market: (Global Perspective)

Pharmaceutical Products consist of two main components – the active pharmaceutical ingredients (API) or bulk drug and the formulation, i.e. the suitable final dosage form. Generally APIs are either produced by chemical synthesis or of plant, animal or biological origins. (Prasad BVS, 2008) Patents are critical aspects in the development and marketing of Pharmaceutical products. A patent can be obtained for new drug molecules, a new indication for an existing drug molecule or for a new drug delivery system of an existing product. Usually product patent life is 20 years in all countries. If drug development and market approval takes about 10 years, a pharmaceutical company gets about 10 yrs to market the formulation. (Prasad BVS, 2008) The excessive high cost of drug development forces drug prices to remain high while the drugs are protected by patents. Not every project does yield in marketable products, so successfully marketed product must cover costs incurred for failed projects.

The current Pharmaceutical market value in 2006 at a global level was more than 608 USD billion USD (Prasad BVS, 2008). The major contributing regions are United States, Japan and Europe. Drug prices vary from country to country. Citizens of developing countries cannot afford expensive medicines those are under patent. Multinational companies (MNCs) must either choose to sell a product at a low price in these countries or face the challenges of piracy or parallel trade. Naturally different types of medication are necessary for treatment of these diseases. The drugs need to be
developed through research will naturally be costly and may not be easy to market in relatively poor countries. This may be one of the reasons why MNCs are reluctant to research and develop new products.

5.4. Trends towards Research and Development

The total world market of pharmaceutical product of the order of USD 500-600 billion and the developed countries spent around 18-20% in research and development whereas the Indian pharmaceutical market is about USD 4-6 billions and total expenditure in R and D is 1.5-2% of the total sales which is considerably low compared to international standards and total fund available for R and D is very less (Prasad BVS, 2008). This is reflected in the number of new molecules discovered in developed nations.

India is making efforts to develop modern technology in Pharmaceutical industry. The major task is to promote R and D, that is at par with the technology of other advanced countries. Basic needs for the development of the Pharmaceutical sector are funds, infrastructure, R and D management and human resources. The Indian government is encouraging private and public sectors as well as foreign investors to increase investment in R and D.

Some positive steps taken by Indian Government in recent years include: (Prasad BVS, 2008)

- recognition of Pharmaceutical industry as a knowledge based industry.
- reduction of interest rates for export financing
- additional tax deduction for R and D expenses.
- reduction of price control for Pharmaceutical
The Indian Pharmaceutical Industry (IPI) seeking to take full advantage of benefits offered by the government has been allocating money to R and D. The focal point are drug discovery, development of drug delivery system, biotechnology and bio-informatics. Companies are reevaluating their strength and concentrating on product segments those are profitable to the company. Many companies are trimming their portfolios to focus on particular therapeutic segments. (Prasad BVS, 2008)

Pharmaceutical marketing is also changing rapidly and companies are making elaborate marketing efforts. Companies like Sun Pharma, Nicholas Piramal and Dr Reddy’s Lab have opted for brand/company acquisition to increase therapeutic reach and market penetration. Such specialization would make the entry of MNCs difficult. Another opinion is that companies with strong marketing force would be attractive for possible take over. Many Pharmaceutical companies are entering into marketing arrangements. Examples are Hoechst Marions agreement with Nicholas Piramal and Ranbaxy’s pact with Cipla. Nicholas Piramal acquired Roche products, a company mainly involved in diagnostic products and Zydus Cadila acquired German Remedies in India. (Prasad BVS, 2008)

5.4.1. Factors related to positive development of Indian Pharmaceutical Industry (IPI)

The Patent Act and Drug Control order of 1970s forced MNCs to shrink their operations in India. As a result, in the past two decades domestic pharmaceutical companies have established operations and are self sufficient in all aspects. For example Cipla Ltd could provide the generic version of AIDS triple cocktail to improvised South African people at USD 350 per patient per year to at a price that is
one-thirteenth its cost in the US. (Prasad BVS, 2008) Indian patent laws allowed local companies to set up operations to produce generic drugs. The prevalence of reverse engineering is controversial, but it suggests that IPI chemists have a strong showing in organic/medicinal chemistry. Indian Pharmaceutical Industry (IPI’s) tremendous potential to produce bulk drugs will be major asset in future drug discovery programmes.

Any pharmaceutical industry needs people from fields of organic chemistry, biotechnology, pharmacology Pharmaceutical science etc. With very well developed and diverse education system, India produces students who can meet these requirements. Computers are increasingly being used in pharmaceutical industry. Thus collaboration between the computer and pharmaceutical industries will help drug discovery and development programmes. The presence of ayurvedic, siddha, unani systems would also provide a vast resource for the drug discovery programmes.

The share of IPI in world market is about 1-2%. Even if 2.5-3% of gross sales are invested in R and D, the IPIs total R and D budget is very small. Individual R and D budget of many US companies probably amount to much more than the cumulative R and D budgets of all companies in India. (Prasad BVS, 2008) Thus availability of funds is a major constraint. Every new drug molecules must be screened using animals first to determine its efficacy, side or toxic effects. Animal rights activities in many cases block the use of animals in R and D experiments. In such case IPI will be forced to turn to other countries for animal studies. The animal right activists are to be informed adequately so a balance can be struck between animal rights and human rights.
Indian regulatory system overlook drug discovery development and delivery system need to be paced up so that delays in approval processes may be avoided. The value of pharmaceutical market in India was USD 6.0 billion in 2004, representing 2% global market, ranking fourth in terms of volume and thirteenth in value terms. The industry is active in the worldwide market for generic and leadership in formulations making the country is self sufficient in most drugs. The development of bulk drugs sector, is actually most important achievement of the pharmaceutical industry in India. (Prasad BVS, 2008)

These are four main factors that helped Indian pharmaceutical manufacturers to emerge as important generic products. The Indian Patents Act of 1970, which has been (enforced since 1972 till Dec 31, 2004). As per this act the Indian parliament granted patent rights only to manufacturing process, rather than to end products were not recognized. Indian pharmaceutical firms were able to take advantage of new patent laws. Patented drugs developed abroad were reverse engineered the manufacturing process and began to produce generics. This helped the local firms to control 30% Indian drug market in 1972 and 77% in late 2004. Due to low prices and quick introduction of the latest wonder drugs IPI could benefit developing world consumer’s and even some western countries. (Prasad BVS, 2008)

The cost of developing a drug from scratch in India could be as low as USD100 million while it would be up to USD 1 billion in West. In other words Indian industries have a significant cost advantage over firms in developed countries. Skilled work forces with strong chemistry skills are available in India. India has the largest number of FDA approved manufacturing plants outside the USA. Until 1988, the
industry was experiencing a negative trade balance. The trade balance turned positive since 1989 onwards; indicating that the country was self sufficient in most drugs and pharmaceuticals. Indicating countries growing technological contribution in this industry. (Prasad BVS, 2008)

5.4.2. Growing contract research

Growing technological capabilities in India and other developing nations can lead to further collaboration in R and D and clinical research between advanced nations and developing countries particularly with India in two areas. First is the R and D outsourcing by western MNCs and second is the growth of clinical trials. Alliances in local companies, contractual outsourcing arrangements and establishing local subsidiaries are good options for enterprises, thinking the strong intellectual potential in India and other developing countries. These outsourcing, activities in developing countries amount to 20 to 30 percent of total global clinical trials. (Prasad BVS, 2008)

Recently, Indian government has amended schedule of drugs and cosmetic regulations of India 1945. This progressive attitude has helped in the environments for clinical research in the country and to attain international standards in pharmaceutical research. Executives of large and small pharmaceutical and bio-tech companies are becoming intrigued with India and they are eager it to launch high quality products for a quicker and efficient manner. While the global pharmaceutical companies are increasing their clinical trial investments in India, many small and big regional companies are considering India in their drug development initiatives. Cost effectiveness, competition and increased confidence in capabilities and skills have prompted many global pharmaceutical players to expand their own clinical research
investments and infrastructure in India. While global pharmaceutical companies and contract research organizations (CRO) are opening up their branches/offices, the small biotech pharmaceutical and R and D companies are looking for preferred partners to conduct their research activities in India. (Prasad BVS, 2008)

The country can accommodate these business expansions because of availability of huge talent pool of investigators and clinical research professionals. India's growth in pharmaceutical bio-technology manufacturing and contract research supported by IT skills has led to promising outsourcing business in various other segments including clinical trial data management and statistical analysis. We have new policy in place since 2006. We now enlist some features of this policy in the next section.

5.4.3. Overall policy framework

The policy draft national Pharmaceutical policy 2006 was necessitated due to several developments during the post reform years. A Price regulation of the essential medicines is an important component of this policy. Since the areas relating to R and D are dealt here, the major policy initiatives in this area are summarized below:

- promotion of Pharmaceutical R and D through the provision of fiscal incentives
- promotion of R and D intensive companies
- Establishment of Pharmaceutical R and D development support
- Development of orphanage drugs
5.4.4. Fiscal incentives for R and D

1.) The fiscal incentives enumerated in Draft National Pharmaceutical Policy 2006 for fiscal incentives for R and D activities

(a.) The benefit of 150% weighted exemption (under section 35(2AB) of Income tax Act of 1961, is to be continued till March 2015.
(b.) This extension is to be extended to depreciation on investment made in land and building for dedicated research facilities, expenditure incurred for obtaining regulatory approvals and filing of patents abroad and expenditure incurred on clinical trials in India.
(c.) Reference standard (sample under test) would be exempted from import duty.
(d.) reference books to be imported for R and D would be exempted from duty.
(e.) Presently there are 101 specified instruments (list 28) required for R and D purpose which are exempted from import duty.

Any other new instrument under certification of Department of Science and industrial research (DSIR) would also be exempt from import duty.

2.) R and D intensive companies

There are some R and D intensive companies fulfilling certain conditions should be given some price benefit for the drugs under Drug Price Control Order (DPCO). The norms under which benefit are to be obtained are

(a.) invest at least 3% of annual sales from over on R and D activities or Rs 500 million per year (average of 3 yrs) which ever is higher on research facilities.
(b.) Employment of at least 200 scientists in India (M.Sc or Ph.Ds employed at least for one year)

(c.) Own and operate manufacturing facilities in India which have been approved by at least two foreign regulatory agencies (US, Europe, Japan, Canada, Australia, Israel, South Africa etc)

(d.) Have filed at least 10 patent applications in India, based on research done in India. Companies fulfilling the above norms would be eligible for the benefit of 200% weighted deduction under 35 (2AB) till 31st March 2015

3.) The Pharmaceutical R and D support fund (PRDSF): At present PRDSF has a corporation of Rs 1500 million (where only interest earning is available for spending) is utilized for funding R and D projects of research institutes and industry in country. It is not adequate to meet the present day and emerging needs of this segment. It has been decided to convert in to annual grant of Rs 1500 million. Priority would be given for R and D in case of diseases which are endemic to India, like malaria, tuberculosis, hepatitis B, HIV/AIDS etc.

4.) Development of orphaned drugs: The central Drug research Institute (CDRI) has over the time developed a number of drug technologies, which could not be commercially produced and marketed. Such technologies could be perfected with a view to enable them to reach the market. The new draft policies have also two new initiatives. They are:

(a.) abolition of industrial licensing for bulk drugs, intermediates and formulations, and
5.) Research Institutes: connected with R and D of Indian Pharmaceutical companies expended, nearly two thirds of total contribution by the industry and the remaining by the Government Research Institutes, primarily under the management of council of scientific and industrial research (CSIR). Central Drug Research Institute, contributed a major share of the small number of new drugs developed by Indian inventors. CDRI is considered to be one of the few public sector organizations in the world which has its own drug development infrastructure. Over the years it has developed and licensed ten new drugs to other private sector companies. Of course most of these have to face strong competition from MNCs. Apart from CDRI, the CSIR administration has other laboratories which are engaged in some form of Pharmaceutical research.

TABLE 5.1. FOREIGN AND INDIAN PATENTS GRANTED TO CSIR AND OTHER GOVERNMENT LABORATORIES ENGAGED IN DRUG RESEARCH 2003-04

<table>
<thead>
<tr>
<th></th>
<th>India</th>
<th>Foreign</th>
</tr>
</thead>
<tbody>
<tr>
<td>CDRI</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>CIMAP</td>
<td>7</td>
<td>29</td>
</tr>
<tr>
<td>IICP</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>IICT</td>
<td>24</td>
<td>39</td>
</tr>
<tr>
<td>Total for 4 above</td>
<td>42</td>
<td>78</td>
</tr>
<tr>
<td>Total for CSIR</td>
<td>275</td>
<td>212</td>
</tr>
</tbody>
</table>
Four of this research institutes under CDRI camp have contributed to above one fourth of patents obtained by CSIR laboratories till 2003-04. (Prasad BVS, 2008)

5.5. The Emerging Research and Development Collaborative Opportunity

Major drug companies started involving into drug research by 1997. Dr. Reddy's Research Foundation in the late nineties started research in medicinal chemistry based at Hyderabad. Reddy's Therapeutics based in US was into high throughout screening and target discovery. The other Reddy's group was into early drug discovery proteomics. Molecular Connection was into bioinformatics research. (Mani Sunil, 2006)

A pharmaceutical major like Nicholas Piramal has already invested USD20 million in researches and development facility and the company has carried out three contract researches. (Mani Sunil, 2006) Ranbaxy have collaboration with GlaxoSmithKline in the area of drug discovery and development. The company has also entered into an agreement with (MMV) Geneva for development of anti-malarial drugs. The Indian arm of Pfizer's clinical research wing is in the process of identifying and evaluating CROs in India. Most Contract Research Organizations are focusing on chemistry, protein, and drug discovery, toxicology screening and clinical fields.

The existing value of contract research in India is close to USD 75 million and is expected to grow manifold to USD2 billion in the coming 10 years. (Mani Sunil, 2006) During the year 2003-04, the export revenue from bioservices in India grew at a rate of 117.4 percent. According to a study by Cygnus Research, contract research
mainly bioservices contributed 13.6 percent of the total industry export revenue of
USD18.17 billion during the period 2003-2004. Astra Zeneca started a major drug
discovery programme on tuberculosis with an initial investment of $10 million and an
additional investment of USD 5 million every year. (Mani Sunil, 2006)

5.5.1. Strategies of Drug Discovery Adopted by Indian Companies

No Indian company has the scale or resources to pursue cutting edge research
involving all stages of drug discovery though the cost of conducting research are
lower in India due to the availability of the cheaper scientific manpower. . (B Rajesh
Kumar and S M Satish, 2007) Indian firms aim to pursue the two basic strategies of
analogue research and out licensing that optimizes the cost and risks. In analogue
strategy, firms will not pursue to find a completely new family of drugs. The research
will be focused at finding a new drug within an existing family that has already been
discovered. This strategy is called analogous because it involves finding a compound
that is analogous to an already discovered compound.(B Rajesh Kumar and S M
Satish, 2007)

The significance of analogous strategy is that it cuts down cost. By focusing on
protein target that are already well established and developing a new drug within a
family which had undergone extensive research, the uncertainties surrounding drug
research can be reduced to a greater extent. But the negative aspect is that the new
drugs developed by this process will not be a big blockbuster as the first drug in the
new family. But an exception to the trend also exists. Pfizer's cholesterol reducing
drug Lipitor was not the first drug in its class to hit the market, but became the best
The analogue strategy was very successfully used by the Japanese drug industry.

The strategy of out-licensing involves licensing the promising compound to a multinational company. An Indian company identifies a number of new compounds in a family that are likely to work and further takes them up to the pre-clinical trial phase. Then the compound is out licensed to a multinational for further development with the condition that the multinational company will have the exclusive rights to market the drug if it succeeded. The multinational company would have to bear the costs of testing. The MNC also have to pay milestone payments a certain amount to the compound discoverer when the compound crosses each stage of clinical development. (B Rajesh Kumar and S M Satish, 2007)

The multinational company's preference for in-licensing a compound from an Indian company can be attributed to the high levels of failure in the new drug development scene. For every 1000 compounds that are identified by a company only 30 cross the barriers. On an average only three compounds get past the first round of clinical trials and finally one reaches the aim. Hence the concept of licensing is gaining prominence. Multinationals in addition to their own compounds under development, scouts for promising compounds developed by other companies in therapeutic areas and then takes these compounds for clinical trials. (B Rajesh Kumar and S M Satish, 2007)

A list of drugs discovered by some leading Indian pharmaceutical companies are given below along with the status of development.
<table>
<thead>
<tr>
<th>Company</th>
<th>Category</th>
<th>No. of Promising Compounds</th>
<th>Stage of Development</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dr. Reddy's</td>
<td>Cardiovascular diseases, Diabetes and cancer</td>
<td>37</td>
<td>9 in Phases I and II</td>
</tr>
<tr>
<td>Ranbaxy</td>
<td>Infectious respiratory and urinary diseases and diabetes</td>
<td>11</td>
<td>2 in Phase I</td>
</tr>
<tr>
<td>Orchid</td>
<td>Inflammatory and infectious diseases, cancer and diabetes</td>
<td>8</td>
<td>3 in Phases I and II</td>
</tr>
<tr>
<td>Glenmark</td>
<td>Respiratory and inflammatory diseases, diabetes and cancer</td>
<td>6</td>
<td>4 in Phases I and II</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Company</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ranbaxys Lab</td>
<td>RBx9841, Overactive bladder</td>
<td>RBx11160, Malaria! infection</td>
<td>Search for outlicensing deal opportunity for RBx 9841. The company has tied up with Medicines for Malaria Venture to develop RBx 11160</td>
</tr>
<tr>
<td>Dr. Reddy's Lab</td>
<td>DRL 11605 Metabolic disorders</td>
<td>DRF 2593 Metabolic disorders</td>
<td>DRL licensed DRF 2593 to Rheoscierce in 2004. The molecule is to enter Phase III RUS 3108 and DRF 10945 were transferred to Perlecan Pharma. DRL's integrated drug development company set up in 2005</td>
</tr>
<tr>
<td>Wockhardt</td>
<td>WCK 1152 Respiratory infections</td>
<td>WCK 771 MRSA Resistant Infections</td>
<td>Trying for a foreign partner to develop its NCE</td>
</tr>
<tr>
<td>Nicholas Piramal</td>
<td>P276 Oncology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lupin Labs</td>
<td>LL4218 Anti-psoriasis, LL4858Anti TB</td>
<td>LL3348 Anti-psoriasis, LL2011 Anti-migraine</td>
<td>Scouting for foreign partnership</td>
</tr>
<tr>
<td>Orchid Chemicals</td>
<td>BLX1002, Antidiabetes</td>
<td></td>
<td>Searching for outlicensing opportunity</td>
</tr>
<tr>
<td>Glenmark Pharma</td>
<td>GRC 3886, Asthma COPD</td>
<td></td>
<td>GRC 3886 was licensed out to Forest Lab for the US market and to Teijin Pharma for a partner.</td>
</tr>
<tr>
<td>Dabur Pharma</td>
<td>DRF 7295 Oncology</td>
<td>TNP Oncology</td>
<td>Scouting for foreign partnership</td>
</tr>
<tr>
<td>Sun Pharma</td>
<td></td>
<td></td>
<td>The company hived off its R&amp;D including its NCE to a new company independent entity called Sun Pharma Advanced research company SPARC</td>
</tr>
</tbody>
</table>

5.6. Clinical Trials in India

India is fast emerging as the hotbed of clinical research. Clinical Research Organisation (CROs) doubled their turnover from USD 5 billion in 1997 to $10 billion in 2002. (B Rajesh Kumar and S M Satish, 2007) The turnover is expected to reach USD 50 billion by 2010. Clinical testing have immense potential as world's top pharma companies are set to focus on the multi billion dollar industry. Globally clinical research was estimated to be a $10 billion industry by 2010. According to McKinsey &c Company 2005 estimated by 2010, global pharma majors would spend up to USD 1.5 billion on drug trials in India. (B Rajesh Kumar, S M Satish, 2007) A Rabobank India report states that India has the largest pool of patients in many categories of diseases like cancer and diabetics. The study also opines that the biggest advantage is with respect to cost. For example, trials for a standard drug in the US can cost up to USD150 million but the same drug can be tested at less than half that amount in India. (B Rajesh Kumar and S M Satish, 2007)

Thus development outsourcing is an attractive area. Around 25 contract research organization (CROs) and almost all multinational pharma companies have started full-fledged clinical trials in the last three years due to lower costs, reliable trials and large patient pool for various diseases. The demand for clinical services in India is growing at almost 100 percent per year. The amendment to Schedule Y of the drugs and Cosmetic Act now allows MNCs to conduct simultaneous trials in India and abroad. Worldwide the average cost of developing one molecule cost about USD 282 million and takes about seven years to complete. (B Rajesh Kumar and S M Satish, 2007)
The growth of clinical trials will have greater impact on the Indian health system. It will improve the record keeping in Indian hospitals especially of patient history. The Indian medical institutions by virtue of association with new drug discoveries will get international recognition as their findings are reported in reputed medical journals. Patients suffering from diseases that have no cure will get opportunity for treatment with the latest drugs that in the normal course would take years to reach the market. In a strategic perspective, the availability of specialized firms for clinical research will reduce the commercial drug development cost which would facilitate the Indian companies to pursue drug patent strategy for growth. With respect to competitors like China, Indian clinical methods are similar to West.

The biggest driver of clinical research is the emergence of Contract Research Organization (CROs) that adhere to ICH norms. About 122 trials are conducted in India. The large native population pool, various disease profiles and robust infrastructure are factors which make Indian as an attractive destination. GlaxoSmithKline conducts the maximum number of clinical trials in India for diseases like cancer, arthritis, epilepsy, heart disease, constipation or vaccines. These trials include Phases II, III as well as Phase IV clinical drug trials. The second position belongs to Astra Zeneca which is having nine investigation centres in India out of 186 clinical trials worldwide. (B Rajesh Kumar, S M Satish, 2007)

The trials of Astra Zeneca in India are for diseases like schizophrenia, bipolar disorder, cancer, diabetes and testotoxicosis. The emergence of developing countries as a hotspot for clinical trials can be attributed to the cost and time involved for the drug development process. The clinical trials on human which is a critical phase in
new drug development account for 40 percent of the total cost. Clinical trials in India, for instance cost 50 percent to 60 percent less than the average cost in US. Time is also a crucial factor for pharma companies. (B Rajesh Kumar and S M Satish, 2007)

A patent will last only for 20 years starting from the moment when the drug is discovered and approved for clinical trials. More than half of the time would have been already gone by the time trials are over and the drugs are finally marketed. Clinical trial itself can last up to ten years. In Western countries it is difficult to recruit patients quickly. Patients enrolled in clinical trials are not financially compensated. The health expenses are almost entirely covered by the government in European countries. Similarly in US patients are covered by health insurance policies. Most clinical trials conducted in emerging economies are multi locations studies.

5.6.1. Worldwide Clinical Trials - A Perspective

The escalating research and developing costs compel global companies that are increasingly considering low cost options in developing and emerging economies for clinical research outsourcing. (B Rajesh Kumar and S M Satish, 2007) In US, 8.9 percent of clinical trials registered with US health authorities are conducted in emerging countries of Asia, 7.4 percent are conducted in Latin America, 7.1 percent in Central and Eastern Asia and 1.6 percent in Africa. Mexico with 429 clinical trials stands out as the most attractive destination for clinical trials, followed by Taiwan with 402 trials and Poland with 200 trials. Lebanon and Brazil accounts for 193 and 161 trials respectively. (B Rajesh Kumar and S M Satish, 2007)
5.6.2. Drug Discovery Services — Contract Research and Manufacturing Segment

The services that actually support the process of discovering new drugs and testing their efficacy is called drug discovery research outsourcing. A contract research organization that handles all the complex aspects of clinical trials prepares the protocols; recruits investigators, forms the ethics committee, monitor the project and manage the database. The Indian industry has witnessed a growth in the amount of clinical trial data over the last decade. (B Rajesh Kumar and S M Satish, 2007)

The ageing population in the West is straining healthcare budgets. Hence, American and European governments are looking for cheaper generics and low cost drugs. Moreover, with the expensive nature of new drug development, pharma companies cannot sustain large R&D spending unless new blockbusters are developed cheaper. In this scenario, the Indian outsourcing and CRAMS fits into the global scenario. (B Rajesh Kumar, S M Satish, 2007)

5.7. Contract manufacturing - Growth perspective

Many Indian companies have turned to contract manufacturing to maintain high growth using their expertise in process research and development mainly reverse engineering. This strategic alternative of contract manufacturing seems viable in the context of huge investment in discovery research. Along with contract research, this avenue will ensure that these companies will be able to leverage their research and manufacturing capabilities and expand business in Indian and abroad. Contract
manufacturing, also known as third party, or toll, manufacturing, is not an entirely new activity for the Indian pharma industry. Most large Indian companies have been farming out production of bulk 'actives' and formulations to third parties (mainly small scale units) in order to circumvent the rigid Drug Price Control Order. (B Rajesh Kumar, S M Satish, 2007)

During the past decades, the trend for outsourcing pharmaceutical products like bulk drugs, drug intermediates, and formulations by multinational drug giants has gained momentum. Companies on account of shifting the focus to high-end value-added operations like marketing have handed over not so lucrative manufacturing tasks to outsiders. Some of the companies that

<table>
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<tbody>
<tr>
<td>Global outsourcing opportunity for pharma &amp; biotech industry</td>
<td>100</td>
<td>168</td>
</tr>
<tr>
<td>Contract manufacturing services for prescription drugs</td>
<td>26.2</td>
<td>43.9</td>
</tr>
<tr>
<td>Contract manufacturing services for over the counter drugs (OTQ)</td>
<td>71.2</td>
<td>100</td>
</tr>
<tr>
<td>Contract research services</td>
<td>14.5</td>
<td>21.9</td>
</tr>
<tr>
<td>Drug discovery outsourcing</td>
<td>4.1</td>
<td>7</td>
</tr>
<tr>
<td>Clinical research outsourcing</td>
<td>9.57</td>
<td>Not Available</td>
</tr>
</tbody>
</table>

outsource aggressively American Home Products, Bristol Myers Squibb, Glaxo Wellcome, Merck, Hoechst Marion Roussel, Novartis, Pharmacia and Upjohn, and SmithKline Beecham. A local subsidiary like Glaxo India is producing ranitidine bulk for Glaxo Wellcome. The shift of bulk manufacturing from Western Europe and the US to India and China is the latest trend due to their inherent advantages, such as low-cost manufacturing, easy availability of qualified workforce and lax environment laws that favour investment in these two countries.

5.8. Research and Development Expenses of Indian Pharma companies

India’s total annual R&D spend of USD 3.15 billion is less than the annual R&D budgets of corporations like Ford (USD 7.4 billion) and GM (USD 6.2 billion). India currently spends only 0.8 percent of its GDP on R&D. (B Rajesh Kumar and S M Satish, 2007) Compared to the global pharmaceutical industry; Indian R&D expenditure is still minuscule, which could have a negative effect in the long run, especially in the era of patent enforcement.

Most of the Indian companies are spending 6-7 percent of their revenues on research and developments compared to the global spend of 12-15 percent of revenues. In 2001, research-oriented pharma companies worldwide invested USD 30.5 billion in R&D which was 18.7 percent higher compared to the year 2000. Typically one of four NCEs that enter clinical trials is finally commercially produced. Moreover only 30 percent of the markets NCEs are able to recoup or exceed the minimum development cost of USD 200 million. The cost of developing new drug has tripled in the last one and half decade to over USD 700 million. Globally, over the last thirty years the
resources allocated to R&D as a percentage of sales have shot up from 11.4 percent in 1970 to 18.5 percent in 2001. (B Rajesh Kumar and S M Satish, 2007)

The increase in R&D expenses of pharma majors had an impact on its net profit. Dr. Reddy's net profit fell by 90 percent to Rs.40 million from 592 million when R&D investment grew by 37 percent to Rs.705 million from Rs.516 million during the period October-December 2004. Ranbaxy doubled R&D expenditure from Rs.565 million in October December 2003 to $26 million in the year 2004 while net profit stood at Rs. 1565 million down from the previous year's Rs.1758 million. Lupin had also raised its R&D spends from Rs.99 million to over Rs.180 million, while the net profits dipped from Rs.400 million to Rs.245 million. (B Rajesh Kumar and S M Satish, 2007)

**TABLE 5.5: TOP R&D SPENDERS IN DOMESTIC PHARMA INDUSTRY – 2006**

<table>
<thead>
<tr>
<th>Company</th>
<th>R&amp;D Spend on Current Account</th>
<th>R&amp;D as Per of Sales</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ranbaxy's Lab</td>
<td>492.5</td>
<td>9.49</td>
</tr>
<tr>
<td>Dr. Reddy's Lab</td>
<td>234.1</td>
<td>9.45</td>
</tr>
<tr>
<td>Sun Pharma</td>
<td>155.1</td>
<td>8.94</td>
</tr>
<tr>
<td>Cipla</td>
<td>120.5</td>
<td>3.87</td>
</tr>
<tr>
<td>Lupin</td>
<td>98.9</td>
<td>5.65</td>
</tr>
<tr>
<td>Cadila Healthcare</td>
<td>81.7</td>
<td>5.42</td>
</tr>
<tr>
<td>Wockhardt</td>
<td>79.8</td>
<td>5.65</td>
</tr>
<tr>
<td>Nicholas Piramal</td>
<td>77.5</td>
<td>4.59</td>
</tr>
<tr>
<td>Torrent Pharma</td>
<td>56.4</td>
<td>5.47</td>
</tr>
<tr>
<td>Aurobindo Pharma</td>
<td>39.8</td>
<td>2.35</td>
</tr>
<tr>
<td>Total</td>
<td>1436.2</td>
<td></td>
</tr>
</tbody>
</table>


Pharma major Wockhardt have increased its R&D spend to around 1250 million from April 2005. This will constitute around 8.5 to 9 percent of the total sales. The company would spend the amount the amount for new drug discoveries, novel drug delivery system and reverse engineering process. In the fiscal year 2004-05, the
company had spent around Rs.850 million for R&D on total sales of Rs.2880 million. (B Rajesh Kumar, S M Satish, 2007) Strides Arcolab the specialty pharmaceutical company has dedicated Strides Technology and research centre to house research facilities of its foreign partners, pursuing research on non fringing process and new drug delivery system under one proof.

### TABLE 5.6: R AND D SPEND BY MAJOR PHARMACEUTICAL COMPANIES IN INDIA

<table>
<thead>
<tr>
<th>Year</th>
<th>USD m</th>
</tr>
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<tbody>
<tr>
<td>1976-77</td>
<td>10.15</td>
</tr>
<tr>
<td>1978-79</td>
<td>12</td>
</tr>
<tr>
<td>1979-80</td>
<td>14.75</td>
</tr>
<tr>
<td>1981-82</td>
<td>29.3</td>
</tr>
<tr>
<td>1983-84</td>
<td>40</td>
</tr>
<tr>
<td>1984-85</td>
<td>48</td>
</tr>
<tr>
<td>1986-87</td>
<td>50</td>
</tr>
<tr>
<td>1991-92</td>
<td>80</td>
</tr>
<tr>
<td>1992-93</td>
<td>95</td>
</tr>
<tr>
<td>1993-94</td>
<td>125</td>
</tr>
<tr>
<td>1994-95</td>
<td>140</td>
</tr>
<tr>
<td>1995-96</td>
<td>160</td>
</tr>
<tr>
<td>1996-97</td>
<td>185</td>
</tr>
<tr>
<td>1997-98</td>
<td>220</td>
</tr>
<tr>
<td>1998-99</td>
<td>260</td>
</tr>
<tr>
<td>2001-02</td>
<td>97.77</td>
</tr>
<tr>
<td>2001-02</td>
<td>130.51</td>
</tr>
<tr>
<td>2002-03</td>
<td>175.3</td>
</tr>
<tr>
<td>2003-04</td>
<td>280.01</td>
</tr>
<tr>
<td>2004-05</td>
<td>392.37</td>
</tr>
<tr>
<td>2005-06</td>
<td>495.19</td>
</tr>
<tr>
<td>2006-07</td>
<td>1430</td>
</tr>
<tr>
<td>2008-09</td>
<td>930.22</td>
</tr>
<tr>
<td>Average (76-2009)</td>
<td>234.80</td>
</tr>
<tr>
<td>Std Deviation (76-2009)</td>
<td>323.78</td>
</tr>
<tr>
<td>Average (2001-9)</td>
<td>491.42</td>
</tr>
<tr>
<td>Std Deviation (2001-9)</td>
<td>434.9</td>
</tr>
</tbody>
</table>

Source: CMIE, 2010
Till 1999-2000 in the Table: 5.6 there is a increasing trend in R and D activities. In 2001 there is sudden fall beginning from 2001 which again picked up in 2003-04 onwards. This relate to changes in the patent laws in India and WTO insistence of acknowledging the patent laws in the developed countries. The resurgence in R and D activities from 2003-04 onwards can be attributed to industries innovative skills circumventing the patent law restrictions insisted by WTO. In an era of development the input towards R and D are expected to be not so uniform hence high variation as denoted by the standard deviation figures are expected to be normal. We expect to get less variation in prereform and more variation in post reform. The standard deviation figures given in Table 5.6 evince this.

5.9. Challenges in drug Development process

As mentioned earlier drug development is a difficult process. It takes about USD 400 million (Rs. 1,682 crore) for a drug from its conception to market of which USD 80 million (Rs.340 crore) is spent on discovery and USD 320 million on clinical trials. But the average revenue per drug is only USD 265 million in its lifetime. More than 90 percent of the new drugs generate sales of less than USD 180 million. About 2/3rd never get any return on investment. It takes about 13 years after filing a patent to get a drug out into the market. (B Rajesh Kumar, S M Satish, 2007) Traditionally this process takes many years and guarantees no outcomes as most new compounds fail the screening process.

Now the pioneers like Dr Reddys Lab and Ranbaxy has been investing in new drug discovery for about a decade. But there isn't a single new drug from an Indian company. Globally, about one in 10 drugs undergoing research will see the light and it
takes about 10-15 years to do so. It is common to expect that a drug may fail. There could be a number of reasons for failure. It may be due to strong side effects or existing better alternatives.

The potential market size may not justify the resources needed to develop drug. Thus there is no single reason on why drugs fail. For the next three to four years no new drug is expected from Indian firms. The number of new drugs approved by the USFDA is down from 53 in 1996-1997 to 21 in 2003-04. Hence, the global picture is also not that attractive. (B Rajesh Kumar and S M Satish, 2007) As per one estimate, nearly 30 percent of drugs sold by big MNCs are licensed. The global failure rate is a little over 40 percent at the pre-clinical stage, rising up to 50 percent during the Phase I, going up further to 70 percent in Phase II and reducing to about 47 percent by Phase III. . (B Rajesh Kumar and S M Satish, 2007)

Drug discovery and drug development are the prerogative of big companies of the developed world because of the enormous cost of development. According to McKinsey Quarterly (August 2004) in clinical trials, it has been observed that the cost involved in acquiring licensed compounds would be far lesser compared to the process of developing the compound internally by the company. The cost saving could be about in the range of USD 1-$9 million. The licensed compounds are found to be twice successful in clinical trials compared to in-house developed compounds. Big pharma companies have steadily increased R&D spending to over USD 30 billion (Rs. 1, 32,000 crore) every year up from $2 billion (Rs.8, 800 crore) in 1980. Studies estimate that pre tax cost of developing a new drug to be USD 800 million which is about six fold increase in 25 years. One study points out that only about 3 out of 10
drugs recover the post tax R&D spend of close to USD 500 million (Rs.2,200 crore).
(B Rajesh Kumar and S M Satish, 2007)

5.9.1. Future Innovations in Drug Discovery

The three breakthrough innovations promise to radically reduce the duration of the drug discovery process and increase the quality of the output. (B Rajesh Kumar and S M Satish, 2007) These are genormics, combinatorial chemistry and High Throughput Screening (HTS). Genomics aims to establish the links between genes and diseases. These efforts had yielded results with respect to genetic targets for obesity and breast cancer. Combinatorial chemistry allows chemist to start with known chemical building blocks and then cheaply and quickly generate thousands of chemical compounds at a much reduced cost. HTS are the result of advances in molecular biology which helps in screening new compounds against drug targets. Now transnational firms are identifying target compounds and taking dosing, delivery system, product information and compliance programmes to address the needs of particular patient sub-segments.

Pharmaceutical companies screen all the molecules they get running into hundreds and thousands to test the biological activeness which is costly in nature. But now the focus is on what is called rational drug discovery. In this method, the focus of research is with respect to a molecule usually a protein which could act as a target in the body for a drug. Molecular modeling and other techniques allow scientists to see whether a particular drug can actually attack this target.

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Efforts are being made and strategies are being drawn to improve the success rate by intelligent synthesis using conventional and modern combinatorial techniques and then screening these sources of chemical compounds. Also plants, microbes, fungi, insects and various venoms are an excellent source of chemical diversity and thus new and novel chemical compounds isolated from these extracts could also be screened.

Another promising source is the drugs, which are being used routinely by clinicians for treating specific diseases but which are known to have strong side effects. They may also be difficult to synthesize, separate and purify. The therapeutic value of some of these drugs can be enhanced by using the basic components of the structure as a base, which gives the biological activity, and modify or substitute those associated structures, which are responsible for the side effects, or may be difficult from chemistry and engineering point of view. Similarly some drugs with high toxicity can be a good source for new drugs. By modifying and directing their delivery to the desired sites in biophases, the dosage and toxicity can be reduced.

Drug discovery research is going on through a revolution in big companies. No matter how animal studies are, human beings responded completely differently. Four properties of drugs are being tested in humans. It consists of how it is absorbed, distributed, broken down or metabolized and finally excreted. Pharma companies call the studies ADME (Absorption, Distribution, Metabolism and Excretion). ADME studies came late in the conventional approach. Now the drug companies are studying drug metabolism early on in a drug's history in parallel with efficacy and animal toxicity tests. During animal studies, molecular biologists have learned to use genetic engineering and clone receptors into animal models.
5.9.2. Status of Drug Discovery in India

It is estimated that Indian companies have so far devoted only a total of USD 450 million on new drug research. Dr. Reddy's has spent some USD 57 million on taking its first new-compounds up to the pre-clinical stage. (B Rajesh Kumar, S M Satish, 2007)

In Indian context, there are at least twelve Indian pharma companies that are involved in new drug development. An estimated 60 new compounds are in various phases of development and testing. This numerical fact is very small when compared to world standards of GlaxoSmithKline and Pfizer, which have about 143 and 140 compounds respectively. But it is an appreciative fact that Indian pharmaceutical companies have started evolving from being mere copycats to discoverers of original drugs. So far every drug that has been created by Indian pharmaceutical industry has been a reverse engineered generic - a copy of a drug that was already discovered by a multinational. The drug design process in all its stages is undergoing fundamental change. Indian pharma companies have to invest in millions of dollars to cope up with the change process.

The human genome mapped 3 billion pairs to be called the code of life. Only one in about 500 makes a difference. Within pairs even one letter makes a difference. The pairs form a sort of twisted ladder. The 3 billion pairs of the four letters are similar for most human beings. In fact, it is estimated that there is only 0.1 percent variation between human beings. But most of these 3 billion pairs are not critical. There are 30,000 to 50,000 genes in the human body that actually perform function. If these genes which control the production of different proteins in the body are identified,
then the related diseases can be easily identified. But it turns out that there are very few single gene diseases like cystic fibrosis or Huntington's diseases. Most others are complex. (B Rajesh Kumar and S M Satish, 2007)

Companies like Sequenom, Orchid Biosciences, Millennium Pharmaceuticals and Nanogen are working on technologies to discover identify and catalogue variety of important genes. Indian companies will immensely gain if they pursue R&D in tropical and global diseases like HIV, TB and malaria since the focus on Western companies are not on them.

International pharma companies have also alliances with National Chemical Lab, Pune, National Institute of Immunology, New Delhi, Indian Institute of Science, Bangalore and Centre for Cellular and Molecular Biology, Hyderabad. (B Rajesh Kumar and S M Satish, 2007) Some companies worn with research institutes in India for this purpose.

5.9.3. The Changing Global Scenario of Research and Development

The future new medicines for chronic diseases are likely to be biological like proteins, genes, cellular therapy, vaccine, monoclonal antibodies, new molecular entity (NME), so the emphasis and focus will shift from chemistry to molecular biology, molecular medicine and receptor pharmacology. From new chemical entities (NCE) to new molecular entity (NME). Although the initial set of patents on therapeutic proteins have expired e.g., HGH, TPA, insulin, interferon, CSF, the regulatory consensus and standards for generic biopharmaceuticals may take another five years. This leaves the
growth of originator biotech companies like Amgen, Biogen, Genentech, Chiron, Serono, and Novo unchallenged. (B Rajesh Kumar and S M Satish, 2007)

Drug discovery is multi-disciplinary and complex science and needs a lot of scientific infrastructure. Recent advances in molecular biology and genetic engineering have enhanced the basic understanding of human physiology and the biological action of drugs on cell receptors and proteins. New tools of drug discovery such as combinatorial chemistry, structure based molecular design and high throughput screening has revolutionized the drug discovery process. (B Rajesh Kumar and S M Satish, 2007)

This new phenomena of drug research has led to the emergence of specialized segments of the innovation chain like basic biomedical research, chemical synthesis, process development, clinical testing, etc. In order to attempt to reduce the time for drug development to half and to improve the success rate of drug discovery, intelligent screening of sources of chemical compounds is required. Furthermore, some of the new sources of NCEs could be plants, microbes, fungi, insects and various venoms. The extracts from these material sources offers scope as a major source of entirely novel structures.

Thus there is tremendous scope for R and D in this sector in India as well as at a global level. Now let us talk about the outsourcing patterns in this industry in the next chapter.