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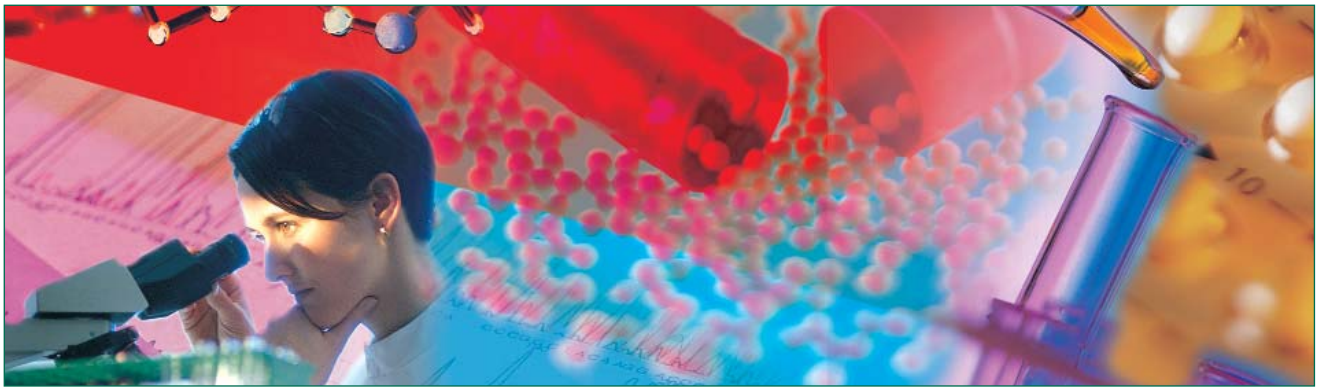
Harnessing the Power of India

Rising to the Productivity Challenge in Biopharma R&D



In recent years, the biopharmaceutical industry has come to recognize that one of its key challenges is to improve R&D productivity. If companies are to address this challenge in earnest, they need to develop optimal R&D strategies. But as the R&D environment continues to grow more and more complex, doing so is becoming increasingly difficult.

What's needed initially is an organizing framework to make sense of the bewildering variety of options. Our own framework specifies five sites for intervention: front-end innovation; external sources; the R&D engine; the political and regulatory environment; and people, team, and culture. By focusing on these five sites, companies can clarify the issues facing them and home in on the strategies best suited to their distinctive needs.

When it comes to retooling the R&D engine itself, one approach is to pursue an offshore R&D strategy—especially in China and India. This report explores the opportunities and risks inherent in conducting biopharmaceutical R&D in India; another recent report examined the China option. Taken together, these reports reveal the unique advantages presented by the two countries. Specifically, the key impetus for offshoring biopharmaceutical R&D to China is gaining enhanced access to a national drug market that promises in the long term to rank among the five largest in the world. India, on the other hand, delivers an established vendor base that promises to immediately turbocharge global R&D engines for biopharmaceutical companies.

These reports are part of a larger series of studies on ways to improve R&D productivity. They follow our introductory report, Rising to the Productivity Challenge: A Strategic Framework for Biopharma, *which presented an overview of the framework and its background.*[1]

Expertise and entrepreneurship abound in India, positioning the country as a powerhouse in R&D. Home to some of the top technical universities in Asia, as well as a large community of entrepreneurial, Western-trained graduates, India teems with resourceful scientists and managers. Notably, nearly every one of these experts is at ease with the English language. This combination creates a business environment rich in enthusiasm and support for global collaborations in R&D.

Small wonder, then, that a 2004 survey of senior executives across all industries ranked India among the top three countries where companies planned to spend the most R&D dollars over the next three years.[2] Certainly this vote of confidence comes as no surprise to the Indian pharmaceutical industry. The domestic players that once antagonized multinational pharmaceutical companies (MPCs) now attract them in droves.

Historically, the Indian pharmaceutical industry focused almost exclusively on generics, operating under a regime that recognized *process patents* but not *product patents*. Under this regime, local companies legally manufactured prescription drugs that were protected outside of India by composition-of-matter patents. As long as the Indian companies deployed an original process to produce these otherwise protected drugs, they operated without fear of reprisal from the Indian government. In this way, the industry came to acquire excellent capabilities in process reengineering—and a tarnished reputation among MPCs.

In early 2005, with pressure from the international community mounting and the World Trade Organization threatening sanctions, India finally instituted a new regime of product patents. This change afforded MPCs the same intellectual property (IP) rights in India that they enjoy elsewhere by extending patent protection beyond manufacturing processes to the drug molecules themselves. Interestingly, the new patent regime did not leave the domestic industry reeling; Indian companies had anticipated the move and shifted their focus from generics to innovative drug discovery. Indeed, local pharma companies have already claimed a chunk of the future innovative market for themselves, boasting more than three dozen new chemical entities (NCEs) in the preclinical phase or in early clinical trials.

The combination of improved IP protection and local pharma companies embarking on innovative R&D projects of their own has changed the way MPCs think about India. The very same MPCs that once denounced Indian pharmas now partner with them—and increasingly entrust them with vital R&D assignments. While the initial objective of such collaborations may have been to access India's proven capabilities, such as process scale-up, MPCs facing declining productivity in their internal R&D departments are now broadening the scope and nature of their relationships in India. In our view, there are three primary advantages to shifting some proportion of biopharmaceutical R&D to India:

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- *Alleviating Bottlenecks in the R&D Pipeline.* Conducting R&D in India can ease backlogs and capacity shortages, particularly in the labor-intensive phases of early-stage chemistry and of data management during clinical study. By marrying proven capabilities in these areas with a broad and experienced vendor base, India offers MPCs a flexible approach to both capacity and pipeline management.

- *Reducing R&D Costs.* Established Indian vendors pay wages that are typically less than one-third—and may be as little as one-fifth—of those paid by their counterparts in the United States, Europe, and Japan. This less expensive talent pool can be accessed through a range of business models, from fee-for-service vendor contracts all the way to MPC-owned R&D centers.

- *Accelerating Clinical Trials.* India's population provides MPCs with an ideal patient base for drug studies. The majority of the country's more than 1 billion people reside in or near major urban centers and are therefore easily reached, recruited, and monitored. Many are also "treatment naïve"—that is, they have not been exposed to other medicines or medical treatments.[3]

The benefits of offshoring R&D to India go hand in hand with certain challenges, however, and MPCs that pursue opportunities in the country must also be aware of the pitfalls. Specifically, players must protect their IP rights, cut through now-legendary red tape in administration and regulation, and overcome an inadequate public infrastructure. How well MPCs navigate the path to success in India will no doubt depend on how well they understand the lay of the land.

India's Strengths Translate into Attractive Opportunities

India's greatest allure is its promise of near-immediate gratification for MPCs that seek to enhance chemistry-related activities and accelerate clinical trials. Because Indian vendors boast

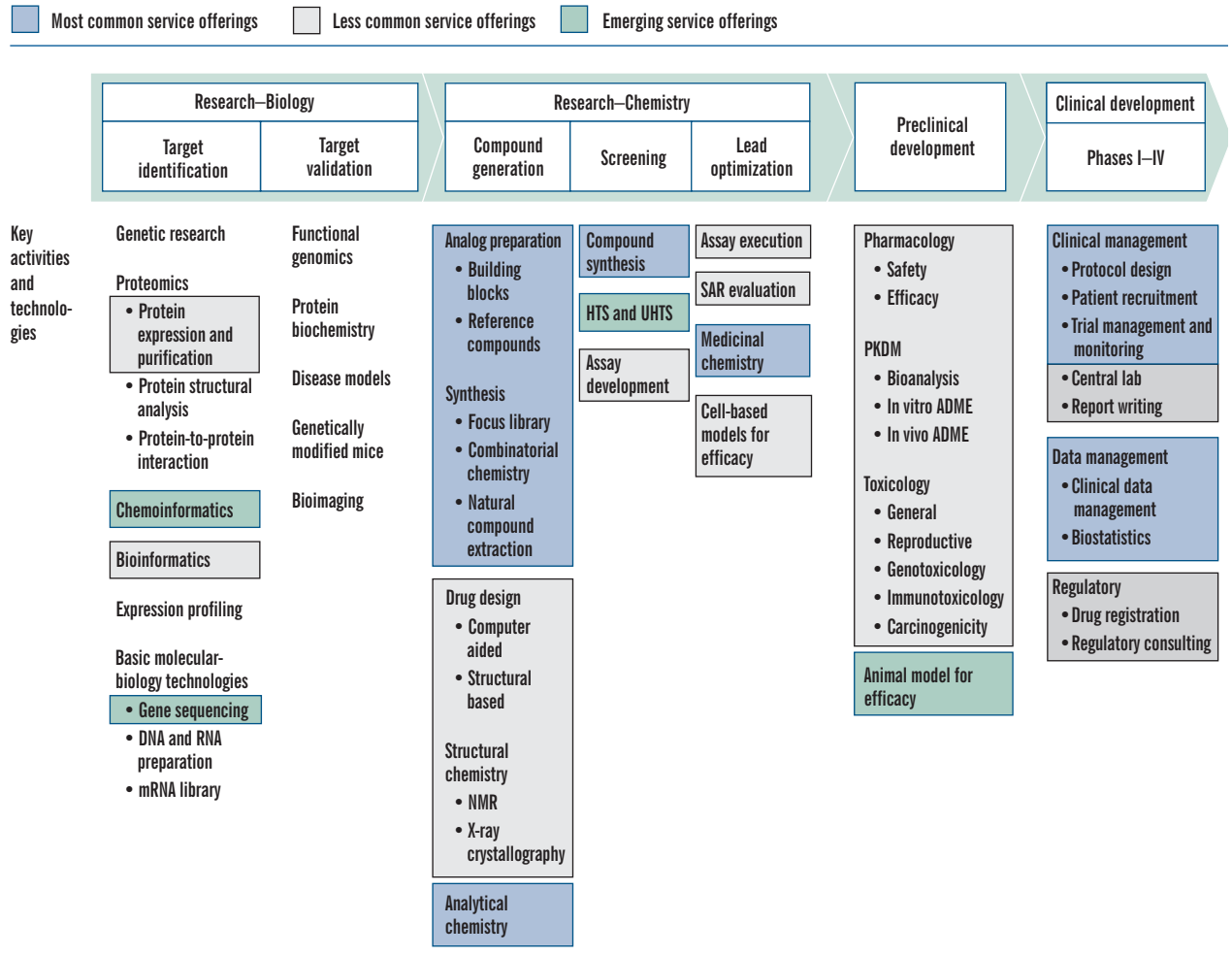
established capabilities in these areas, MPCs can tap into them—and reap their benefits—quickly. Domestic expertise is also growing in the areas of preclinical trials and biology-related activities. (See Exhibit 1.)

Proven Prowess in Chemistry and Data Management. Drawing on the country's rich legacy in process reengineering, Indian vendors in biopharmaceutical R&D have developed capabilities in scale-up, process optimization, and manufacturing. The strong domestic capabilities in data management and information technology have long made India an attractive location for the labor-intensive activities involved in clinical data management and biometrics. MPCs have eagerly availed themselves of these skills, securing high-quality output in chemistry on a par with that of U.S. labs—but at as little as one-fifth the cost.

Simultaneously, India's recent shift to drug discovery has triggered the domestic pharmaceutical industry to expand its repertoire in chemistry. Over the past three years, with tax incentives providing an impetus to boost investment in their own R&D, the ten local companies with the highest revenues have more than doubled their R&D budgets—from an average of 2.8 percent of sales to 7 percent—and many have similarly doubled the number of R&D personnel. The size and scope of chemistry departments have expanded accordingly, reinforced by an influx of repatriated Indians. Drawn to the

EXHIBIT 1

VARIOUS OPPORTUNITIES EXIST ALONG THE VALUE CHAIN



SOURCE: BCG analysis.

new opportunities in their homeland, these professionals are returning, armed with expertise in managing complex and high-end chemistry activities developed through years of working in MPCs.

An increasing number of Indian vendors are building end-to-end chemistry offerings and selling them as a bundle of services in drug design, analytical chemistry, and assay development. Others are combining technical skills with their familiarity with local business practices and regulations to offer joint-venture and build-operate-transfer opportunities for MPCs seeking a longer-term presence in the country.

Speed and Agility in Clinical Trials. India has rapidly become a preferred destination for clinical trials, and the pace at which this shift has occurred is striking. India's rapid growth on the world stage has been fueled in part by global contract research organizations such as Quintiles Transnational. Quintiles has been conducting global and local clinical trials from its facility in India since 1997. In a recent quality audit, the U.S. Food and Drug Administration rated this facility on a par with top facilities in the United States and Europe.

But by far the biggest factor driving clinical studies to India today is the critical competitive advantage that the country holds over Western locales. Because of the nation's vast and highly dense population, patients in India can be enrolled more quickly, in greater numbers per clinical site, and at a lower cost than nearly anywhere else.

Clearly, MPCs' enthusiasm for India as a trial locale is justified, yet it still should be kept in check. First, in the most desired sites, the public infrastructure is stretched nearly to full capacity, and investments will be needed to accommodate further demand. Second, offshoring later-stage trials to India does not position an MPC to enhance its access to a large drug market—in contrast to other emerging locales, such as China, where offshoring has this advantage. Given its traditional reliance on generics and its focus on low prices, the Indian market for new ethical drugs will, at best, stay in the middle of the pack relative to other promising locations for offshoring.

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Emerging Skills in Preclinical Trials. As India's capabilities in preclinical research develop, MPCs are becoming increasingly comfortable outsourcing various substeps to Indian vendors. But offshoring preclinical studies from end to end is not a practical option in the near term.

Indian services in preclinical trials have evolved in response to two moves by local companies. First, many vendors have been upgrading labs and vivaria, the centers that manage and house research organisms and samples. Second, many have also been developing expertise in conducting pharmacokinetic, drug-metabolism, and toxicity studies in rodents and, to a lesser extent, in dogs. By 2004, Indian pharmaceutical companies had already advanced some 37 NCEs of their own into preclinical trials or later development stages.

Traditionally, MPCs approached the preclinical phase in India with trepidation, since approvals for such trials demanded a great deal of time and labor—at least by U.S. and European standards.[4] Thanks to legal gains, applications proceed more smoothly today, and MPCs can expect reasonably prompt approval for proposed trials. Despite this progress, however, India still has few facilities in which to study non-human primates and few labs that meet Western good laboratory practice (GLP) standards.[5]

A Long-Term Option on Biology. Considering that Indian pharmaceutical companies focused almost exclusively on process reengineering for decades, it isn't surprising that their capabilities in biology do not create a significant offshoring opportunity in the near term.

Local industry has, however, been collaborating with the government to sow seeds that will bear fruit in the biology arena in the long term. Over the past five years, for example, India's Department of Biotechnology

has spent more than $230 million to advance the biotech space. The agency has spread its investments across local pharmaceutical companies, public projects establishing biotech parks, and educational institutions building or expanding graduate programs in biology.

The Risks—Although Real—Can Be Mitigated

If India seems an obvious choice for offshoring R&D, it is not without its challenges. Even as the country promises MPCs major cost savings, smoother-flowing pipelines, and expedited clinical trials, it also exposes them to several risks. India is still struggling with a reputation for weak IP protection, a resource-draining bureaucracy, and a public infrastructure that is already groaning under the weight of a burgeoning high-tech industry.

Still, the overall risk-and-return profile for offshoring in India is favorable. India's challenges are hardly menacing, and they are declining as policymakers and industry players strive to remove obstacles. They are also easily mitigated.

Protection for IP Rights. Under the new regime of product patents, Western-style protection for IP rights is now in force in India, but skeptics question whether it will be enforced. Many MPCs have expressed misgivings about how consistently and thoroughly the new laws will be applied.

No doubt, caution is warranted about some elements of the laws. The extent to which the laws will uphold exclusive marketing rights, for instance, remains to be seen. But serious concerns may be overstated and should not cause MPCs to rule out involvement in India.

In reality, any intellectual property generated in India receives full protection in European and U.S. markets under those countries' regulatory frameworks. Furthermore, India's Contract Act provides alternative statutory protection in India, particularly for sensitive R&D data and know-how from the discovery phase. The powers created by the act and its related laws correspond closely to those of similar statutes in the United Kingdom.

India's challenges are hardly menacing and are declining as policymakers and industry players remove obstacles.

Although the laws have not yet been tested in pharma cases, precedents in the outsourcing of IT and business processes prove that they can be enforced effectively. Finally, MPCs can take steps to prevent IP-rights issues from arising at all. For example, they can require local vendors to assign a researcher exclusively to a single project, maintain communication firewalls between projects, and even keep client names confidential.

Bureaucracy. The famously slow and heavy hand of Indian bureaucracy presents a daunting challenge. Certain documentation requirements—for exporting human tissue and blood samples, for example—exceed those in the United States and Europe. Furthermore, some approval procedures remain frustratingly lengthy, such as those for breeding or importing genetically modified animals.

In fairness, however, the burden of India's bureaucracy is being reduced, especially for preclinical and clinical trials. Approval times for these trials are typically limited to three or four months. In general, the government is taking steps to make it easier to execute biopharmaceutical R&D, and any residual stumbling blocks are being cleared. For example, the government is sponsoring the creation of two breeding centers that will supply genetically modified animals to Indian vendors. Furthermore, facilities for testing nonhuman primates are accessible—beyond the private sector—through government-funded research centers such as the Central Drug Research Institute in Lucknow.

Still, until the thicket of red tape thins out significantly, MPCs can avoid getting caught by partnering with savvy local vendors, as Altana Pharma has done. To establish a foothold in India, Altana formed a joint venture with Zydus Cadila in 1998, thereby achieving a relatively smooth market entry into the country. In 2003, Altana established a wholly owned subsidiary

in India—to which it later transferred the development activities of the joint venture.

Infrastructure. The public infrastructure in India's largest metropolitan areas, the so-called first-tier cities, adequately meets the demands of clinical trials and other biopharmaceutical R&D. But as clinical trials gain in popularity, MPCs will need to offshore their work to second-tier cities, where companies are not always ensured adequate hospitals—to say nothing of a reliable source of electricity and water and a sound system of roads. India will therefore need to accelerate its pace of development if it is to dominate as the preferred location for global clinical trials. Fortunately, the country's infrastructure and logistics are already improving, in keeping with its general economic surge.

Plugging into India and Enhanced R&D

Deciding *whether* to engage in India is not nearly as difficult as deciding *how.* Which services would best support one's strategy? Which business model would be most likely to foster success?

On the basis of our experience with clients and our own research, we have found that there are two general options for harnessing India's capabilities in R&D. The first is an activity-based approach we call cherry picking; the second is a project-based approach that deconstructs the value chain for delivering innovation. MPCs can choose between these approaches or combine them in any number of ways. Then, once they have determined how opportunities in India can advance their global strategy, they must decide on the right business model for harnessing those opportunities. (See the sidebar below.)

Cherry Picking. We define cherry picking as the process of selecting individual activities, typically those that are routine and labor intensive, for offshoring. Under this approach, through vendor arrangements or captive facilities, a collection of discrete activities across multiple projects or therapeutic areas are conducted in India at a significant cost savings compared with the cost of using domestic vendors or conducting these activities in-house. As the capabilities of vendors expand and MPCs gain experience and increased comfort working in India, the number and scope of these efforts

A UNIQUE FORMULA FOR INVESTING IN INDIA

AstraZeneca (AZ) began blazing a trail into India in 1984, when drug discovery was still in its infancy in the country. AZ established a *captive base,* an R&D center that since 2000 has focused on developing a drug for tuberculosis. Later this year or early next, the center is expected to launch AZ's first drug targeting TB, a product that has the potential to reduce the duration of treatment for the disease.

Because the R&D center in India has exceeded expectations, it will likely be expanded, but AZ's investments extend beyond the captive facility. The company also makes use of a *collaboration model* by pursuing shared-development programs that draw on the R&D capabilities of Indian players. For example, AZ has joined forces with Torrent Pharmaceuticals to develop a drug for hypertension. Under this arrangement, AZ's R&D headquarters in Sweden provided the target, and Torrent is handling the full gamut of chemistry activities as well as preclinical and early-stage clinical trials.

Other MPCs, such as Novartis, have taken another tack, initially keeping Indian involvement at arm's length and opting for a pure *outsourcing model.* This move allowed Novartis to take a highly simplified approach to offshoring large volumes of custom synthesis and analog preparation to Indian vendors.

The number of R&D vendors in India continues to rise, the range of their capabilities continues to expand, and the chemistry that is being outsourced is growing increasingly complex. For example, the Life Sciences Division of the Indian company Talent Capital Group was recently awarded a contract that will engage 60 of its employees full-time on lead generation, lead optimization, and early animal studies for an MPC.

increase. Tasks commonly offshored to India today include medicinal and analytical chemistry, drug design, data management, and the implementation of clinical studies.

Deconstructing the Value Chain. With so many promising leads now emerging early in the R&D process, MPCs are finding downstream workflows jammed. An approach that deconstructs the value chain seeks to ease the bottlenecks in MPC pipelines. It is exemplified by shared-development agreements between MPCs and Indian pharmaceutical companies, such as recent notable deals between GlaxoSmithKline and Ranbaxy Laboratories and between AstraZeneca and Torrent Pharmaceuticals. In such collaborations, an MPC provides a target or lead-related information, handing over considerable control to the Indian partner. The vendor then assumes responsibility for the project's end-to-end lead selection and optimization, for selected preclinical activities, and for early clinical trials. The primary advantage of this approach for MPCs is that it provides a cost-effective and flexible solution to expanding capacity.

Choosing the Right Business Model. When it comes to a strategy for investing in India, one size does not fit all. Each MPC must establish its own formula, taking into account variables such as previous offshoring experience, concerns about security and control, aversion to risk, and budget. But the most critical determinant of a company's chosen approach is the nature and scope of its planned activities. For example, clinical trials, data management, or less complex chemistry activities might be safely outsourced to an established local vendor. Advanced chemistry work or preclinical trials, in contrast, might require a local collaborator with proven end-to-end capabilities or a captive facility tooled with top-notch equipment and staff.

As MPCs scale up their R&D offshoring, they will eventually require a mechanism—most likely a local center—to coordinate the myriad vendors and collaborations. Instituting such a center will mark their switch to an *integrated offshoring model*—a holistic approach that seeks to fully exploit the opportunities in India by balancing collaborations and vendor-based relationships while also building smaller captive R&D bases for specific priority activities. To date, no MPC has attained this state, but a select group, including AstraZeneca, seems to be evolving toward it. This model also appears likely to emerge as the preferred option in the near future.

In the more distant future, a fully mature model—one that closely resembles the model already in operation at several top multinationals in other industries—is likely to dominate. (See the sidebar above.) We believe that biopharmaceutical companies will follow the evolutionary path set down elsewhere, progressing beyond opportunistic approaches such as cherry picking to elevate R&D facilities in India to the status of integral and critical operations. Under this scenario, the typical Indian center of an MPC would develop world-class, end-to-end capabilities and, within the next decade, would emerge fully assimilated into the MPC's global R&D

GE's R&D CENTER: A LIGHT BULB GOES ON IN INDIA

To test the R&D waters in India, General Electric launched its John F. Welch Technology Centre in Bangalore in 2000. For the first three or four years, the center remained clearly subordinate to its U.S. counterpart. The group in India worked on projects that originated in the United States, took direction from project managers located there, and received their training during regular visits from senior managers based in the United States. In sum, the center supported projects rather than ran them.

Today is a very different story. The $80 million facility now employs more than 2,200 scientists, researchers, and engineers, and its domain owners and experts are based in India. It has graduated into a multidisciplinary hub in its own right—one of GE's largest outside the United States. The John F. Welch Technology Centre focuses 20 to 25 percent of its efforts on pure research and competes confidently with other R&D hubs for top-drawer projects in product development.

network as a full-scale R&D hub. (See Exhibit 2.)

* * *

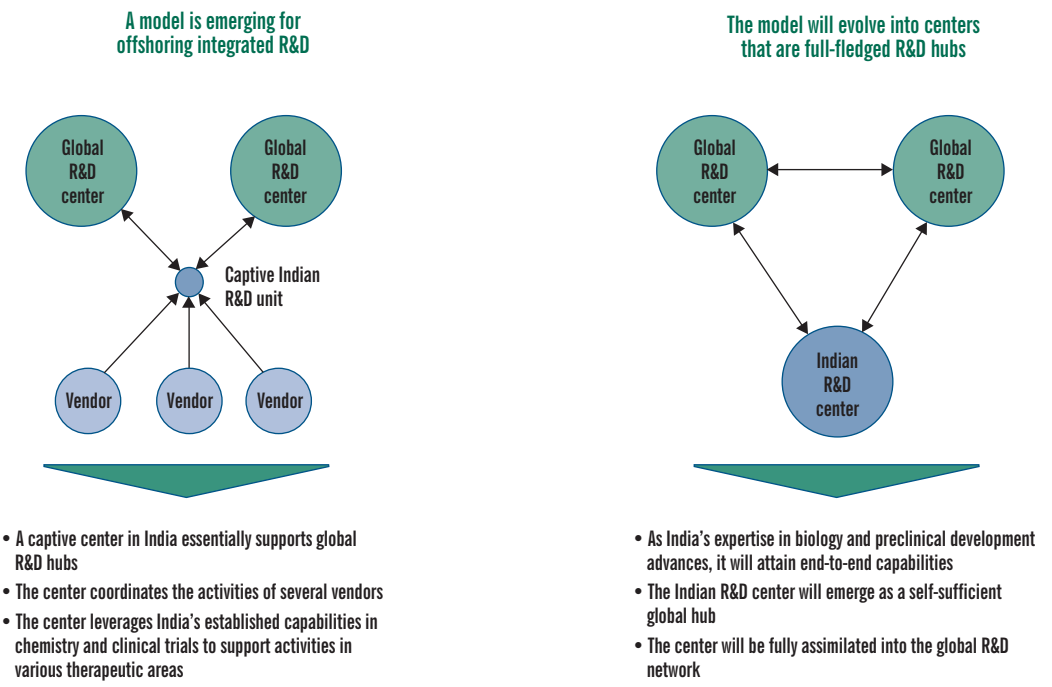
Economic globalization once seemed to be defined entirely by developed countries that outsourced bulk manufacturing work to developing countries. With surprising speed, R&D work has joined manufacturing as one of the key areas for offshoring. India is both a driver and a beneficiary of this trend.

Multinationals in a multitude of industries have come to appreciate India's impressive qualifications: a liberalizing and fast-growing economy and a deep talent pool of responsive, enterprising, English-speaking graduates. For MPCs specifically, the country's world-class skills in chemistry and information technology and its large treatment-naïve patient population provide added allure.

MPCs that take the long view will see that Indian R&D offers more than inexpensive custom synthesis or biostatistics work—or even solutions to bottlenecks in the pipeline. Soon enough, the entire R&D package will be readily available in India, and, in due course, MPCs will treat their Indian operations as another vital hub in the global R&D network. In pharmaceutical R&D, India will no longer be considered a developing country, as its hubs acquire equal status with their counterparts in Europe and the United States.

EXHIBIT 2

FULL-SCALE R&D HUBS SHOULD EMERGE IN INDIA WITHIN THE NEXT DECADE



SOURCE: BCG interviews and analysis.

Notes

1. *Rising to the Productivity Challenge: A Strategic Framework for Biopharma,* BCG Focus, July 2004.

2. The senior executives surveyed ranked China first, the United States second, India third, and the United Kingdom fourth among the nondomestic locales where they planned to spend the most R&D dollars over the next three years. Economist Intelligence Unit, *Scattering the Seeds of Invention: The Globalisation of Research and Development,* September 2004.

3. Even in regions of India where the majority of patients are not treatment naïve, many patients have been exposed only to older-generation medicines, as is the case with diabetes patients in first-tier and second-tier Indian cities, for example. Such patients are generally more willing to switch treatments and enroll in a clinical trial than are Western patients—who already receive more advanced and newer-generation medicines.

4. A common perception in the industry was that animal rights activists in India were effectively restricting approvals for preclinical trials through their presence on the Committee for the Purpose of Control and Supervision of Experiments on Animals and on the Institutional Animal Ethics Committees (IAECs). In June 2005 an amendment to India's Schedule Y eliminated such concerns by establishing clear guidelines for using animals in preclinical trials and mandating that the majority of the members of each IAEC be independent scientists and experts.

5. As of September 2005, only five Indian labs were certified as operating in compliance with GLP; 13 more were awaiting certification.

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