



Featured Article

Demystifying the Intricacies of Asian Clinical Trials

By Jessica Liu, MD

Senior Director of Clinical Operations

Head of Asia-Pacific, Global Clinical Operations, INC Research



With every aspect of drug development moving east, there are only two kinds of clinical trial sponsors: those running sites in Asia, and those thinking about running sites in Asia.

For the latter, Asia appears from afar an impenetrable black box. While that box is rumored to hold significant cost savings and access to the fastest-growing healthcare market in the world, tapping into it means navigating regulatory and operational challenges compounded by language barriers.

Even for drug and device developers with established clinical trial sites in Asia, expanding from one country to the next can pose challenges. Each country has its own distinct cost structure, population base, medical practice standards, infrastructure, government policies and cultural differences.

Selecting the optimal Asian countries in which to establish or expand a clinical trial depends on the unique goals and priorities of each sponsor, as well as the indication and type of treatment being developed. That's why companies from emerging biotech start-ups to the largest pharmaceutical players have engaged CRO partners with in-depth knowledge of the Asian landscape. A few of the considerations each sponsor should discuss with their CRO partner include:

Cost Considerations

Most drug developers are well aware that conducting preclinical research in Asia is far more cost-efficient than conducting the same research in America or Western Europe. And many drug developers are rapidly discovering the same is true with clinical trials.

Running trial sites in China, Thailand, the Philippines, or Malaysia can save a sponsor 60 percent compared to running equivalent sites in the U.S. Most countries in Asia are at least 20 percent to 30 percent more cost-efficient than their western counterparts. But there are exceptions to every rule: for instance, investigator salaries and other trial costs in South Korea and Japan can be just as high if not higher than in the Western world.

The Numbers Game

With more than 4 billion people, Asia offers sponsors a deep pool from which to draw clinical trial participants. And for late-stage clinical trials in indications like diabetes or cardiovascular disease, which can require tens of thousands of patients, establishing Asian trial sites to tap into that pool is critical. In particular, sponsors of such trials may want to consider enrolling patients in highly populous countries like India, China, Indonesia, Japan, the Philippines, Thailand and Malaysia.

At the same time, however, sponsors must be aware that competition for clinical trial participants in countries like China is increasing. A country like South Korea may be less populous than China, but it still boasts roughly 50 million people and, as an emerging region for clinical research, it may offer less competition for enrollment.

The incidence of the target disease in each country's population also may play a role in trial site planning. Asia offers relatively more patients for first-line and second-line cancer drug evaluation than the West, where such patient stores have been largely exhausted. Highly developed Asian countries have a higher incidence of diseases common in the West, like obesity and diabetes, while diseases like tuberculosis are more common in Southeast Asia. Some countries, like India, have diverse patient populations afflicted with diseases of both the developing and developed world.

Evaluating Medical Practice

There are certain diseases for which the standard-of-care in Asia is similar to that in the western world, including breast cancer, lung cancer and diabetes. Sponsors of clinical trials in these indications can feel relatively comfortable establishing trial sites in any Asian country. But for many indications, medical practice standards differ both from East to West and between the different Asian regions. In such circumstances, sponsors seeking to mirror Western standards-of-care would do well to consider limiting their trial sites to Singapore, Taiwan, Hong Kong and South Korea.

Getting the Job Done

Principal investigators in the U.S. and Western Europe have been running clinical trials for 40-plus years, but their counterparts in Asia are lucky to have half as much experience. Thus sponsors should be prepared that Asian trial sites – even those that have adapted Western-style medical practices – may need more assistance when it comes to following protocol and differentiating between medical practice and clinical research.

Similarly, sponsors should not assume that all potential Asian trial sites will have the infrastructure – even fax machines or freezers – needed for a clinical trial. A good CRO partner will help a sponsor work with investigators to bring such sites what they need, as such an investment can be well worth the effort. Fortunately, vendors of clinical trial services from data storage to cold-chain supply are following the Eastern migration of research and making everyone's job easier.

Political Factors

Each Asian country's policies on protocol approvals, insurance regulations, import licenses and myriad other factors can affect a sponsor's ability to establish and run clinical trial sites. Ironically, countries like China and Thailand, which have historically been considered "easy" targets for clinical trials, are now increasing their regulations and making the trial review and approval process more formal, demanding and time-consuming for sponsors. China in particular is associated with a relatively long lead time for getting protocols approved and trials operational. Meanwhile South Korea and Taiwan are starting to realize that participation in global clinical trials is critical to advancing their medical practice standards, and they are working to ease regulations and facilitate protocol reviews.

Rules and Regulations

The regulatory bodies in South Korea and Taiwan, as well as in Singapore, have adopted an FDA flavor to their practices, so sponsors may not feel as much culture shock when dealing with them. Yet each Asian country has its own regulatory idiosyncrasies – in China, for example, reviews take on a project-based nature and sponsors should never assume that what worked in one application will be directly applicable to another. No matter how harmonized Asia may appear, the cookie-cutter approach simply doesn't work.

Clinical trial sponsors must consider their regulatory strategy in Asia as part of their overall business strategy, not as an afterthought. It's a process that needs to be started early, yet it is dynamic and should be revisited often. A good regulatory strategy will help a sponsor deliver the data needed for approval, save money on registration, and ensure effective reimbursement.

Cultural Considerations

Language barriers can be easily overcome by CRO partners with offices across Asia, and sponsors are often pleased to learn that investigators in most Asian countries are eager to participate in clinical research. It is viewed as a way to advance their quality of care and position themselves on the cutting edge of scientific innovation. Regulatory reviewers, too, are often eager to help, if a sponsor knows what questions to ask and how to ask them. And in countries like India, a high degree of patient respect for physicians can translate into high compliance and low drop-out rates.

Yet there are certain cultural considerations that sponsors need to address upfront with their investigators. For example, some Asian researchers may believe that their participation in a trial gives them the right to publish data on their findings, while sponsors require at least some degree of control over the publication of trial data. Such issues are best managed by through good communication prior to the start of enrollment.

A Question of Ethics

As the fastest-growing pharmaceutical market in the world, China is a major consideration in the marketing plans of most drug developers. Biotechnology and pharmaceutical companies are often interested in establishing trial sites in China as part of a plan to support eventual approval in Chinese markets, and the same is true of Japan.

In addition, there are certain diseases that present a serious unmet medical need specifically within Asian populations, such as foot-and-mouth disease. Such indications obviously lend themselves to Asian clinical trials.

Yet if a sponsor has no plans to launch a drug in certain Asian countries, perhaps because the populations of those countries would not be able to afford the drug, then conducting clinical research in those countries may present ethical challenges.

The right CRO partner is aware of such ethical considerations and can guide sponsors through this and other issues mentioned in this article, as well as the many other obstacles associated with running clinical trials in Asia. While challenging at first, the rewards to sponsors in terms of rapid enrollment, cost-savings and market access are not just upside, they are essential to remaining competitive in the drug development world of today and tomorrow.

For more information on INC Research's clinical services and therapeutic expertise for Asia, please contact Dr. Jessica Liu at jliu@incresearch.com or visit www.incresearch.com.

About the Author

Jessica Liu, MD is the Senior Director of Clinical Operations for Asia-Pacific Rim, INC Research. Dr. Liu received her Medical Doctorate from the prestigious University of Beijing (China) and has a Diploma in Pharmaceutical Medicine from the University of Basel (Switzerland). She started her career as a resident physician in the endocrinology Department of the Peking Union Medical College Hospital (PUMCH) in Beijing, China, followed by 15 years of valuable experience in clinical research, during which she conducted and managed Ph I-IV clinical studies across multiple therapeutic areas. During her career Dr. Liu has worked in the Chinese affiliates of global pharmaceutical companies taking on increasingly responsible roles in clinical operations, project management and medical affairs giving her a depth of the expertise in running global clinical trials. Her experience and expertise on the Asia-Pacific region deepened as she managed international projects out of the European Headquarters office for a global CRO in Brussels, Belgium, for more than 3 years. Dr. Liu continues to manage global operations in support of biotech and pharmaceutical companies with a specific expertise on conducting clinical trials in the Asia-Pacific Rim in her current senior leadership role at INC Research. She is based in Beijing.