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# Pharma focus

Mega Ace Consultancy

MONTHLY REVIEW OF THE INDIAN PHARMA SECTOR

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## Outsourcing Clinical Trials

# Inevitable Trends

Clinical research has been predominantly an activity restricted to North America and Western Europe in the latter half of the 20<sup>th</sup> century, largely due to institutional variance with regard to intellectual property rights and product patents in rest of the world. With the gradual universalisation of institutions relating to patents and IPR under the WTO regime this bias in clinical trials is reducing. Thus by 2006 North America and Western Europe accounted for 55% of global clinical trials and the share of these two regions is expected to further decline to 38 % in 2010. In 2006 India's share was 3% and is likely to be around 5% in 2010.

The reasons for India's low share are that while its institutions favoured her becoming a 'generic giant', they did not foster an environment for new drug discovery or research resulting in low demand for clinical trials. This situation will, however, alter in course of time as more Indian companies restructure their activities. Moreover, the institutional change has created an enabling environment for 'outsourcing' clinical trials from North America / Western Europe to India. The recent increase in

India's share in clinical trials is largely on account of 'outsourcing' / transfer of work by overseas entities / companies to India, to Subsidiaries located in India, Joint Ventures or specialised Clinical Research Organisations. It is estimated that 'outsourced' clinical research / trials account for around 40 % of the R & D spending globally.

Though Clinical Research Organisations in India originated in the early 1980s, the work was largely restricted to bio availability / bioequivalence studies. It is only in the 21<sup>st</sup> century, more particularly after 2005 that such organisations have undertaken Phase ii & III trials and project management with respect to NCEs from pharmaceutical companies. This has led to a proliferation of such organisations in India. Moreover, opportunities have opened up in the IT sector, particularly with respect to clinical data management / monitoring / dispersal.

While geographical redistribution of clinical trials, particularly to developing / emerging economies like India, is the obvious trend that is likely to emerge globally for economic reasons, advantage of availability of target 'population' and assurance of stable skilled workforce,

there seem to be reservations amongst many foreign companies about the wisdom of outsourcing such work to Indian companies. A concern expressed by some multinational companies is that data confidentiality might be compromised and that the laws are not 'secure' enough with respect to protection against misuse of shared information. Indian companies, on the other hand, disagree with this perception and express the view that this is a 'strategic stance' taken to extract maximum advantage from deals 'outsourced' to India. A few Indian companies express the view that many multi-nationals are reluctant to share information on clinical trials as there has been a tradition in the global pharmaceutical industry to place in the public domain data on a selective basis to gain commercial advantage and camouflage shortcomings of the product.

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# Clinical Trials, Transparency & Institutional Change

While major pharmaceutical companies have necessarily to share all information on clinical field trials proposed to be carried out / being carried out with regulatory authorities, there is reluctance on their part to provide material details in the public domain. This 'opacity' inhibits the process of building information necessary to evaluate the contemporary status of research, clearly identifying the focus areas and gaps.

Another area of lack of transparency is in making available in the public domain all data collected during clinical trials, which companies necessarily share with regulators. It has been generally felt that companies have a tendency to release data on clinical trials selectively. This makes an 'independent' and 'holistic' assessment of results difficult. While it is true that the Regulator could possibly access all data, it is important that results of clinical trials must be in the public domain so that they may be subjected to the equivalent of a 'peer' review. In the absence of this companies could publish results that are biased and drugs may not turn out to be as claimed by the 'innovator'.

With a view to making the process of research in the pharmaceutical sector more efficient and improving the quality of new drugs the World Health Organisation has been staunchly advocating for institutional measures that bring about greater transparency to clinical trials. One lead taken in this context is the advocacy and creation of a 'clinical trials registry'. The value of registration goes far beyond the administrative benefits of having a complete collection of all trials. Clinical trial registers may facilitate recruitment

into clinical trials by raising awareness of their existence among potential participants and health-care practitioners. They may also lead to more ethical and successful research by avoiding the unintentional duplication of research already under way elsewhere. Moreover, these would make it clear which trials are being conducted so that people can anticipate their results.

Many countries, including India, have initiated this measure. However, in India's case not all clinical trials are as yet registered because it is so far being done on a voluntary basis. An institutional measure that has been suggested in India's case is either to legislate in this regard or to ensure that the regulator makes such registration mandatory as a pre-requisite for granting permissions.

The recognition of the need for reliable evidence to improve health care and to facilitate the synthesis of the results of research into systematic reviews has fuelled the demand for access to the findings of all research, as have the needs of the numerous other stakeholders in clinical research. In this context, before the WHO is a proposition to consider making mandatory the publication of findings of all clinical trials. An informal institutional step that has already been taken in this regard is to persuade a group of journals to only publish papers on research findings of those companies that place their complete data set in the public domain.

While debate on these issues is taking place in international forums and academic circles, transparency, driven by institutional change, can only come about once uniform formal rules / laws are created across nations.

## What are Clinical Trials?

A clinical trial is any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes. Clinical trials may also be referred to as interventional trials. Interventions include but are not restricted to drugs, cells and other biological products, surgical procedures, radiologic procedures, devices, behavioural treatments, process-of-care changes, preventive care, etc. This definition includes Phase I to Phase IV trials. The WHO regards trial registration as an internationally-agreed set of information about the design, conduct and administration of clinical trials. These details are published on a publicly-accessible website managed by a registry conforming to WHO standards. The registration of all interventional trials is considered to be a scientific, ethical and moral responsibility for the purpose of information dissemination enabling informed decision making and improved awareness of similar or identical trials enabling research partnerships & collaborations among others. The Declaration of Helsinki states that "Every clinical trial must be registered in a publicly accessible database before recruitment of the first subject".

*Market Entry Services*

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# Industry Analysis

## Dr. Reddy's Lab

Dr. Reddy's Lab, an emerging global pharmaceutical company, was established in 1984 by entrepreneur-scientist Dr. Anji Reddy with just \$40,000 in cash and a bank loan of \$120,000. Dr. Reddy's Laboratories had humble beginnings. But the appetite for growth and the desire to make a difference has made it the second largest pharmaceutical company from India today. It is one of the largest Indian pharmaceutical companies having revenue of \$1.4 billion in 2009-10 and CAGR of 25%. International business generated around 85% of the revenue in 2009-10. The company has strong portfolio of business with vertically integrated approach.

### Three Core Businesses:

- Pharmaceutical Services and Active Ingredients,
- Global Generics, includes branded & unbranded generics;
- Proprietary Products, which includes New Chemical Entities (NCEs), Differentiated Formulations, and Generic Biopharmaceuticals.

**Global Location:** US, UK, Germany, India, Russia, CIS, Romania and Venezuela

**Manufacturing Expertise:** It has 16 world-class manufacturing facilities of which 9 have a long history of regular USFDA inspections. Annual capacity of nine billion tablets/ capsules a year.

**R&D Expenses:** R&D expenses grew by 20% to Rs. 3847 million. As a share of

total revenue, R&D expenditure was at 6% in 2008-09, compared to 7% in 2007-08. The rise in R&D expenses was primarily on account of increase in greater development activity in the Global Generics and proprietary business segments.

### Financial Snapshot

Rs. in Crore	Mar-07	Mar-08	Mar-09	Mar-10
Sales Turnover	4045.32	3449.7	4239.8	4401.1
Net Profit	1176.86	475.3	560.9	846.1
Total Share Holder's Fund	4373.36	4811.8	5259.1	5914.5
Total Debt	329.9	462.3	640.3	563.2
Earnings Per Share(Rs.)	69.45	27.62	32.25	50.15

### Share Price Movement

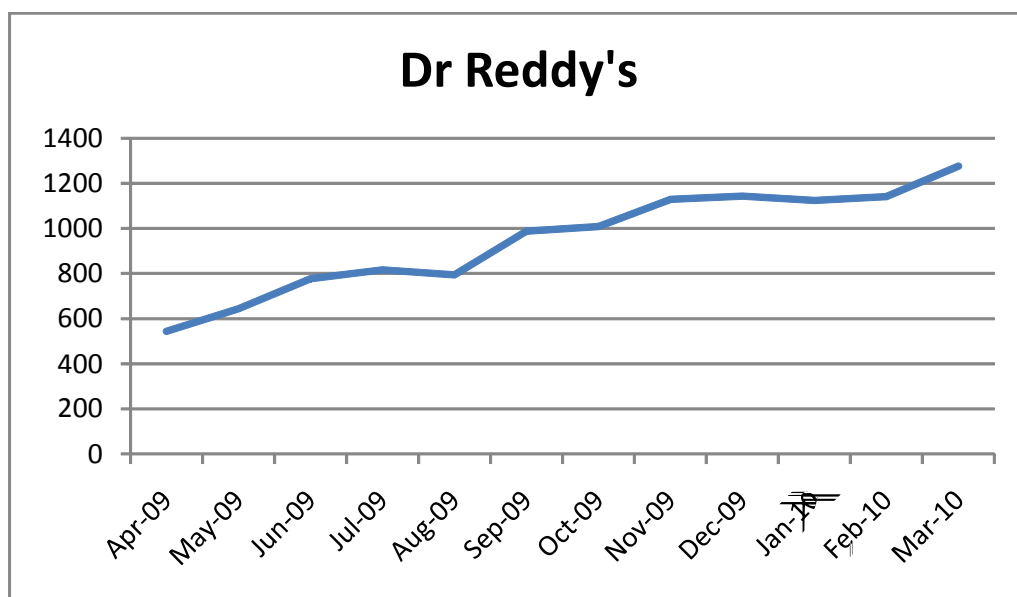
Market Capitalisation	Rs. 20178.91 Cr
Promoter's Holding	5.11%
Face Value	Rs. 5
52 Week High	Rs. 1317.9
52 Week Low	Rs. 546.7

### Mega Ace Consultancy Knowledge Services

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Month	Dr Reddys
Apr-09	544.35
May-09	644.85
Jun-09	777.85
Jul-09	817.55
Aug-09	794.65
Sep-09	988.1
Oct-09	1,009.15
Nov-09	1,129.45
Dec-09	1,143.80
Jan-10	1,125.25
Feb-10	1,142.70
Mar-10	1,276.80



# Industry News Updates

## Glenmark in licensing pact with Sanofi-Aventis

Glenmark Pharmaceutical Limited has entered into an agreement with Sanofi-Aventis to grant Sanofi-Aventis a license for the development and commercialization of novel agent to treat Chronic pain. Pharmaceuticals licensed its chronic pain molecule to Sanofi Aventis for an upfront payment of \$20 million (approximately Rs 89 crore, in a cumulative deal of \$325 million (Rs 1,449 crore). Glenmark is one of India's few companies involved in original drug research. According to the company CEO & MD "Costs of drug development is inhibitive, so the Indian company needs to sell molecules it discovers, in an out-licensing agreement with partners who can fund development till it is ready to be marketed" Glenmark is expected to strike more such deals in the future.

## Aurobindo Pharma on growth spree

According to the company's news report Hyderabad-based leading Indian active pharmaceutical ingredient (API) manufacturer, Aurobindo Pharma is setting up a new injectable manufacturing facility in its existing facility at Bhiwadi, New Delhi. The company is investing about Rs 15 crore from internal accruals to commence by December 2010. Aurobindo Pharma obtained Health Canada approval for its abbreviated new drug submission for topiramate tablets is the generic equivalent of Janssen-Ortho Inc, Topiramate tablets are indicated as adjunctive therapy for patients with partial onset seizures or primary generalized tonic-clonic seizures and falls

under the central nervous system (CNS) therapeutic category. This is Aurobindo's ninth product approval from Health Canada.

## Orchid in pact with US co for oral non-antibiotic drug

Chennai Based Orchid Chemicals & Pharmaceuticals announced that it has entered into an out-licensing and distribution agreement with the US-based pharma company Alvogen for marketing eight of Orchid's oral non-antibiotic generic formulations in the US market. According to the company press release, under this agreement, Orchid will develop and manufacture eight oral non-antibiotic formulations for licensing to and marketing by Alvogen in the US. Alvogen will source these products from Orchid exclusively. The products will be manufactured at Orchid's facilities, which are approved by the USFDA. Alvogen would pay certain dossier licence fees to Orchid based on development and regulatory milestones and share profits arising from marketing of these products in the US with Orchid. Both the companies would share the legal expenses and bio-study costs. These formulations licensed to Alvogen under the agreement comprise products in the high-growth therapeutic segments of CNS and Osteoporosis among others. The combined addressable market size of these products is around \$8 billion.

## FDA Approval for Sun Pharma Generic Namenda Tablets

According to the press release Sun Pharmaceutical has received FDA approval for its abbreviated new drug application (ANDA) to market a generic

version of Forest Laboratories' Namenda 5mg and 10mg tablets.

Sun was amongst the first ANDA applicants to submit a substantially complete ANDA with a paragraph IV certification to the '703 patent. Sun's subsidiary is eligible for 180 days generic exclusivity. Memantine (Namenda) helps treat the symptoms associated with Alzheimer's disease or dementia.

## Spurious Drugs Seized in TN

The recent unearthing of expired drugs scam by the Tamil Nadu Drug Control Department and the state police brought to light some of the gray areas of the Drugs & Cosmetics Act. These drugs were found in many cases to be more than five to ten years over their expiry period. They were being sold as new at many shops and traded by many dealers who were altering the batch numbers and expiry dates on the wrappers using special chemicals. The Act is rather silent on handling of expired drugs of pharmaceutical companies. Every pharma company will have a build up of stocks of expired products as the potency of most of the drugs does not normally last more than two or three years. The pharma companies are believed to be collecting the expired drugs from the trade channels and destroy them regularly. It is more of a voluntary act by the pharma companies. And there is no monitoring of the destruction of goods of the companies by the state drug authorities. The seizure of Rs 5.5 crore worth of expired drugs belonging to one company by the TN state authorities from a dump yard is a testimony to this hard reality.

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