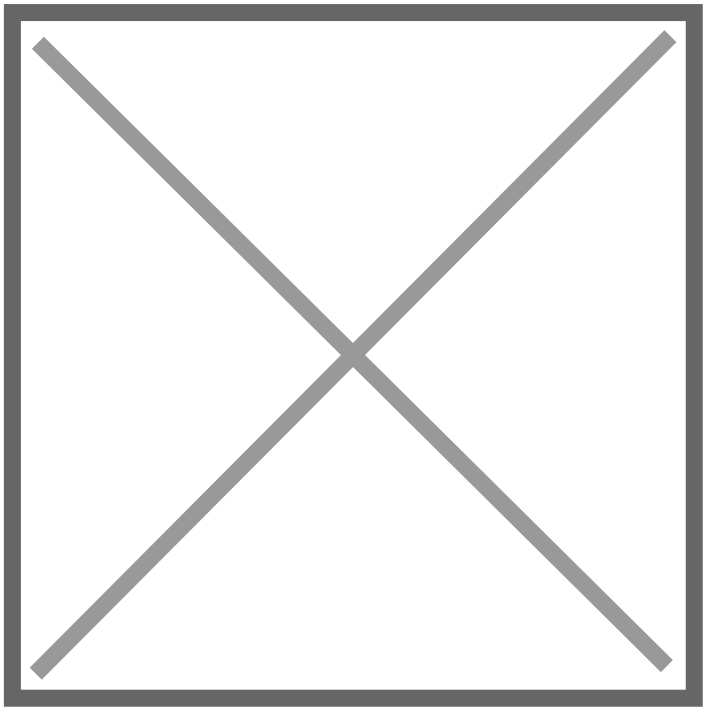


India CROs: On the fast track

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This financial year has seen some positive developments in the Indian CRO industry, yet the regulatory environment and lack of trained inspectors continue to be areas of concern for companies operating in India. A BioSpectrum special report on the emerging trends in the CRO market in India.

Inside: Key findings of Asia Pacific CRO Survey

The clinical trial industry in India is undergoing a positive metamorphosis. It is gradually being viewed as a drug discovery rather than a mere drug development destination, with more companies looking at innovation.

According to the BioSpectrum-ABLE annual survey 2010-11, the Indian CRO industry has been growing at a rate of 23 percent and clocked total revenue of ₹3,245.97 crore ($709 million) in 2010-11, over last year's (2009-10) segment revenue of ₹2,639 crore ($576.4 million). This constitutes about 19 percent of the total biotechnology industry revenue for the fiscal.

The players operating in the Indian segment include multinational CROs that still dominate the nation's market, Indian CROs, multinational pharmaceutical companies and Indian pharmaceutical companies. While the first three categories of companies are into global trials, Indian pharmaceutical companies usually look at conducting local trials. The major global players with a presence in India are Quintiles, PPD, Parexel, ICON, Pharmanet, Kendle, i3 Inventiv, Theorem Clinical Research (formerly called Omnicare Clinical Research), Inveresk Research, MDS and SCIREX.

Some of the India CROs going global

Sl. No.	Name of company	Countries targeted
1	Synchron	Vietnam
2	Siro Clinpharm	South East Asia (Malaysia)
3	Veeda Clinical Research	South East Asia (Malaysia) /USA
6	Max Neeman	Global regions not disclosed
7	Excel Life Sciences	Worldwide
9	CliniRx	US/Europe

The major Indian players in the market are Siro Clinpharm, GVK Bio, ClinInvent, Ecron Acunova, CliniRx, Asian Clinical Trials, Jubilant Clinsys, Vimta Labs, Lotus, Lambda Therapeutics, Clinigene, Max Neeman Medical and International, Synchron Research, Diagnosearch Life Sciences (earlier called iGate Clinical Research), Veeda Clinical Research and Actimus Biosciences.

Compared to the previous two fiscals, when the CRO industry was hit by the global economic downturn, the year 2010-11 saw some positive developments in this segment. Both the companies and the Indian government (the Drug Controller General of India or DCGI) were proactive in creating a favorable environment for clinical trials, while consolidation in the global landscape, in the form of mergers and acquisitions, too had its cascade effect on the India CRO industry.

Favorable trends and developments

According to market observers, the decade-old India CRO industry has successfully overcome early challenges, including the 2008 slump, to report decent growth figures. Ã¢â?¬Å?It has crossed the early challenges of setting up and establishing of businesses and successfully managing trials,Ã¢â?¬? said Dr Arun Bhatt, president, ClinInvent. Ã¢â?¬Å?Now, it has to sustain and grow in a challenging environment.Ã¢â?¬?

While lower costs has been a crucial factor in making India an attractive destination for global companies looking to conduct large-scale trials, there are other factors like skilled and knowledgeable investigators and expertise, increased compliance towards quality issues, a large patient pool and unmet medical needs of the population also help to lure foreign companies. Ã¢â?¬Å?The focus areas are cardiology, endocrinology, anti-psychiatric, respiratory, diabetic and anti-infection drugs,Ã¢â?¬? said Mr Anil Panwar, CEO, Fortis Clinical Research.

Another favorable trend is the CROs engaging in new business development and expanding their range of services.

Dr Yati Chugh, managing director of Lotus Labs, Bangalore, said the growth trend was particularly in the areas of data management, pharmacovigilance and clinical trial management. Ã¢â?¬Å?Until 2000, none of the companies were really offering these services, so these areas need a lot of investment,Ã¢â?¬? he said.

Dr Ajit Nair, president, Asia operations, Siro Clinpharm, expressed a similar opinion. Ã¢â?¬Å?The fields of data management and medical writing have seen a significant increase in the country. There is a trend of significant amount of work related to data services going to the BPO sector of big IT companies,Ã¢â?¬? he said. Mr Sudip Sinha, vice president and country manager Ã¢â?¬â?? India, CliniRx Research, too pointed out that the CROs were approached for end-to-end study and program management rather than sponsors outsourcing individual activities to different CRO players.

Contract staffing is also common largely due to problems of recruitment and retention of experienced clinical staff in the country, with demand outweighing supply. Ã¢â?¬Å?The average staff attrition rate in firms operating in India is 45 percent,Ã¢â?¬? said Dr Chugh.

Home-grown CROs are also aggressively looking at expanding to other markets. Ã¢â?¬Å?Indian CROs are looking at South East Asian countries to expand their operations followed by East European nations. They are focusing on oncology, diabetes, CNS and respiratory as their key therapeutic segments. The Indian arms of global CROs too have started consolidation,Ã¢â?¬? said Dr Nair.

Siro Clinpharm, in early 2011, launched operations in Malaysia. Veeda Clinpharm too has announced that the final steps were in place for the commissioning of its CRC Veeda phase I unit at Ampang Hospital in Kuala Lumpur, Malaysia. Having established its presence in Thailand, Synchron Research is looking at tapping the growing South East Asian market, with Vietnam being the favoured destination.

Increasing clinical trials

The number of clinical trials in the country has increased significantly. According to estimates, there are 30 CROs conducting BA/BE trials and 50 CROs looking at phase I-IV trials. Major companies into BA/BE studies are Lambda Synchron, BA Research, Veeda Clinical Research, Vimta, Bioserve, Accutest, Accunova and Lotus Labs. Only a few companies in India are into phase I trials due to issues of large scale investments in infrastructure.

Ã¢â?¬Å?The number of trials are increasing along with the number of job opportunities in this sector. This growth is giving impetus to small CROs that are just starting,Ã¢â?¬? said Prashant Patil, manager-business development, Asian Clinical Trials.

The Government of India has also initiated a number of steps to create a transparent and favorable environment for clinical trials. In 2009, the DCGI made it mandatory that all clinical trials have to be registered with the Clinical Trials Registry of India (CTRI) before any subject is recruited for the study. As of January 2011, according to the CTRI, the total number of trials registered is 1,584 as against 806 trials between January-December 2010. Ã¢â?¬Å?As part of the industry's evolution, a good number of phase II and III trials are now being entrusted to the country. Earlier, most of the trials conducted in India were in phase IV,Ã¢â?¬? said Dr Chugh. Quintiles India conducts, by far, the largest number of trials in the country.

Dr Ramanjaneya, managing director of SMO India, said the overall scenario was good in terms of the number of studies carried out, international companies coming to India and the total investment. Ã¢â?¬Å?From the regulatory side, the industry is looking for quicker approvals from the DCGI. Dissemination of correct information about clinical trials to the general public is very necessary,Ã¢â?¬? he said.

Shortage of inspectors & investigators
The most common grievance of the companies operating in the segment is the shortage of trained investigators and inspectors in the country. While data on the total number of inspectors is not available, industry observers said it was not the number but the quality of inspectors that was more important.

Ã¢â?¬Å?The inspectors in India are expected to play superman roles. They are asked by the agency to inspect everything and anything under the purview of the agency. They are expected to inspect labs, manufacturing plants, distributors, ayurvedic companies, cosmetic companies, pharmacies, biotech plants and also CROs,Ã¢â?¬? said Dr Shivprakash Rathnam, managing director, Synchron Research Services. Ã¢â?¬Å?For the good of the industry, there should be a separate wing or department for CRO inspections. They need special training to inspect GCP and GLP compliance in labs. In this way they can control the CRO industry efficiently without any ethical issues.Ã¢â?¬?

Dr Bhatt also said that inspectors need to spend time in hospitals with investigators to understand how the clinical trials are conducted. Ã¢â?¬Å?They also need to get an understanding of how monitoring and QA are carried out by the sponsors. The current experience suggests that the inspectors conduct the inspection more like policemen than professionals. The inspectors require training on how to behave professionally as quality compliance experts with the investigators and companies,Ã¢â?¬? he said.

Inspectors in India also require training on international norms and requirements. Ã¢â?¬Å?Indian CROs are inspected regularly by international regulatory bodies. During such inspections, the Indian inspectors should be allowed to participate as members of the team,Ã¢â?¬? said Dr Chugh. Ã¢â?¬Å?This would help train our inspectors and also bring Indian regulators at par with international counterparts.Ã¢â?¬?

India still faces the paucity of investigators and lack of sites. At present, a total of 2,000 investigators are overseeing clinical trials across various sites in India. Estimates point out that India requires an additional 25-30 percent investigators. Industry experts said that the way to overcome this challenge is to tap the potential in tier II and III cities and by training investigators on good clinical and lab practices at regular intervals.

The regulatory landscape
With the global market for clinical trials in India growing, the DCGI is getting more number of applications. Delay and uncertainty in approvals is now the biggest regulatory challenge. Ã¢â?¬Å?The government should look at ensuring faster approvals as slow pace is one of the main reasons why multinational companies are reluctant to invest in India,Ã¢â?¬? says Dr Ramanjaneya of SMO India. Ã¢â?¬Å?India is proving to be an attractive destination for conducting trials and the government should understand that and allow for faster approvals.Ã¢â?¬?

Mr Sinha of CliniRx Research said the delays in approvals were of significant concern in cases where India was a participant in pivotal, global, multi-centric trials. Ã¢â?¬Å?Global sponsors tend to include other South East Asian countries to avoid study program delays. The government should look into a multi-tiered approval process,Ã¢â?¬? he said. According to Dr Shiva Murthy Nanjundappa, director, CR and BD, Quartesian CR, there should be no cap on the maximum number of approvals. Ã¢â?¬Å?If they say 10 percent or 20 percent of the projects will be approved, it is unethical. It should be based on the ethical standards and safety and quality of protocols. If all the projects fulfill the need, then all of them should be approved,Ã¢â?¬? he said.

Theoretically the approval process should take about 12-14 weeks. The time-lines often get extended due to various reasons. Ã¢â?¬Å?This includes providing rationale for the number of patients to be recruited in India (percentage of patients in a protocol to the global number), providing approvals of western countries participating in the study, and providing justification for age of certain population to participate in studies,Ã¢â?¬? elaborated Dr Nair of Siro Clinpharm.

Lack of regular interaction between CROs and officials from regulatory agencies is another point of concern. Dr Shivprakash Rathnam stated that this kind of interaction was minimal or non-existent in India. Ã¢â?¬Å?They never understood each other well. Therefore, the CRO industry is suddenly getting a negative feedback and hence is in defensive mood.Ã¢â?¬?

M&A effects on India
The global landscape saw a spree of merger and acquisition (M&A) activities in 2011. The most prominent deal was INC Research's acquisition of Cincinnati-based CRO, Kendle. Before this, INC also acquired Australia-based CRO Trident Clinical Research. Some other M&As saw private equity firm Nautic Partners acquire Omnicare CR in April, Clinipace Worldwide buy Swiss CRO PFC Pharma Focus in May and private equity-owned inVentiv Health's acquisition of PharmaNet.

There are two schools of thoughts on the cascading effects of these M&As on India. On one hand, experts said this could, to some extent, lead to consolidation in the Indian industry. Ã¢â?¬Å?Consolidation was expected and is happening. It is good for

small players as they may not be able to sustain the competition,Ã¢â?¬? said Dr Nanjundappa. Consolidation will not just expand existing operations but also give CROs opportunity to gain experience. Ã¢â?¬Å?These are really interesting and will surely help the industry to consolidate its business interests. Besides that, the industry will gain experience and maturity in the long run,Ã¢â?¬? said Mr Panwar of Fortis Clinical Research. Mr Prashant Patil of Asian Clinical Trials agreed that M&As bring with them the necessary expertise that can boost a company's revenue, especially for those that are not doing well. Ã¢â?¬Å?So, on the whole they do help the industry although they create tougher competition for smaller CROs,Ã¢â?¬? he said.

It has made the market more competitive. Ã¢â?¬Å?Due to consolidations and M&A activity in recent times within the clinical research industry, the spirit of competitiveness is more as is the focus on watching over the shoulder on what competitors are doing,Ã¢â?¬? said Mr Sinha of CliniRx Research.

On the flip side, another school of experts said that these M&As could impact the existing R&D programs, which in turn will effect the Indian industry to a certain extent. Ã¢â?¬Å?The major impact of global M&As is a reduction in the number of R&D programs. This has resulted in decrease in the number of phase III trials,Ã¢â?¬? Mr Bhatt of ClinInvent said.

The trend is quite recent and it will be too early to predict. Ã¢â?¬Å?Post acquisitions or mergers, synergy looks rosier on paper than in practice and a lot will depend upon how both partners navigate their way through myriad issues lying ahead of them, including cultural and personnel issues apart from the financial ones,Ã¢â?¬? said Dr Nair of Siro Clinpharm.

Clinical trials in India

Phases	No of trials
Phase I	145
Phase II	369
Phase II	792
Phase IV	162
Total	1468

Therapy-wise distribution of clinical trials in India

Diseases	No of trials
Cancer	277
Cardiovascular	200
Central Nervous System	96
Diabetes	211
Metabolic diseases	246

Source: Clinicalstrials.govÂ (as on August 22, 2011)

Companies into drug discovery/BA/ BE studies

Sl. No.	Companies	Studies
1	Vimta Labs	BA/BE
2	Synchron Research	BA/BE
3	ClinInvent	BA/BE
4	TCG Life Sciences	Drug Discovery
5	Advinus Therapeutics	Drug Discovery
6	Aurigene Discovery Technologies Limited;	Drug Discovery
7	Lotus Labs	BA/BE
8	Accutest	BA/BE
9	Reliance Life Sciences (Clinical Research Group)	BA/BE

10	Reliance Clinical Research	BA/BE
11	Jubilant Clinsys	BA/BE
12	Fortis Clinical Research	BA/BE

Life sciences companies with CRO subsidiaries

Sl. No.	Principal /Promoter Company	CRO
1	Piramal Healthcare	Wellquest Clinical Research
2	Ranbaxy/Daiichi Sankyo	Fortis Clinical Research
3	Claris Life Sciences	Xcelris Labs
4	Intas Pharmaceuticals	Lambda Therapeutics
5	Biocon	Syngene/Clingene
6	Aurobindo Pharma	Axis Clinicals
7	Suven Life Sciences	Asian Clinical Trials
8	Alembic	Alembic Research Centre
9	Vlife Sciences	Novalead
10	TCG Life Sciences	Clininvent
11	Reliance Life Sciences	Reliance Clinical Research

Top MNC CROs in India

Sl. No.	Company	Year of Establishment in India
1	Quintiles	1997
2	PPD	2004
3	Parexel	2007
4	ICON	2005
5	Kendle	2005; now globally acquired by INC research
6	Theorem Clinical Research (formerly Omnicare Clinical Research)	2002

7	PRA	2007
8	Covance	2009
9	Pharmanet	2003; Now Acquired by inVentiv Health
10	ClinTec International	2001

By Nayantara Som (with inputs from Rahul Koul and Manasi Vaidya)