FROST & SULLIVAN

Asia: Preferred Destination for Clinical Trials

Executive Summary

WHAT

The clinical trials process is complicated and time-consuming, requiring substantial investment. Biotechnology and pharmaceutical companies in the United States (US) and Europe face escalating clinical trial costs and challenges in both recruiting and retaining patients. Additionally, companies have to navigate through complex regulatory processes.

To overcome, these challenges, US and European biotechnology and pharmaceutical companies outsource their clinical studies to contract research organizations (CROs).

This white paper highlights research on why Asia is a key destination for clinical trials.

WHY

Availability of vast patient pools, high-quality infrastructure, comparable quality and lower costs appeal to US and European companies.

There are 3 key benefits in outsourcing clinical trials to Asia:

- **Resources, Capabilities and Speed:** Elements unique to Asia include large treatment-naive patient pools, numerous clinical trial centres with advanced equipment and technology, comparable incidence and prevalence of Western diseases. The region's knowledgeable physicians and Key Opinion Leaders (KOLs) provide attractive environments for clinical trials and facilitate speedy trials; while low healthcare spend by many governments in Asia makes clinical trials an attractive way for patients to access innovative therapies in these countries.
- **Worldwide Data Acceptability:** Data from clinical trials in Asia is routinely accepted as part of US Food and Drug Administration (US FDA) and European Medicines Agency (EMA) regulatory submissions. KOLs from Asia are often members of international expert groups and citable academic output from Asia is growing rapidly. Data from inspections conducted in Asia by US FDA and EMA show low levels of adverse findings versus the US or European Union (EU), indicating high international compliance to standards.
- **Cost-Effectiveness:** Costs in Asia for procedures, diagnostic tests and visits are generally 30-40% lower than the US and European countries.

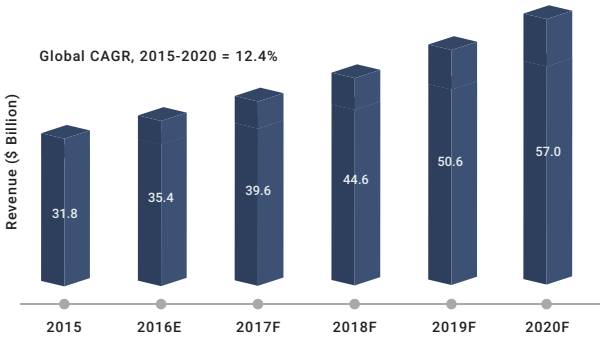
WHO

Key factors to consider when selecting a CRO:

- **Capability:** The CRO should have a capable in-house team with strong project management skills and a keen understanding of regulatory requirements. A client-centric and flexible approach to project delivery is another attribute to look for. The CRO should also offer scalability of IT systems and sophisticated quality systems.
- **Experience:** Expertise in specific therapeutic areas, study types and trial phases; proven track record of trials in the biotech sector and with multi-region trials; and a thorough understanding of regulatory audits.
- **Network:** CROs should have a local presence and networks, and strong relationships with the principal investigators, KOLs, and institutions. CROs should also be flexible in their approach to working with multiple regional specialist CROs.

**Note: The currency used in the document is USD.*

Outsourcing To CROs Is On The Rise



The practice of outsourcing clinical trials by biotechnology and pharmaceutical companies to CROs continues to grow.

Globally clinical trials are expected to grow at a CAGR of 12.4% to reach USD57billion in revenue by 2020 from USD31.8 billion in 2015.

Global Companies Face Challenges In US & EU

Low participation in trials has encouraged biopharma companies to pursue clinical trials beyond the US and Western Europe.

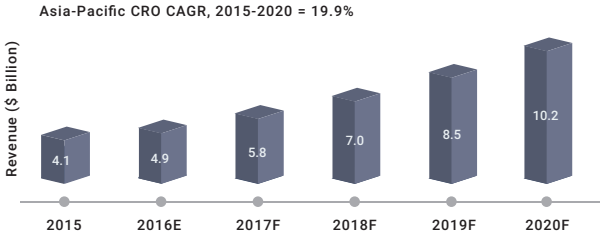
The time and costs associated with conducting trials in the the West has grown significantly due to higher insurance fees, increased administrative and resource costs. Lengthy timelines also compound these issues.

Asia Pacific Is The Hub For Outsourcing

Asia Pacific is becoming an increasingly attractive market for clinical trials.

According to a Frost & Sullivan report, in 2015, over 50% of global clinical trials had sites in Asia Pacific. In this region, sponsors are attracted to the large number of treatment-naive patients, comparable incidence and prevalence of Western diseases and high quality data, along with cost-effectiveness.

Asia Pacific's CRO Market Is Also Growing Rapidly



Asia Pacific clinical trial revenue is growing at a CAGR of roughly 20%, as compared to 11% for rest of the world (ROW).

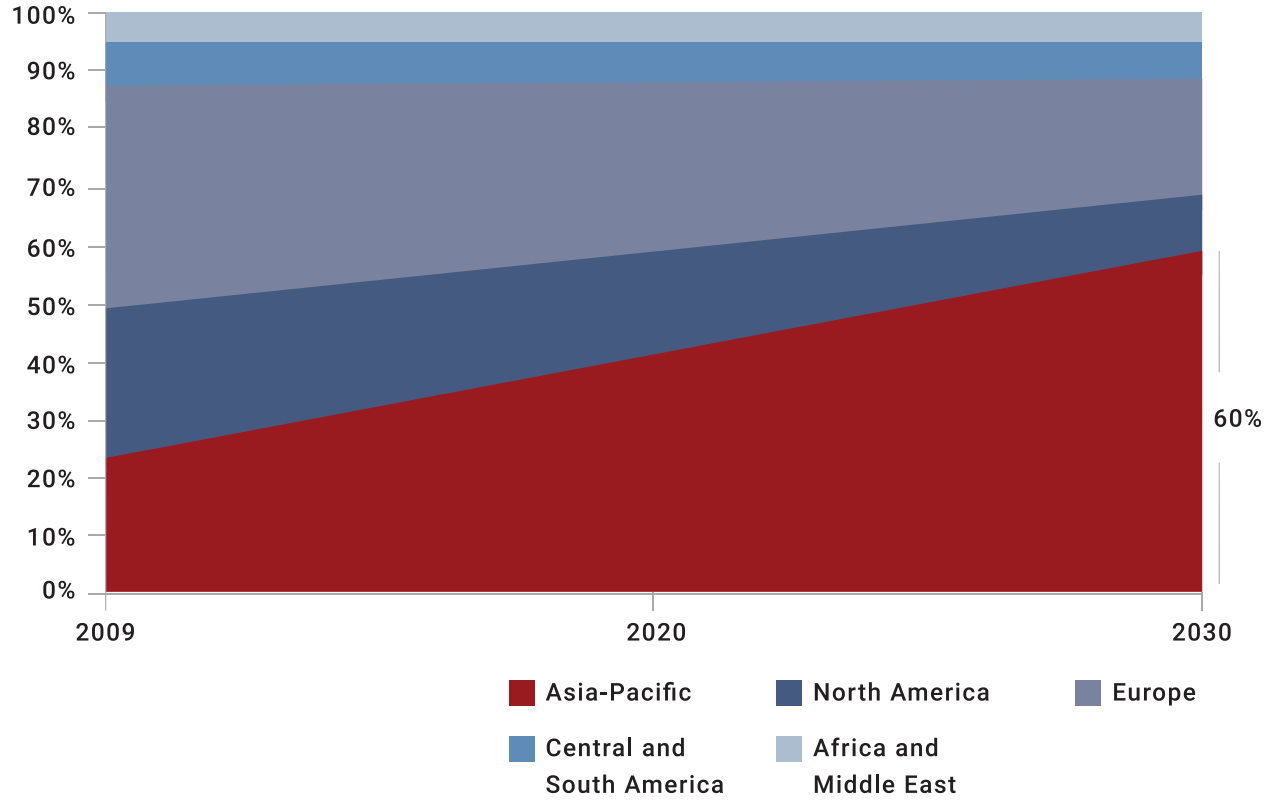
This strong growth is partially driven by an increase in outsourcing penetration which is 15% in Asia, versus 29% in ROW.

Key Reasons For Outsourcing Clinical Trials To Asia

The 3 key reasons biotech and pharma companies consider Asia as a top choice to conduct clinical trials are resources, capabilities and speed; worldwide data acceptability; and cost efficiencies.

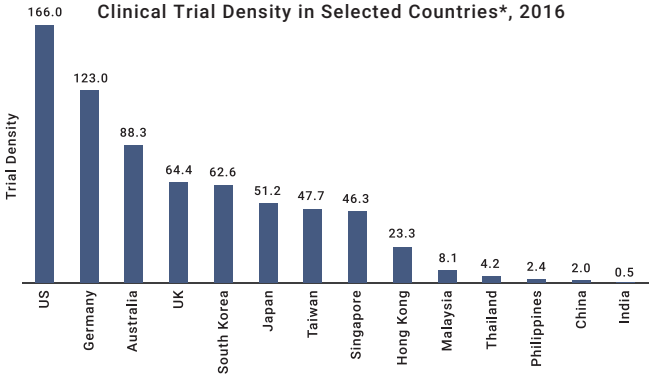
I. Resources, Capabilities and Speed

1. Middle Class Consumption Share by Region, 2009-2030F



In 2009, the global middle class was estimated at approximately 1.8 billion. This demographic is expected to grow to 3.2 billion people by 2020 and reach almost 5 billion by 2030. At present, Asia's middle class accounts for 28% of this global population and is expected to grow to 66% in 2030. The emerging middle class in developing countries is a potentially important consumer market for biopharmaceutical companies, warranting early engagement at the clinical trial stage.

2. Treatment-naive population



Asia provides a large and concentrated patient pool ideal for the speedy recruitment of trial subjects.

The large treatment-naive population presents a significant opportunity for biotechnology and pharmaceutical companies.

**Number of industry initiated trials per million population 2016.*

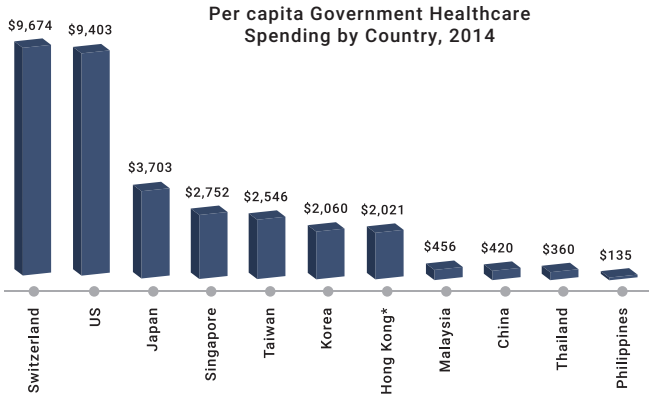
Case Study: High Recruitment Rate

Background
A European biopharma company conducted a Phase III study for a neurosensory condition across sites in Bulgaria, Czech Republic, Germany, Hungary, Poland, Russia, Serbia, Spain, Taiwan and Thailand.

Study Results
"Taiwan and Thailand are together expected to recruit 29% of the total study population. After enrolling 88% of the total patient population, Thailand is the highest recruiting country."

Depending on the indication, Asia has several large patient pools concentrated in major sites. For example, we initiated studies targeting chronic hepatitis patients in a few sites in South Korea and Thailand and recruited many patients from just those sites. This enabled us to achieve faster recruitment and obtain quality data.
Paul Gineste, Clinical Operations Director, Abivax

3. Low Government Spending



Per capita government healthcare spend is lower in Asian countries than in the US and Western Europe.

Clinical trials are an effective way for patients in Asian countries to access to innovative therapies.

The medical systems in many countries in Asia don't pay for certain drugs for patients, which makes the patient look at clinical trials to get access to best medical care and an opportunity to cure their disease. This was a great advantage for us.
Bruce Given, Chief Operations Officer, Arrowhead Pharmaceuticals

4. Similar Disease Patterns

Asian countries show similar incidence rates of major diseases to Western nations, providing a comparable environment to conduct clinical trials. Some diseases show spikes in prevalence (e.g. Liver Cancer in Taiwan) which may be attractive to sponsors focusing on these conditions.

5. Infrastructure

Asia has large hospitals and clinical trial centers to run large-scale clinical trials. The largest hospital in Asia, the Chang Gung Memorial Hospital in Taiwan, has 9,000 beds; while the largest one in US, the New York Presbyterian University Hospital, has only 2,478 beds. Some South Korean and Japanese hospitals also maintain a de-identified patient and trial database for fast patient identification, such as Korea's SCI Consortium.

We conducted a feasibility study for a global CRO who was looking for patients with very specific inclusion and exclusion criteria. We were recruiting for Type I diabetes-associated nephropathy in Phase IIa. The need was for adults between the age 20 to 50 years, with type 1 diabetes mellitus for ≥ 8 years, lab result of ≤11.0% HbA1c and excluding patients on non-insulin antidiabetic medications. Within 5 days, we were able to scan our database to identify 28 patients through our 3 hospitals' endocrinology departments. The database not only helps identify patients rapidly, but also helps assess the eligibility design and feasibility.

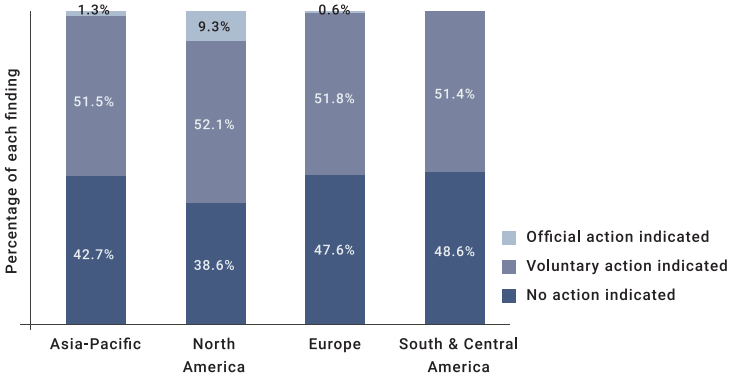
Dong-Kyu Kim, Secretary General,
SCI-Consortium of Clinical Trials Centers at University Hospitals

II. Worldwide Data Acceptability

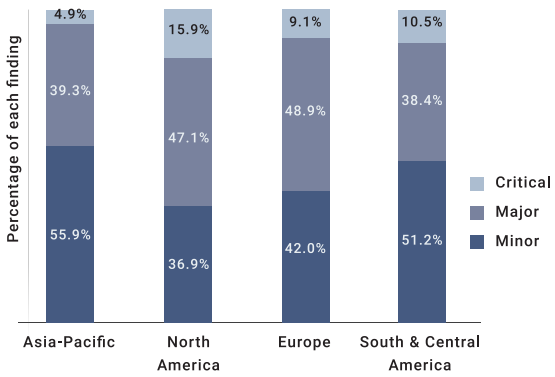
1. Low rates of issues in regulatory findings

Asia has low rates of official actions taken by the US FDA and critical EMA inspections, reflecting the high level of international quality compliance.

FDA Inspections by Type, 2000-2015

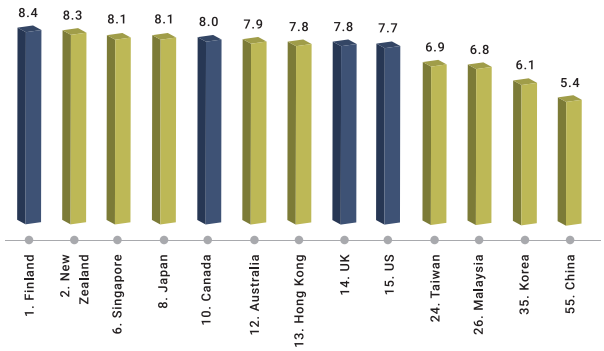


EMA Inspections by Type, 2000-2012



2. IP rights protection

IP Rights Index, Global, 2016



IP rights in Asia continue to improve with many important clinical trial markets in the top quartile of 128 countries monitored.

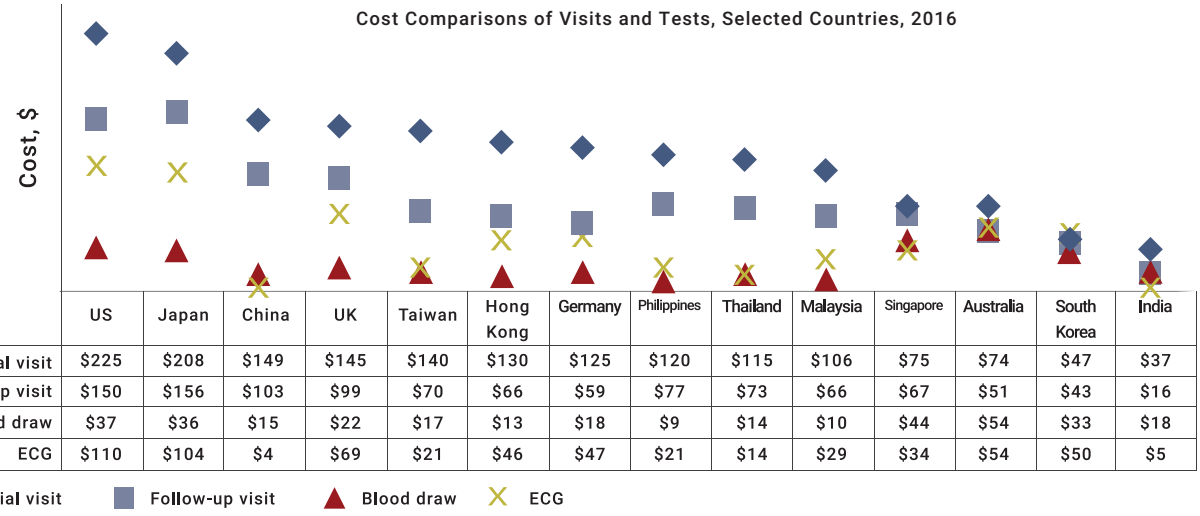
**The IP Rights Index comprises protection of IP rights, patents, and copyrights; and compares 128 countries.*
Source: The International Property Rights Index 2016, accessed 23 August 2016.

We always include Asia-Pacific sites in our global trials and are impressed by the quality of education, care to patients and commitment to R&D at these locations. The regulatory activation times have been in line with Western countries and recruitment rates have exceeded our expectations. Even the data quality was exemplary in terms of number and time to address the queries.

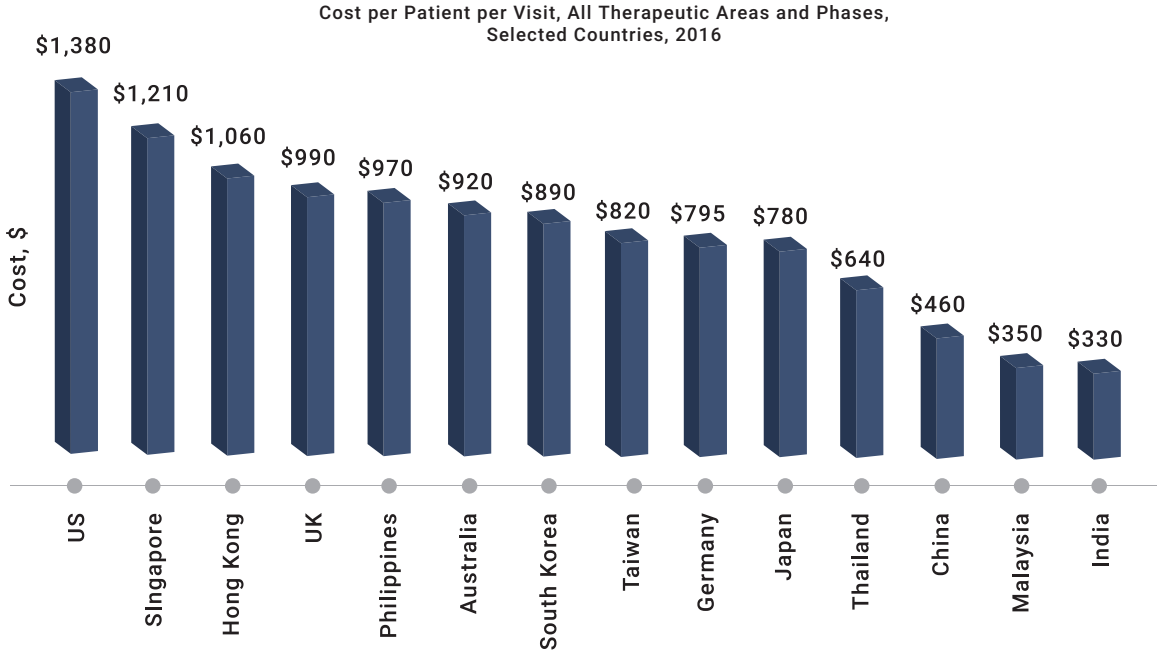
Associate Director, Clinical Trial Management, US Biotechnology Company

III. Cost Efficiency

Low operational costs position Asia as a highly attractive destination for clinical trials, when compared with the US and Western Europe.



	US	Japan	China	UK	Taiwan	Hong Kong	Germany	Philippines	Thailand	Malaysia	Singapore	Australia	South Korea	India
Initial visit	$225	$208	$149	$145	$140	$130	$125	$120	$115	$106	$75	$74	$47	$37
Follow-up visit	$150	$156	$103	$99	$70	$66	$59	$77	$73	$66	$67	$51	$43	$16
Blood draw	$37	$36	$15	$22	$17	$13	$18	$9	$14	$10	$44	$54	$33	$18
ECG	$110	$104	$4	$69	$21	$46	$47	$21	$14	$29	$34	$54	$50	$5



Key Challenges of Working In Asia

I. Regulatory Complexities

1. Engagement and Timelines

Undertaking clinical trials in Asia requires an appreciation that the regulatory regimes are heterogeneous. The Institutional Review Board (IRB) approval, regulatory, import licensing and contract negotiations are undertaken simultaneously in some countries, while others carry them out sequentially.

2. Standard of Care

In the US, Europe and Australia, standard of care is generally provided by the patient's normal payer during a clinical trial. In most Asian countries however, sponsors are required to pay for the standard of care. Nevertheless, total cost of running studies in Asia continues to provide cost savings in the region of 30% to 40% as compared with the US and Western Europe.

II. Infrastructure and Legal Issues

1. Infrastructure barriers in some areas

Asia's R&D and infrastructure is mostly concentrated in wealthier metropolitan cities. While there has been significant progress in technology adoption for use in hospitals and patient services, there may be infrastructure issues in smaller cities or fast growth cities with insufficient infrastructure investment.

2. Logistics complexities in megacities

Megacity growth rates have resulted in traffic congestion in a few Asian cities. Road transport logistics must therefore be planned in advance in these cities to ensure diagnostic samples or investigational products are not compromised.

3. IP protection

Asian governments have created a more robust IP protection system over the last few years. India and China have made substantial improvements in IP legislation alongside efforts to digitize operations and hire additional staff. Indonesia has launched policy statements and actions for IP protection.

III. Language and Cultural Hurdles

1. Local languages and English variability

Most Asian countries use and understand English, although they primarily use their local language for communication. Since English is the most commonly used language in global research, many Asian countries require translation of trial documentation; although in some counties, this may only apply to patient materials. English proficiency also varies slightly across Asia; with differences in word usage, meanings and accents, so documentation translation should be done with local experts.

2. Cultural norms

Saving face, heterogeneous belief systems, perceptual reporting and high trust in physicians are some factors that need to be considered while planning design and analysis of trials.

3. Local medicine practices

Cultural diversity in the practice of medicine, such as Ayurveda or Chinese medicine, may affect trial execution and results.

4. Gift giving

Modest gift giving in businesses as a goodwill gesture is a common practice in some countries. Western companies should implement clear policies and reporting to ensure compliance with global standards.

5. Informed consent

Treatment decisions, including trial participation, may require broader discussion with family members before an individual is willing to provide consent.

Key Factors In Selecting A CRO For Early Phase Clinical Trials

Last Word

Asia is quickly becoming a clinical research powerhouse facilitated by the availability of a vast treatment-naive patient pool, superior clinical infrastructure and talent, and low cost.

Disease incidences that mirror rates of Western countries create an attractive environment for conducting trials. Government spending on healthcare in Asian countries is relatively low compared to the US and Europe, so clinical trials motivate and help patients to access innovative therapies. Asia has large, state-of-the-art clinical trial centers which meet patient enrollment and retention goals, generate high-quality data and are led by skilled investigators.

As transparency in the regulatory environment in Asia improves, the region is poised to become the preferred destination for clinical trials.

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This white paper has been sponsored by Novotech, Asia's largest independent contract research organization (CRO).

About Novotech - www.novotech-cro.com

Established in 1996 and headquartered in Sydney, Novotech has a strong presence in the Asia Pacific region, with operations in all key regional markets including Australia, New Zealand, China, Korea, Taiwan, Hong Kong, Philippines, Singapore, Malaysia, Thailand and India. Novotech also has worldwide reach through the company's network of strategic partners.

Novotech provides clinical development services across all clinical trial phases and therapeutic areas including: feasibility assessments; ethics committee and submissions, clinical monitoring, data management, statistical analysis, medical monitoring, safety services, central lab, report write-up to ICH requirements, project management and vendor management.

Novotech is a fully Quality Endorsed Company compliant to the ISO9001:2000 standard.