

Drug Development in China: Lessons Learned from Years of Clinical and Small-Molecule Experience

by [Lan Huang](#)

“Today we recognize that, to successfully protect US public health, we must think, act, and engage globally. Our interests must be broader than simply those within our own borders.” —Margaret Hamburg, US Food and Drug Administration (FDA) commissioner, 2009–2015



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Many major pharmaceutical companies — including Pfizer, Novartis, Eli Lilly, Sanofi, and Bayer — have research and development centers as well as clinical and commercial activities in China. Their sales revenues are increasing with the rapid growth of China’s healthcare market, which depending on the estimate is double or triple the country’s current gross domestic product (GDP) growth of 6.7% (1).

China saw 3.6 million new cancer cases in 2012, with 2.2 million cancer deaths that year. GlobalData forecasts incidents of non–small-cell lung cancer (NSCLC) in particular to rise there at 4.7% annually from 2015 to 2025, with sales of lung cancer therapies increasing tenfold. China is the second largest pharmaceutical market in the world and forecast to grow from US\$108 billion in 2015 to \$167 billion by 2020 (2).

No matter their size, all new markets pose challenges for pharmaceutical companies. Recently, a major Western drug-company executive told me that his company had spent eight years attempting to start a presence in China and had experienced great difficulty doing so. My company is

developing innovative drugs both time- and cost-efficiently using a unique US–China integration model. Understanding the internal infrastructure of the country and of its China Food and Drug Administration (CFDA) will help other drug manufacturers work there and create more innovative treatments for patients in need around the world.

Developed Infrastructure and Quality Data Generation

Generating FDA-quality data for clinical trials conducted at Chinese sites is achievable. Non-US clinical trials costs are reduced (relative to Western studies) for everything from clinical care and operational costs to documentation and training. In addition, recruitment is faster in Chinese trials than in those conducted in the West, which ultimately shortens their overall timelines (3, 4).

Healthcare infrastructure in China has developed significantly over the past decade. Global contract research organizations (CROs) can help generate US good clinical practice (GCP) data there, and their clinical competence has matured in the past 15 years. I know this firsthand, having cofounded a clinical CRO called Paramax International that conducted clinical trials in China for global companies. (It was ultimately sold to the global CRO company RPS and later to Warburg Pincus.) Over a dozen major institutions capably serve as trial sites and are reviewed by the US FDA. Their systems and methods withstand the scrutiny of those reviews, and the sites are managed by scientists who received training in the West.

The US FDA encourages the biopharmaceutical industry to make greater use of centralized monitoring and central data review. We have implemented that in our clinical trials, with an added benefit of further assuring that clinical data are generated at the highest quality. Selected Chinese CROs provide robust data presentations with Western site data to the US FDA. It's important for them to confirm that they are capable of fulfilling requirements under the centralized monitoring regime.

China Food and Drug Administration

More drugs currently are submitted for approval than the CFDA has time to review, but it does plan to hire additional personnel. Drugs that can obtain priority review include

- those being developed by domestic companies
- innovative drugs not yet approved elsewhere
- those that address national priority medical conditions
- those being developed by scientists who have received China's Thousand Talent Innovator Award.

Registering a Category 1 new drug market approval with the CFDA requires transfer of the manufacturing process to a Chinese company or facility, conducting studies to demonstrate chemical equivalence (and sometimes also bioequivalence) to product produced outside China, complying with good laboratory practice (GLP) standards, and submission and approval of a clinical trial application (CTA, similar to an investigational new drug application (IND) in the United States), as well as a new drug application (NDA). Several competitive advantages come with implementing this strategy. Qualifying as a Category 1 innovative drug speeds up product review. In addition, performing clinical trials in China has historically provided quicker, and larger, patient enrollment at a lower cost.

The ability to navigate through the ambiguity of the CFDA website and published guidelines is key. Also helpful is having a cultural understanding, prominence in China's scientific ranks, and a working relationship with the regulatory body. Safe drug candidates that demonstrate noninferiority on primary end points and superiority on secondary end points can be (and have been) approved by the CFDA.

Finally, Chinese data meet US GCP standards and thus can be included for US FDA filings. For afatinib tablets, a first-line NSCLC drug approved by the FDA in July 2013, Boehringer Ingelheim used patient data that mostly originated from China in its pivotal trial (72%) (5). And AstraZeneca's gefitinib received EMA approval as a first-line NSCLC drug with 99% of its pivotal trial data from China (6). Ongoing phase 3 trials are being conducted for AstraZeneca's osimertinib, Bayer's sorafenib, and Pfizer's crizotinib using patient enrollment in China.

Most of all clinical trial sites are located outside of the United States. According to a 2010 report by the US HHS office of the inspector general, 80% of applications to the US FDA for drugs and biologics contain data from non-US studies (6). Further, 78% of all subjects were enrolled in foreign sites, and 10 drugs approved by the US FDA in 2008 had all-foreign trial subjects. China offers both opportunities and advancements to biopharmaceutical innovators. Thus, when cost and time efficiency are important in developing best-in-class drugs for patients' unmet medical needs — all while upholding the highest standards — this country should be at the forefront of our minds.

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