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Biocon India Group

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"Earn as you learn." For 25 years this unofficial philosophy had served Biocon well. Starting out in the enzyme business in 1978, the Bangalore-based firm had gradually expanded into the pharmaceutical industry. Expertise in manufacturing enzymes led to mass production of generic drugs, which in turn gave Biocon the experience to establish Syngene, a subsidiary contract research organization (CRO) serving the global pharmaceutical market. At each stage Biocon had built on both its recently developed capabilities and the political, biological, intellectual, and financial benefits of the Indian environment to move into new areas of opportunity. By early 2003, Biocon had parlayed earning and learning into a firm that boasted 800 employees and annual revenues of US$75 million.

Yet the time had come to consider whether this growth model was reaching its limits. In the eyes of Biocon India Group's Managing Director, Kiran Mazumdar-Shaw, Biocon's newest subsidiary, Clinigene, seemed an ideal way to capitalize on the company's technical strengths by offering services in clinical trials. There was concern, however, that Clinigene could also be an enormous distraction, consuming precious resources in an area in which Biocon had little direct experience. Moreover, if Clinigene did prove profitable, its very success could be a Pyrrhic victory: the subsidiary could rapidly outgrow its parent and damage the company's hitherto collaborative culture. The growth could even sidetrack Mazumdar-Shaw and Biocon's directors into pursuing a possibly futile dream of creating one of the only fully integrated drug discovery and development companies in India. Yet if Biocon chose not to pursue the promise of Clinigene, it might be trapped forever in the brutally competitive generic pharmaceuticals market, unable to tap its potential as an innovator. Springboard, pitfall, or detour: Mazumdar-Shaw knew that the shareholders expected her to predict Clinigene's and Biocon's future correctly, and soon.

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The Indian Pharmaceutical Industry

The Indian pharmaceutical industry had been shaped to a great extent by economic policies since independence in 1947. Initially, pharmaceutical multinational corporations (MNCs) from Europe and the United States dominated the local market. In the 1960s, India's government established local bulk drug manufacturers Hindustan Antibiotics Ltd. and India Drug and Pharmaceuticals Ltd. to compete with the MNCs' overseas bulk-drug operations for supplying local formulation plants.

In 1970, the government passed two regulations that affected the pharmaceuticals industry: the India Patent Act (IPA) and the Drug Price Control Order (DPCO). The India Patent Act prohibited "product patents for any invention intended for use or capable of being used as a food, medicine, or drug or relating to substances prepared or produced by chemical processes."[1] As a result, any drug on the market could be reproduced without retribution. The Drug Price Control Order gave the Indian government the authority to set prices for drugs sold on the local market.

Starting in its earliest days, the industry experienced phenomenal growth. A combined bulk drug and formulations output of 168 Rs. crore[2] in 1965 grew to 19,737 Rs. crore 35 years later, an annual growth rate of 15%. Roughly two-thirds of the output stayed in the domestic market, which by the year 2001 was also growing at 15% annually. The remaining one-third – 6,631 Rs. crore – went to the export market, which had a 21% growth rate.[3] By the beginning of the 21st century, over 20,000 pharmaceutical companies were operating in India.

Fueling these companies and their export market was the global pharmaceutical industry's trend toward outsourced research, development, and manufacturing. Facing slimming pipelines and escalating costs – an average of US$800 million to bring a new drug to market – major pharmaceutical firms increasingly saw outsourcing as the best, perhaps only, way to boost speed, reduce problems faced during regulatory processes worldwide, and cut costs by 30% to 35%.[4] Revenues for clinical research companies worldwide in 2000 were estimated at $7 billion and expected to grow at 30% per year.[5]

When choosing to outsource, global pharmaceutical firms tended to focus on three areas of the drug discovery and development value chain (see **Exhibit 1**):

- *Research and development (R&D)*. Drug discovery usually required considerable quantities of particular molecules with which to experiment. A contract research organization (CRO) could make target and even custom molecules to order.
- *Clinical trials*. A drug typically went through four phases of clinical trials to determine whether it worked consistently, for a large population, without toxicity or major side effects. (See

[1] "Intellectual Property Rights in India", www.indiaonestop.com (April 2003).

[2] 1 crore = 10,000,000 Indian Rupees = approximately US$200,000.

[3] http://www.indiainfoline.com/sect/phfo/cu01.html; http://www.indiainfoline.com/bisc/thre.html.

[4] Swati Chaturvedi, "Outsourcing in Pharmaceutical Industry," Frost & Sullivan (2008), http://www.bionity.com/articles/e/49803.

[5] Kiran Mazumdar-Shaw, "The Biotechnology Boom: Can India Meet the Challenge?", speech to the Asia Society (March 13, 2001).

Exhibit 2.) A CRO might offer services in some or all phases, including finding the patients, working with hospitals and doctors, and managing the data.

- *Manufacturing*. Once the drug was tested and approved, it could be produced in bulk according to the set formula and process. Manufacturing, though not always simple, tended to be the least value-added of the three outsourcing areas and thus the most price-competitive.

By the year 2000, leading pharmaceutical firms were outsourcing roughly 25% of all their work in these areas. [6]

Increasingly the country of choice for outsourcing of pharmaceutical products, whether finished or intermediate, was India. India had a large pool of English-speaking scientists and professionals who were well-educated and well-trained. They were also cheap: a Ph.D.'s salary in India averaged approximately $15,000, while the equivalent in the United States was closer to $100,000.[7] India's population was genetically diverse, which provided researchers with easily accessible ethnic genetic structures and a well-balanced group from which to recruit for clinical studies and to whom companies could eventually sell their products.

Clinical trials services, in particular, were emerging as prime targets for outsourcing to India. Clinical trials represented the most expensive part of the drug development chain: nearly 60% of total development costs, of which nearly 70% went to patient recruitment and medical personnel.[8]

Meanwhile the Indian government had recognized the tremendous growth potential of the medical biotech industry, and so had set up both internal and external supports to encourage the industry's growth, especially in the areas of R&D and biotech facilities.[9] In 1986, the federal government created the Department of Biotechnology within the Ministry of Science and Technology. Some Indian states, such as Karnataka, had taken the initiative to build international-standard biotech parks. In addition to building facilities for research and development, business incubation, and biotech companies, Karnataka also eased tax, duty, and lease obligations for residents of the biotech parks.[10] Biotech was also beginning to attract venture capital funding, although it remained the minority source: 10%, or about 300 Rs. crore, of outside funding was believed to come from VCs, compared to 40% from banks, government sources, and internal resources. Most Indian biotech and pharmaceutical firms counted on organic growth or acquisition, not outside funding, to fuel any expansion.

[6] Mazumdar-Shaw, op. cit.

[7] http://lists.essential.org/pipermail/ip-health/2001-December/002504.html.

[8] The Tufts Center for the Study of Drug Development, cited in http://www.pfizer.com/research/clinical_trials/clinical_trials.jsp (October 2008); Chaturvedi, op. cit.

[9] http://dbtindia.nic.in/overview.html (March 2003).

[10] http://www.bangalorebio.com/docs/BiotechPolicyf.doc.

The Biocon India Group

Biocon India was established in 1978 by Kiran Mazumdar-Shaw, the Managing Director, as a joint venture with Biocon Ireland to bulk manufacture enzymes. Mazumdar-Shaw had begun her studies planning to become a master brewer like her father, an unusual occupation for a Brahmin family from the alcohol-prohibiting state of Gujarat. But after graduate school, when she found that the industry wasn't ready for the first woman master brewer, Mazumdar-Shaw turned to business opportunities using fermentation processes to produce enzymes for various purposes. From a shed in an undeveloped part of Bangalore, she began producing mass papain and isinglass, two enzymes that used raw materials which were already abundant in India and necessary for the production of beer. In 1989, Biocon Ireland was acquired by Unilever. As part of Unilever, Biocon began producing enzymes for Unilever's food business. In 1998, Biocon India bought out Unilever's share in the company and became an independent, privately owned entity.

Biocon

Central to Biocon India's success in its early days was its ability to recreate a fermentation process that was dominated by Japanese companies in the early 1980s. Biocon's Chief Scientist, Shri Suryanarayan, visited Japanese factories to understand their methods for the solid state process of fermentation, and developed a pilot plant in 1989. By 1995, a second plant was required, three times the size of the original plant. During this time, Shri and his R&D team built a unique and subsequently patented fermentation reactor, called the PlaFractor™, which greatly simplified the fermentation process and created greater control, thereby reducing waste and inefficiency.

It soon became clear that the capabilities and resources developed to produce enzymes could be easily applied to the lucrative healthcare market. In 1997 Biocon India entered the $12 billion market for generic statins, a group of drugs targeted at lowering cholesterol. It launched Lovastatin in Canada, Mexico, Eastern Europe, and Southeast Asia. After Merck's patent on the drug expired in 2001, Biocon took the opportunity to sell in all countries. With Lovastatin and other statins – Simvastatin, Provastatin, Atorvastatin, etc. – Biocon became the first company to produce healthcare products through solid state fermentation.[11]

Syngene

Meanwhile, by the early 1990s, Biocon's scientists were developing significant abilities not just as brewers or manufacturers but as chemical and biological researchers. In 1994, Mazumdar-Shaw and her team therefore decided to convert that expertise into a new business, Syngene. A separate company within the Biocon India Group, Syngene was the first Indian CRO to serve pharmaceutical and biotech companies – primarily international – in the areas of synthetic chemistry, molecular biology, and informatics. Syngene provided its clients with bulk volumes of target molecules, reagents, and custom molecules for early-stage drug discovery and development. In the process,

[11] "The World of Biocon," *BusinessWorld* (December 2, 2002).

Syngene was building the skills and infrastructure to discover original molecules. Here again was the "earn as you learn" philosophy, a philosophy that helped foster a strongly collaborative culture throughout Biocon India.

The Biocon India Culture and People

Biocon India prided itself that the cornerstones of its culture were openness, trust, and collaboration. Visitors often remarked that everyone – senior leaders, key scientists, lab employees – constantly walked in and out of the buildings and corridors, discussing ideas and exchanging views with colleagues from Biocon and its subsidiaries. Biocon valued its people's accessibility, and as Tara Jayaram, Head of Quality Assurance, noted, "Kiran [Mazumdar-Shaw] encouraged us to collaborate from the beginning, and we are passing on the same corporate values to our people as we grow." Chief Scientist Shri Suryanarayan took pride in being available by cell phone rather than hunkering down in his office: "This is how we at Biocon India find our opportunities."

Employees were encouraged to avoid hierarchies in the interest of doing the best job they could. "At [Biocon India], we work without hierarchies," explained Jayaram. "I don't need to go through layers to reach the person that I need; that is not the culture we have here. It is perfectly acceptable, and encouraged in fact, that people go directly to the person they need to reach without waiting for permission, approval, whatever. This is how it was when I joined, 15 years ago when we were only 43 employees, and this is how it continues to be today."

A key element of the Biocon India open culture was trust among colleagues. "Take away people's insecurities," pointed out Mazumdar-Shaw, and creativity and passion would flow. Shri Suryanarayan estimated that it took an average of two years to strip away a new hire's wariness and see him fully embrace the collegial culture at Biocon. To ease and streamline this acceptance, Biocon had invested in both numerous creature comforts – special transportation, free lunch and snacks, on-site health checkups, etc. – and a strongly meritocratic hiring and performance management system. Performance rewards were based not merely on an individual's achievement but on the performance of her team, so as to foster excellence and reinforce collaboration.

Thanks to its cultural and financial successes, Biocon India had become a highly desirable place to work, allowing it to hire the best minds in the sciences. According to Nirupa Bareja, Head of Human Resources, "We want people with scientific backgrounds because it makes it much easier for people to talk to each other. They are familiar with the jargon, accustomed to scientific concepts, and this facilitates dialogue and fitting in." Importantly, Biocon India Group's people were also business-oriented, typically coming from industry backgrounds (Novo Nordisk, Astra Zeneca, etc). Yet senior managers were keenly aware that background and industry experience alone were not enough. As Jayaram remarked, "I rejected a candidate that was exceptional in his scientific background, because he did not have the collaborative attitude that is so essential to Biocon."

Clinigene

Emboldened by the strength of Biocon India's culture and its two subsidiaries, Mazumdar-Shaw and her senior team developed a vision: to become a fully integrated drug discovery and development company. The Biocon India Group already possessed or was developing the capabilities for conducting research and development, manufacturing pharmaceuticals, and marketing its products. Besides animal testing, Biocon's missing link in the traditional pharmaceutical value chain was the ability to run clinical trials (see **Exhibit 2**).[12]

Thus in the year 2000 Biocon India launched a new subsidiary: Clinigene. Clinigene sought ultimately to offer a broad range of clinical trial services, recognizing that drug development could span two different areas that consequently required different types of clinical studies. Generally, generic drugs required bio-equivalence and bio-availability (BE/BA) clinical studies to prove that the generic drug worked as well as the off-patent original drug. But for new drugs, much more elaborate clinical trials had to be conducted.

In the few years since its launch, Clinigene had focused not on organizing trials but on clinical lab services, BE/BA studies, and partnership coordination with hospitals. As Chief Operating Officer Dr. A. S. Arvind noted, "By building up capabilities in conducting BE/BA studies and clinical trials, Clinigene fills a key missing gap in the drug discovery and development value chain for Biocon." According to Dr. Nadig, Vice President of Medical Services, the services contributed to "Clinigene's ability to conduct high quality clinical research from start to finish."

Yet launching Clinigene raised multiple concerns, largely because it was not clear how soon Biocon India Group would need its capabilities. Biocon India was still several years away from developing its own drug molecules. Rather than put Clinigene on hold until in-house demand kicked in, Mazumdar-Shaw expected Clinigene to sustain itself with external clients in the CRO business. More than two years after Clinigene's creation, doubts remained about the risks it posed, risks particularly in market positioning, culture, publicity, and ethics.

Market Opportunity

Clinical research in India was beginning to take off, and was forecast to explode during the next decade. Contract research organizations (CROs) were emerging as the key players in this market. Lotus Labs, for instance, was growing at a rate of 100% per year, and one study predicted that Indian CROs would grow from 0.7% of the global market in 2002 to 20% in 2010.[13] Within India, CROs based in Bangalore accounted for 2% to 3% of the total CRO activity in India, which was estimated at Rs. 250 crores in 2000, and were expected to continue to grow over the next few years.[14]

[12] Animal testing was currently outsourced, and there were good reasons to continue doing so. It required different capabilities and investments, which were very specific to the animals, and from which it was difficult to leverage the resources for other activities.

[13] *BusinessWorld* (October 14, 2002).

[14] Vijaya K., "Bangalore: Jostling with the game of clinical research," Expresspharmapulse.com.

This high growth potential could represent significant opportunity for Clinigene to reap revenues as a CRO player. On the other hand, Clinigene would have to position itself carefully. Indian CROs were focused primarily on serving the need for BE/BA studies in the market, and although a few were beginning to offer services in clinical trials, some pharmaceutical MNCs were wary of outsourcing such critical and sensitive tasks to a largely unproven Indian industry. Meanwhile foreign CROs, such as Quintiles, and the in-house data management centers of big pharmaceutical companies, such as GlaxoSmithKline and Pfizer, were focusing their efforts on serving higher-value needs of the market, particularly data management and Phase III clinical trials (see **Exhibit 3**). Clinigene's current capabilities positioned it in the low- to medium-value segment of the value chain. Moving up the value chain might be more profitable in the long run but would entail significant costs, both financial and cultural.

Organizational Culture

Mazumdar-Shaw and her team also recognized that Biocon India Group could end up a victim of Clinigene's success. Were it to succeed in capturing a significant slice of a growing market, Clinigene could conceivably grow to a size that overshadowed Biocon and Syngene. Such aggressive growth meant the diversion of time and resources. It also meant a large influx of new employees and little time to inculcate the Biocon culture – particularly the two years cited by Shri Suryanarayan. New organizational designs and procedures might need to be introduced and enforced, in a company that prided itself on loose structures and casual hierarchies. Moreover, the nature of clinical trials required that much of the work be done in partner hospitals. Physically dispersed among trial sites, rarely able to wander the corridors or enjoy Biocon's facilities, the Clinigene employees could easily end up disaffected, or at least loyal only to Clinigene rather than its parent Group.

Publicity and Ethics

Clinical trials dealt with humans, and thus carried significant risk to the CRO sponsoring the clinical trial. Although rigorous and stringent conditions were imposed by the industry and government bodies, the risk still fell upon the company running the experiments. Furthermore, this risk could have multiple dimensions: financial losses from failed clinical trials and compensation to victims, ethical challenges for employees eager to achieve results and unsure where subjectively measured "good ethics" lay, and damage to reputation and even organizational survival if questions were publicly raised about the company's impact on humans and society.

In the media, Biocon India Group had enjoyed coverage ranging from quiet approval to fawning praise. But if a Biocon subsidiary were to run clinical trials in India, a developing nation with a significant population living in poverty, it could receive negative and destructive attention for the first time. The issue of human participation in clinical trials, never a simple topic, grew far more complex when the use of illiterate and arguably ill-paid subjects raised questions of patient consent and abuse. In the United States, for example, any actual or perceived infringement of clinical trials ethics – not

providing informed consent, preventing control-group subjects from seeking medical treatment, etc. – frequently provoked references to the Tuskegee Syphilis Study (1932-1972), "arguably the most infamous biomedical research study in U.S. history."[15] As some Clinigene staff had recently pointed out, clinical trials could easily become politicized, particularly when a Western MNC used an Indian company like Clinigene to test drugs on Indians for largely Western use. In its desire to grow into a model firm – a rare Indian example of a fully integrated drug discovery and development company – Biocon India Group might find itself accused of deliberately inviting neocolonial imperialism, foreign exploitation, and subjugation to the West.

Seeing the Future

Mazumdar-Shaw was excited by Clinigene's bright prospects. Yet she also recognized the importance of caution. True, Clinigene was making money, attracting clients, and filling gaps in the Biocon India Group value chain. But it also significantly increased the company's risks, risks not just of embarrassment or failure but of dangerously swift success.

If Biocon India Group were to grow, then it needed to expand – to Mazumdar-Shaw this seemed certain. She could push Clinigene to get all the business it could, even though it could end up dwarfing the rest of the company and sapping the core culture. Alternatively, she could ensure that in the short term Clinigene only took business for services that were relatively safe, albeit lower-value, and waited to run clinical trials until Syngene was ready to test its own original molecules. Perhaps Clinigene was sidetracking the firm, forcing its senior team to run a start-up all over again; if so, the simplest (though more immediately expensive) approach would be acquisition: buy a budding clinical services CRO, preferably one that would add expertise and client relationships but could be kept at arm's length from the Biocon culture. "Earn as you learn" had worked in the past. Whether the one would soon sabotage the other: that was part of the future Kiran Mazumdar-Shaw now had to predict.

Study Questions

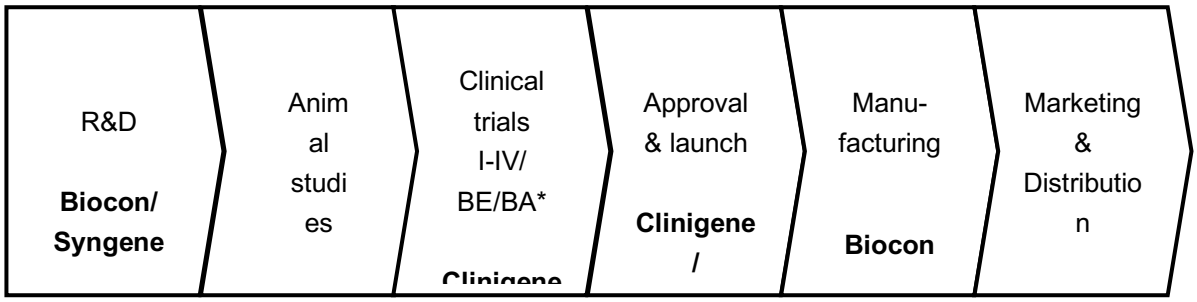
1. What are the advantages and disadvantages of starting and operating a pharmaceutical firm in India?
2. Is the Indian CRO market attractive?
3. What is the best way for Biocon India Group to expand?

Case Write-up Question

What is the best way for Biocon India Group to expand, and what factors should it consider?

[15] http://en.wikipedia.org/wiki/Tuskegee_Study_of_Untreated_Syphilis_in_the_Negro_Male (October 2008).

Exhibit 1 Typical Drug Development and Discovery Value Chain, including Services of Biocon India Group's Companies



* BE/BA: Bio-equivalence/bio-availability.

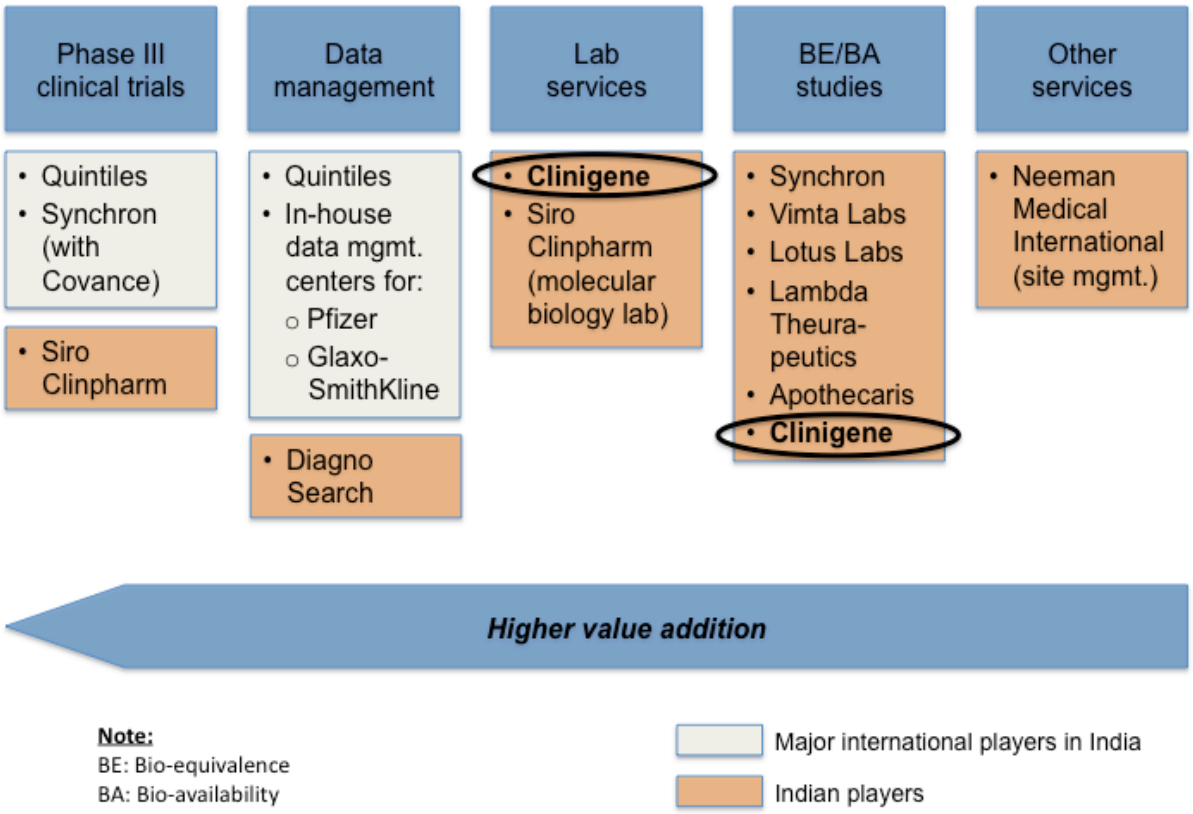
Source: Case authors.

Exhibit 2 Clinical Trials in India

Phase	Objective	Status	Criteria for Subject Selection	Number of Subjects	Duration of Study	Cost in India, compared to US
I	Determine whether drug has toxic effects on healthy humans	Allowed only for molecules discovered in India	Healthy males between ages of 20-30 years	20-100	0.5-1 year	<50%
II	Determine whether drug works and if there are any short-term side effects	Allowed if Phase I trials are conducted in India	Volunteers with indication	A few hundreds	1-2 years	<50%
III	Determine efficacy of drug over a large population and if there are any long-term side effects	Allowed if Phase II trials are conducted in India	Volunteers with indication and additional medical conditions	A few hundreds to a few thousands	2-5 years	<50%
IV	Test existing medicines in new dosages for effective-ness against other ailments/ conditions	Can be conducted	Volunteers with indication	A few hundreds to a few thousands	1-2 years	N/A

Source: Study by Ernst & Young, BusinessWorld *(October 14, 2002), 40.*

Exhibit 3 Indian and Foreign Contract Research Organizations (CROs) in the Clinical Research Market



Source: Case author interviews; study by Ernst & Young, BusinessWorld *(October 14, 2002).*