EMERGING CLINICAL RESEARCH OPPORTUNITIES IN INDIA:
A NEW SOURCE OF PATIENTS FOR COMPETITIVE CLINICAL TRIALS
Given India’s past regulatory environment, biopharma companies have been reticent to conduct clinical trials in this country over the last few years. That is changing, however. With its vast population, growing economy, major disease burdens, improved regulatory environment, and strong research infrastructure, the Indian market is now emerging as an ideal destination for clinical research. An especially important fact for sponsors seeking a less competitive landscape for study candidates is that only 1.4% of all global trials are currently conducted in India. However, the opportunities do not come without challenges. A successful entree into this market is best accomplished by using partners with extensive country, state and local experience. This includes a provider dedicated to the recruitment of patients and sites for clinical trials in India.

The Emerging Clinical Research Opportunities in India

A vast population and growing economy

India’s population of more than 1.3 billion people, or 17.75% of the total world population, is growing. According to UN estimates, it is expected to overtake China’s by 2025 to become the world’s most populous nation. According to the 2011 Census data, India is home to 104 million elderly people (aged 60 years and above), 53 million women and 51 million men. It is also a well-educated population with a workforce that has better English language skills than many Eastern European markets. There are more university graduates with degrees in India than there are people in South Africa or Poland.

This significant population makes India the world’s third largest economy in purchasing power parity terms. Its recent economic growth (7.0% GDP) has been a significant achievement, driving rapid urbanization and an increasingly large new middle-class.

The Search for Hard-to-Find Clinical Trial Patients

For sponsors of clinical trials in highly competitive therapeutic areas, such as Inflammatory Bowel and Cardiovascular Disease, finding enough study subjects in the United States and Western Europe has become a major challenge. When multiple companies are researching similar compounds, the number of patients in active research sites is limited, there are not enough investigators, and/or existing research sites are full, the result is a backlog of trials and high costs for recruited patients. In order to accelerate research and development in crowded therapeutic areas, sponsors need to find new sources of patients.
A rapidly growing healthcare industry

Specifically, healthcare has become one of India’s largest sectors, both in terms of revenue and employment. During 2008–2022, the market is expected to record a Compound Annual Growth Rate (CAGR) of 16.28%, with the total industry size expected to reach $372 billion by 2022.\(^5\)

This growth is being driven by several factors:
- Dual disease burden (infectious and non-communicable)
- Rising healthcare awareness
- Increasing levels of disposable income
- Growing population and urbanisation

Another significant accomplishment for India has been the growth of its pharmaceutical manufacturing. Currently, India has the highest number of FDA-approved manufacturing plants outside the U.S.\(^6\) It is also a leader in the field of generic manufacturing, with products registered and taken all over the world.

Once known as exporters of bulk Active Pharmaceutical Ingredients (APIs), Indian generic drug makers have managed to gain a foothold in regulated markets such as the U.S. and Europe.

This augurs well for Indian companies, which are also experiencing growth momentum in their domestic market.\(^7\) It is opined that clinical research will follow this success, with India eventually becoming one of the dominant research destinations.

A significantly improved regulatory environment

In an effort to put India back on the global clinical research map, the Indian government has taken great steps forward to speed up approvals, remove intermediaries and provide more transparency. The Central Drugs Standard Control Organization (CDSCO), whose main objective is to standardize clinical research and bring safer drugs to the Indian market, has made its vision clear: “To Protect and Promote Public Health in India”.\(^8\)

Over the past decade, the regulatory climate in India has fluctuated wildly, creating an uncertain research climate for biopharma companies. After finally becoming fully TRIPS compliant in 2005, India emerged as a favourable destination for the conduct of clinical trials. With its timely completion of trials, large patient pool, highly skilled medical investigators and related professionals, India’s share of the global clinical trial market subsequently grew from 0.9% in 2008 to more than 5% in 2012.\(^9\)
However, legacy infrastructure challenges and sometimes less efficient regulations resulted in many unfortunate complications on clinical trials. During late 2011 and early 2012, the existing regulatory framework and patient safety guidelines were challenged. This led to sweeping changes, the introduction of an onerous and restrictive three-tier approval process, and new regulations. Unfortunately, the unintended consequences were excessive timelines, as well as a significant increase in cost and effort to adhere to the new regulations. This led to many research institutions and investigators discontinuing clinical trials in India.

To reverse this situation, The Ministry of Health convened an Advisory Council in 2015 to formulate more practical policies related to the approval of clinical trials and new drugs. Following extensive input from various stakeholders – sponsors, CROs, investigators and the pharmaceutical industry – the committee recommended changes to the regulatory framework with an objective to revive the industry, while ensuring that trials are based on sound science and the highest ethical standards. Of significant importance for sponsors of clinical trials, they initiated:

- The CTA review timeline of 180 days maximum, as compared with unspecified timelines before.
- A pre-trial checklist provided by the Regulatory Authority to help sponsors ensure that their CTA dossier meets all the information requirements from the outset, avoiding potential delays.
- The ability to include an application for an import and export “No Objection Certificate” (NOC) license in the CTA. Previously this was not applied for until after CTA approval.
- Removal of the requirement to apply for “Export No Objection Certificate” from the CDSCO in order to export clinical trial biological samples from India.
- Online submission of regulatory application and monitoring of the status of an application.

Since the introduction of the regulatory reforms, India is well positioned for growth in the clinical research arena. There has been a rapid increase in the number of clinical research projects approved in India: 84 in 2016 and 59 in the first six months of 2017. Importantly, sponsors, CROs, sites and investigators all share a sense of optimism regarding the changes and increased activity.

A population in urgent need of medical treatment

Although India continues to struggle with the burden of communicable diseases associated with a developing country, every state now has a higher burden from non-communicable diseases and injuries than from infectious diseases. The contribution of non-communicable diseases to health loss — fueled by unhealthy diets, high blood pressure, and hyperglycemia — has doubled in India over the past two decades.

Cardiovascular diseases have now become the leading cause of mortality in India, with a quarter of all mortality attributable to CVD. Ischemic heart disease and stroke are the predominant causes and are responsible for >80% of CVD deaths.
Eight years ago, the overall estimated IBD population in India was 1.4 million, which was the second highest number after the USA (with 1.64 million) and one of the largest across the globe.\textsuperscript{13}

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\includegraphics[width=\textwidth]{ibd_population_bar_chart.png}
\caption{IBD population (\times 10^6)}
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\textsuperscript{13} Source: karger.com

Although public healthcare in India has achieved several important milestones, the vast majority of India’s population are treatment naïve or inadequately treated. Access to care remains limited by a number of factors such as a shortage of healthcare infrastructure, the number of trained providers relative to the vast population, and limited health financing options. Currently, only 15% of the population is covered by government health insurance companies and 2% by private health insurance. Moreover, health awareness and education, accurate and timely diagnosis, adherence to and completion of doctor prescribed treatment are still neglected, even today.\textsuperscript{14}

All of this leads to an increase on the demand side of healthcare while the supply side remains relatively constrained. It also points to a vast number of patients who are potentially ready and willing to gain access to better healthcare and new therapies by participating in clinical research studies.

**Tapping the Clinical Research Opportunities in India**

Arguably, India offers great potential for sponsors seeking new sources of study subjects, but it also represents significant challenges for the uninitiated. The use of knowledgeable partners is essential, including a provider dedicated to the recruitment of both patients and sites for clinical trials in India. In order to help a sponsor successfully maneuver through this uncharted territory, a provider must possess a range of experience and capabilities.
Familiarity with all three categories of healthcare delivery in the public sector

It is imperative to have a partner that understands how all levels need to work together in a cohesive manner to effectively deliver care to the majority of the population.

- **Government Hospitals run by state government or central government:** The majority of the Indian population access these hospitals for general and speciality consultations. Because they are run by government, a minimum fee is charged for services. Many of the government hospitals are also teaching institutions that provide undergraduate and post-graduate education.

- **Private Hospitals run by corporations, individuals or groups of clinicians:** Many corporate hospital chains exist in India, such as Fortis, Apollo, Max, Escort, and Columbia Asia, to name a few. These hospitals are usually expensive and primarily used by upper middle to high income classes.

- **Trust Hospitals:** They have subsidized rates for patient treatment and are utilized by large populations.

Strong relationships and access to existing infrastructure

Successful site and patient selection requires a provider that has strong relationships that it can leverage with both hospital management and investigators in hospitals across all three major categories of institutions where clinical trials usually take place.
The ability to mitigate sponsor concerns about India's regulatory process

Although there are a lot of similarities to the Western standards of clinical research, there are also grey areas that often raise unfounded concerns among sponsors. The right partner in India will have the deep knowledge and experience to eliminate any misconceptions that may still linger from the earlier regulatory environment, such as:

Liability risk
Misconception: India's liability risk is out of sync with other countries. This persists from the post-2012 regulation requiring compensation for any patient injured on a trial, irrespective of whether or not the investigational product was responsible for the injury.

Fact: This has been corrected in the new regulations and are now in line with other countries.

Lagging IP framework
Misconception: Running a trial in India is somehow at higher risk of intellectual property theft. By not running projects in India, sponsors think they can somehow prevent their IP from being reverse-engineered by the generic pharmaceutical industry.

Fact: India is TRIPS compliant and enjoys IP protection.

A solid track record of success

Sponsors need to know that a partner can commit to reasonable timelines for study approval and start, deliver on committed patient numbers, and provide confidence of data quality and integrity.

Clearly, for any sponsor that wants to take advantage of the emerging clinical trial opportunities in India, an experienced, knowledgeable, and well-connected partner such as Synexus is essential. Synexus and its Indian affiliate, S4, offer sponsors the ideal entree into the market. Together, these two independent companies combine the experience of the leading site management organization with S4's local market knowledge in India to support pharmaceutical companies and CROs in their mission to take advantage of the patient recruitment potential and cost-saving opportunities in India. Synexus/S4 have access to 35 sites across the major Indian cities and cover the whole spectrum of Civil (public sector), Trust and Private/Specialty hospitals.

With staff strategically positioned at hubs within sites across the country, as well as experience across a broad range of therapeutic areas, the teams provide management and project support onsite, effectively managing the relationship between sites and sponsor and/or CRO, and streamlining the research experience for the sites, investigators and patients.

These established relationships allow access to wards, outpatient clinics, and importantly, the principal investigators across a broad range of therapeutic areas. These investigators typically have an undergraduate degree from an Indian university with specialization and fellowships from international (USA / European) universities. Many sit on global advisory boards for multinational biopharma companies and are frequent contributors at international meetings and congresses.

Synexus/S4 are also fully versed and experienced in India’s regulatory process, as well as the practical issues of conducting a clinical trial such as investigator selection, language and cultural nuances.

Finally, as a testament to their track record of enrollment and data certainty, Synexus/S4's current list of research clients is extensive, with 33 studies ongoing at 14 sites across India.
Conclusion

In their competitive races to market with new compounds, the companies that know how to tap the emerging potential of the Indian clinical trial market by leveraging the appropriate and knowledgeable partners stand to reap huge gains. When this happens, everybody wins – sponsors, patients, as well as the Indian healthcare system and economy.

References:
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Synexus is a world class Site Network Organization with global expertise spanning patient recruitment, trial planning, management and patient retention. We recruit and retain more engaged patients, at fewer sites, and in less time than traditional centers, enhancing the quality and efficiency of our customers’ drug development programs. Our success is based on a simple, but crucial, principle: we place the patient at the heart of everything we do.