1.0 Dr. Reddy’s Laboratories Limited

1.1 Background of Company

Dr. Reddy’s Laboratories Limited (DRL) was established in 1984 to produce bulk drugs for domestic markets. The company’s process technology was based on indigenous efforts. The first product was Methyl Dopa - a technologically difficult product. This product was exported to USA through a multinational company. The company subsequently in late 80s made a number of sophisticated products for multinational companies and the quality of products made by company, was found to be better than the best in the world. The company displaced a number of well-established suppliers from Europe and Japan. During 90s, the company introduced branded finished formulations in the less regulated markets in CIS, Middle East, South East Asia and Africa. From late 90s, the company has started exploiting US patent and regulatory system to introduce generic products in time, to gain market exclusivity and establish brand image. It is the first Indian based company to receive 180 days exclusivity for a generic drug in USA. Its latest product Amlodipine Maleate has made a sale of US$ 2.0 billion during 2002.

The company has global operations with a strong focus on US, Europe, Russia, China and India. Its portfolio of products consists of 70 Active Pharmaceutical Ingredients (API), 100+ Branded Formulations, 11 Generic Pharmaceuticals, 1 Specialty pharmaceutical, 7 new chemical entities in clinical trials. It has world class manufacturing facilities consisting of 6 US FDA approved API plants, 7 formulation plants out of which one is dedicated for US and European market. Its sales turnover for 2002-03 was US$ 380 m. This comprised of 35% API, 38% Branded Formulations, 24% Generics and others 3%. Its revenue came from US (32%), India (36%), Russia (9%), Europe (8%) and others (15%).
1.2 Background of R & D Centre

The company has two research centres in India located at Hyderabad. One centre is involved in process research and the other one is involved in the technology development. The former centre develops novel innovative processes for known molecules as well as for new molecules developed by the company. The technology development centre is involved in new chemical entities and new product development. The company has setup an independant research foundation under the name of Reddy Research Foundation, which overseas the corporate research. The company has scientific staff strength of 550+ out of which 260 work exclusively for drug discovery projects and custom synthesis business. The company has increased its R & D budget by several folds during last few years. The details are given in Table 6.1

Table 6.1 R&D Expenditure of DRL

<table>
<thead>
<tr>
<th>Year</th>
<th>R &amp; D Exp. (in Rs.)</th>
<th>R &amp; D as % of Sales</th>
</tr>
</thead>
<tbody>
<tr>
<td>1997-98</td>
<td>70,748,983</td>
<td>2.12</td>
</tr>
<tr>
<td>1998-99</td>
<td>93,950,378</td>
<td>2.20</td>
</tr>
<tr>
<td>1999-00</td>
<td>132,707,704</td>
<td>2.69</td>
</tr>
<tr>
<td>2000-01</td>
<td>415,441,101</td>
<td>4.22</td>
</tr>
<tr>
<td>2001-02</td>
<td>980,309,229</td>
<td>6.13</td>
</tr>
<tr>
<td>2002-03</td>
<td>1,338,000,000</td>
<td>8.00</td>
</tr>
</tbody>
</table>

During the current financial year, the company plans to spend about 10% of its sales turnover on R & D.

1.3 R & D Project Content

Right from the beginning the company had established an in-house R & D unit, the charter of which was to develop:
I) Lab scale process for pharmaceutical products with a good market potential worldwide.
II) Alternate routes of synthesis for products already commercialized. Study of impurity profile of products.
III) Products for human care, Analytical method development, Quality improvements and packaging development.

This in-house R & D unit was meant to provide technology support as well as to undertake process and product development (technology up gradation) activities. Based on its experience of active pharmaceutical ingredients (APIs), the company started Custom Chemical Synthesis (CCS) Business Unit. This unit caters to the following needs of multinational pharmaceutical companies that wish to outsource their requirements:

- Contract Research
- Custom Synthesis
- Contract Manufacturing

CCS’ cutting edge lies in its experience and expertise, spanning a range of technologies, talented team of chemists experienced in all aspects of process development such as process chemistry, analytical chemistry, process engineering, manufacturing services, safety, health and environment, large manufacturing capacities, modern infrastructure, complete with sophisticated instrumentation. The CCS Business Unit is equipped with a skilled and experienced process development team consisting of nearly 100 scientists, including 15 PhDs.

It was in 1993 the company decided to make an investment in basic research to start new drug discovery programme. The institutional capabilities of the Discovery Research Unit at DRL span a wide range of areas including:

- Molecular Modelling & Drug Design
- Organic Synthesis
- Natural Product Chemistry
Currently, nearly 160 researchers are actively involved in the drug discovery program. They focus on early phase discovery and pre-clinical studies of newly synthesized compounds for the treatment of cancer, diabetes, dyslipidemia, inflammation and infections.

In order to enhance the value of these early stage compounds, the company actively collaborates with government agencies, academic institutions and regulatory bodies. A few organizations are listed below:

National Cancer Institute (NCI), USA; St Jude Children's Research Hospital, USA; Indian Institute of Chemical Technology (IICT), Hyderabad, India; University of Hyderabad, Hyderabad, India; National Institute of Nutrition (NIN), Hyderabad, India; Centre for Cellular and Molecular Biology (CCMB), Hyderabad, India and Nizam's Institute of Medical Sciences, Hyderabad, India.

The company has diversified into biotechnology. The biotechnology division deals with therapeutics, vaccines and diagnostics. Molecular biology, cell culture, fermentation, downstream processing and hybridoma technology are the focus areas. DRL's core competency is in the recombinant proteins technology platform. Company claims that their technology, multiple expression systems (E.coli, yeast and mammalian cells) ensure high expression levels in yield apart from cost and market leadership.

DRL was the first company in India to develop a molecule - from the molecular biology stage to production. GRASTIM (generic name: filgrastim), the human Granulocyte Colony Stimulating Factor (hG-CSF), is a recombinant protein used in chemotherapy-induced neutropenia and in bone marrow transplantation.
The company has identified biogenerics as a significant market area and is in the process of setting up bulk recombinant protein production sites and formulation facilities that meet US FDA specifications. Company has a pipeline comprising several recombinant proteins in various phases of development for treatment of cancer, diabetes and cardiovascular diseases.

DRL has recently set up a separate subsidiary, Zenovus Biotech Ltd., to develop the technology platform for monoclonal antibodies. This is because, today approx. 22% of all products in clinical developments are monoclonal antibodies.

1.4 R & D Globalisation

The company has consistently moved along the R & D value hierarchy during the last 10 years of globalisation. The company has exploited domestic technological capability to export high-tech products and also entered into licensing arrangements, contract research and custom synthesis business. The company’s activities are explained below:

Active Pharmaceutical Ingredient and branded formulations in less regulated markets

The company has posted record revenues in its global API business. Revenue from this business accounted for 35 per cent of the total revenue for the year ended March 31, 2003.

Key Skills being exploited are: Synthetic and analytical chemistry and full range of dosage forms

Generics Drugs in USA

11 Abbreviated New Drug Applications (ANDAs) submitted to US Food and Drug Administration by DRL have been approved and products are marketed by the company in USA. 23 additional ANDAs are pending approvals out of which 7 are first to market opportunities. Company has filed 14 ANDAs in 2003 and it hopes to file 15-18 NDAs in
2004. The company has also challenged the validity of 17 patents granted to MNC pharma companies.

ANDAs are required to be filed when an existing drug is manufactured by a different non-infringing process. The first to file company gets market exclusivity for 180 days in USA after the expiry of original patent.

Key Skills being exploited are: Innovation, Global Regulatory Expertise, Formulation, Patent and Manufacturing Expertise, Drug Delivery Capabilities and Speed to Development.

During the financial year 2002-03, Generics division has reached a turnover closer to the $100 million mark.

During the year, the Company filed 14 drug master files (DMFs) in US, which is almost double the number of DMFs filed in previous financial year, taking the total to 40.

**Specialty Pharmaceuticals**

Key Skills being exploited are: Product Identification, Drug Delivery and Formulation. The company has introduced new salt version of Amlodipine Maleate and already touched sales of 2 billion US$ during 2002.

**New Chemical Entities**

Development of new chemical entities or molecules as drugs represents highest order of research hierarchy in the pharmaceutical industry.

7 compounds are under development (diabetes, cancer, metabolic disorders, and anti-infectives) at DRL. The summary of current status of NCEs is given in Table 6.2
### Table 6.2 Dr Reddy’s Laboratories Ltd. – NCE pipeline

<table>
<thead>
<tr>
<th>Compound</th>
<th>Therapeutic Area</th>
<th>Development Status</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>DRF 2593</td>
<td>Diabetes</td>
<td>Phase II completed</td>
<td>Insulin Sensitizer</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Licensed to Novo Nordisk</td>
</tr>
<tr>
<td>DRF 4158</td>
<td>Metabolic disorders</td>
<td>Preclinical completed</td>
<td>Indicated for Insulin resistance and associated disorders</td>
</tr>
<tr>
<td>DRF 4832</td>
<td>Metabolic disorders</td>
<td>Late Preclinical</td>
<td>HDL Elevator, Clinical Development in Europe</td>
</tr>
<tr>
<td>DRF 1042</td>
<td>Cancer</td>
<td>Phase I completed</td>
<td>Topoisomerase-I inhibitor</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Clinical Development in Europe</td>
</tr>
<tr>
<td>DRF 1644</td>
<td>Cancer</td>
<td>Preclinical completed</td>
<td>Topoisomerase-I inhibitor, Clinical Development in Europe</td>
</tr>
<tr>
<td>DRF 11057</td>
<td>Bacterial Infections</td>
<td>Preclinical</td>
<td></td>
</tr>
<tr>
<td>DRF 10945</td>
<td>Metabolic disorders/Dyslipidemia</td>
<td>Preclinical</td>
<td></td>
</tr>
<tr>
<td>RUS 3108</td>
<td>Cardiovascular</td>
<td>Preclinical</td>
<td></td>
</tr>
</tbody>
</table>

Key Skills being exploited are: World-class chemistry, Rapid pre-clinical development skills, Target identification and validation and High throughput screening.

The company has already licensed New Chemical Entities to multinational firms for further development. According to company’s agreement with Novo Nordisk, Novo will take up clinical trials, regulatory approvals and global marketing of the drugs, and DRL, as per the agreement will be sole global manufacturer of the drug. DRL will also co-market the drug in India. DRL will receive upfront payment and milestone payments for three phases of clinical trials over 54 months after which it will get royalties on global sales.
The company has developed competence in structure based drug design. But today, drug research is affected by the developments in the biotechnology sector. The other approach being followed for drug discovery is target based design. This requires knowledge of genomics and molecular biology.

In order to meet the needs of its biotech research, the company established in November 1999, a small laboratory in Atlanta, USA under the name of Reddy US Therapeutics Inc. This is a biopharmaceutical company dedicated to discovering novel therapeutics that addresses unmet medical needs in diabetes, inflammation, lipid metabolism, oncology and cardiovascular disease. Their proprietary technology platform, the CMS pathway, enables Reddy US Therapeutics to target several diseases from a single research focus.

The company has hired 20 scientists of American, Chinese and Indian origin. In order to support the biotechnology lab the company has opened another laboratory called Aurigene Discovery Technologies in Bangalore for Protein expression work. As number of pharma companies also outsource protein expression work, and in order to provide such service to other research based companies, Aurigene has opened another satellite lab in Boston consisting of 10 scientists that helps in business development and technical coordination with Bangalore lab, where most of the work is carried out. The 25% of company’s R & D budget is spent in USA.

The company claims to have already integrated their research activities in India and Atlanta. They leverage the chemistry and pharmacological capabilities of their labs in India and early stage research capabilities of their labs in Atlanta to create further synergies.

DRL has filed 67 patents with Indian Patent Office in the financial year 2002-03. The company has also filed 67 USA patents and 54 PCT applications for patents so far.
Today DRL is a diversified emerging specialty company. In 3-5 years it wants to become integrated global mid-sized company. In the long term (5-7 years) it wants to become Global discovery – led pharmaceutical company.

Starting with bulk actives (APIs) company used innovation in process development to build a strong and profitable business. DRL then entered the branded finished dosages business in India. Their efforts in this business made it possible for them to bring affordable medicine to the people. The cost advantage they created by innovation enabled them to extend their branded finished dosages business to other global markets such as Russia, UK, and some of the Latin American and Asian countries, including China. Over a period of time some of their brands have become leaders with increased share in these markets. DRL started building a base for the US generics business in 1992 and within ten years, the company has quite a few successes to their credit. DRL felt encouraged to enter the specialty business segment in the US with its own branded finished dosage forms. The company now has one of the most exciting generics pipeline in the US industry, with the potential of introducing drugs whose innovator sales last year topped US$ 19 billion.

Even as the company is building a strong base for generic entry in the US, it has taken on the ultimate pharmaceutical challenge - drug discovery research while readying itself for the post-2005 era, when product patents will be recognized in India. When the company started its drug discovery program in 1993, everyone in the industry viewed it with scepticism. This ambition, they said, would not be within the reach of a medium scale Indian company. The company today has a pipeline of seven New Chemical Entities (NCEs) including two in clinical development. Three NCEs were out-licensed to MNCs for upfront and milestone payments. Of these one has completed phase-II clinical development and another went all the way to phase-III clinical development, before it was withdrawn due to its side-effect profile. Company’s efforts and the progress it has made during the last decade have proved that they are up to the drug discovery challenge. However, the bigger challenge is to take a molecule from research pipeline all the way to the market place cost-effectively. DRL recognizes this limitation because it is in the development phase, where the major expenditure in taking new molecule to the market
place resides. In the development part of the value chain, the company is focusing on using various types of alliances to reduce cost, reduce cycle time and evolve value chain linkages. According to the company, this enables them to manage the risk profile of their R&D assets through alliances and will also help them to build complimentary skills.

Bowonder et al. (2003a) have described the changing competitive landscape of the global pharmaceutical industry and have also analyzed the strategies of DRL (Bowonder et al, 2003b).

Fig. 6.2 shows the Globalisation of R&D at Dr. Reddy’s Lab.

![Diagram showing the Globalisation of R&D at Dr. Reddy’s Lab](image)

**Fig.6.2 Globalisation of R & D by Dr.Reddy’s Laboratories Limited**

This case clearly shows how within a period of ten years, a company whose R & D strength was in process research has been able to move up the R & D value hierarchy to undertake basic research in new chemical entities and new drug delivery systems. Their impressive patent portfolio validates our proposition that Domestic Affiliated R & D is moving away from imitative research to innovative research.
This case perfectly fits into our framework, where a company in a protected market uses in-house R & D efforts to reverse engineer the existing products and processes to meet the demands of domestic market. Over a period of time the company finds opportunities for exports and develops new innovative and cost effective processes to beat the international competition and finally uses that capability to become a global player whereby 60% of its revenue comes from foreign markets. The company then leverages domestic technological capabilities to export high-tech/knowledge based products and services and participate in global knowledge generating activities by licensing and research partnerships. The setting up of Aurigene Discovery Technology and US Reddy Theraupetics in USA reinforces the concept of “home base exploiting” and “home base augmenting,” type R & D proposed by Kuemmerle (1997).