Conducting Clinical Trials in China: Chinese and U.S. Regulatory Considerations

By Joy Liu and Arthur Mok

In recent years, both pharmaceutical and device manufacturers have increased their clinical trial activity in Asia, and in China in particular. Among the main drivers of clinical trial growth in China are large patient populations and potentially lower costs and time savings. Conducting clinical trials in China presents its own set of regulatory challenges, however, which must be navigated carefully. This article presents an introduction to the Chinese regulatory framework for conducting clinical trials, focusing on the process by which an applicant obtains clinical trial approval from China’s State Food and Drug Administration (SFDA). It also highlights certain U.S. Food and Drug Administration (FDA) requirements that may be relevant for companies seeking to use clinical data from trials conducted in China to support a U.S. marketing application.

The Applicant

Prior to conducting a drug or device clinical trial in China, a manufacturer must obtain a clinical trial approval from SFDA.

Applications for clinical trials to be conducted in China may only be submitted by a “domestic applicant,” which is defined

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as an institution “legally registered within the territory of [the] People’s Republic of China that independently assumes civil liability.” A foreign manufacturer may, however, submit a clinical trial application for an “import drug,” which is a drug that has been approved overseas but has not yet been approved for marketing in China. In addition, overseas applicants may submit clinical trial applications if the trial in China will be part of a multi-center, international trial of a drug already approved or in Phase II or Phase III trials overseas. SFDA may, however, require the applicant to conduct Phase I trials in China prior to commencing such a multi-center international trial.

Approval of the Application

A clinical trial applicant must submit its application to a local drug regulatory department of SFDA (Local Agency), usually the one located in the province, autonomous region or municipality where the applicant is located. The Local Agency conducts a preliminary review of the application and, if application requirements are met, issues an acceptance notice to the applicant. The Local Agency then conducts on-site inspections of the applicant and, for biological products, collects product samples for testing. The Local Agency must deliver its review opinions, inspection reports, and the application to SFDA’s Center for Drug Evaluation (CDE) within 30 days of the Local Agency’s acceptance of the application.

CDE has five days to accept the application. It must then conduct a technical review of the application and provide its review opinion to SFDA within 120 days. SFDA then has 40 days to issue a final approval decision. The timelines for technical evaluation by CDE and final approval by SFDA are shortened for certain fast track products (e.g., new chemical entities, HIV/AIDS medicines, orphan drugs and products for “malignant tumors”)—100 days instead of 120 for CDE evaluation and 20 days instead of 40 for SFDA final approval. Thus, it can take up to 195 days (or 155 days for fast track products) to obtain an approval to begin a clinical trial. More time may be required if CDE or SFDA request additional information.

Other Chinese Regulatory Considerations

Similar to requirements for IRB approval of clinical trials conducted in the United States, there is a requirement for the protocols of clinical trials to be conducted in China to be reviewed and approved by an independent “ethics committee.” There are, however, a number of regulatory provisions that are unique to the Chinese regulatory system. For example, clinical trials in China may be conducted only at hospitals that are pre-selected and accredited by SFDA. As of 2010, there were approximately 2100 SFDA-accredited trial sites in 295 accredited hospitals located throughout China. In addition, clinical trials in China are subject to certain minimum numbers of patients, although requests for exceptions may be made for “rare or special diseases.” At least 100 patients are required for Phase II trials, 300 for Phase III trials and 2000 for Phase IV trials. Furthermore, trials for vaccines are prohibited unless the vaccine is already approved overseas.

Using Data from Trials Conducted in China to Support U.S. Marketing Applications

A foreign study not conducted under an investigational new drug application (IND) may support an application for U.S. marketing approval of a drug or biologic if two conditions are met. First, the study must have been conducted in accordance with good clinical practice (GCP), which is defined in this context to as the standards for ensuring that “reported results are credible and accurate and that the rights, safety and well-being of trial subjects are protected.” Second, FDA must be able to validate the data from the study through an on-site inspection, if it deems such an inspection necessary.

A marketing application based solely on foreign clinical data that meets FDA criteria for marketing approval may be approved if: the foreign data are applicable to the U.S. population and U.S. medical practice; the trials were conducted by investigators “of recognized competence” and FDA is able to validate the data through an on-site inspection, if necessary. Applicants are encouraged to seek guidance from FDA prior to submitting an application that will rely solely on foreign data.

Conclusion

The regulatory framework for conducting clinical trials in China is quite distinct from that of the United States. While a clinical trial may begin in the United States 30 days after submission of an IND, barring any clinical holds, sponsors of clinical trials in China must first obtain an approval from SFDA, which could take 195 days or longer. In addition, while an overseas entity may submit an application to conduct clinical trials to be conducted in the United States, an application to conduct clinical trials in China generally must be submitted by a domestic applicant. These regulatory differences necessitate significant advanced planning for trials that are to be conducted in China and, depending on the sponsor, may require strong relationships with Chinese contract research organizations.
Clinical Trials

In addition, companies conducting trials in China that intend to use the data from such trials to support a U.S. marketing application must be careful to ensure data quality and compliance with GCP. ▲

4. Provisions for Drug Registration, Art. 44.
17. Provisions for Drug Registration, Art. 32.
22. 21 C.F.R. 314.106(b).
23. 21 C.F.R. 314.106(c).

Anthony C. Celeste Begins as Senior Advisor at EAS Consulting

EAS Consulting Group, LLC, a leading consulting firm specializing in FDA regulatory matters, has appointed Anthony C. Celeste as the firm’s Senior Advisor, serving the EAS President and expanding the company’s consulting, auditing and training services. He will also provide expert consulting advice to EAS clients on a broad range of food and drug topics.

Mr. Celeste joins EAS after a distinguished, 50-year career split between serving in senior-level manager management positions at the Food and Drug Administration and developing and managing one of the nation’s most reputable regulatory consulting firms, AAC Consulting Group, Inc.