ROPES & GRAY ALERT

China Life Sciences

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China FDA Clarifies Legal Consequences of Clinical Trial Data Inspections

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China's recent drug regulatory reform has emphasized that clinical trial data must be authentic and reliable. However, the legal consequences for breaching data integrity requirements in clinical trials remain ambiguous. On August 24, 2016, the China FDA ("CFDA") issued a draft *Guideline for Handling Issues Identified in Clinical Trial Data Inspections* ("Draft Guideline"). The Draft Guideline aims to clarify what constitutes data forgery and the legal consequences of noncompliance in clinical trials for different stakeholders. The CFDA is currently seeking public comments on the Draft Guideline.

Previously, the CFDA issued on July 22, 2015, a circular requiring all applicants of 1,622 pending drug registration applications to self-inspect their clinical trial data and compliance with the Good Clinical Practices (GCP). The circular highlighted several priority areas for the self-inspection, such as consistency of the final data for analysis with the original raw data, documentation of changes, compliance in handling of samples and investigational products, management of subject screening, inclusion and exclusion, keeping track of protocol deviations and reporting of adverse events. Upon self-inspection, applicants voluntarily withdrew around 80% of the pending applications, including domestic and imported drug applications. Based on the submitted self-inspection results, since early 2016 the CFDA has initiated five rounds of onsite inspections over selected clinical trials, including some Phase I to III trials and some BE studies. Among the first three batches of completed inspections, 30 drug applications were rejected, in most instances based on findings of false clinical data.

To provide more guidance on the legal consequences of these CFDA-led inspections, the newly issued Draft Guideline mainly addresses the following:

- Division of liability between applicants/sponsors, clinical trial institutions/sites, and clinical research organizations (CROs). While sites and CROs shall bear liability for those data integrity issues, they are directly responsible for, the sponsors ultimately bear all the legal liabilities for the submitted clinical data and drug application dossier.

- Types of GCP breaches that constitute data forgery. The Draft Guideline gave a specific list of violations of relevant sections of GCP that constitute data forgery. Among others, hiding certain trial data or not presenting the complete data set is considered data forgery, which can lead to CFDA's ban on the applicant's future applications (see the bullet below).

- Ban on future applications. Companies that have forged clinical trial data are banned from refiling an application for the same product with the CFDA for the next three years. In particular, if data forgery is found to have occurred after November 11, 2015, the CFDA will directly reject the current application under review, and the applicant will be banned from filing any applications for any drug products for one year.

- Implementing a blacklist. Based on the Draft Guideline, blacklisting will apply not only to the sponsors, sites and CROs involved in data forgery, but also to the responsible individuals within these entities.

- Suspension of studies at study sites. If study sites are found to be involved in data forgery, or to have committed other serious GCP violations that threaten subject safety or data integrity, the sites must immediately suspend subject enrollment, rectify the misbehavior, and refrain from undertaking any new trials.

- Discretion in imposing penalties. Applicants can be exempted from penalties if they voluntarily report all identified issues through self-inspection and withdraw the questionable applications. There will be leniency in penalties if applicants fully cooperate with the investigation and timely explain and correct the identified noncompliance. On the other hand, applicants who decline, deter, or avoid inspections can face higher penalties.

We encourage life sciences companies to arrange necessary audits of ongoing clinical trials, evaluate the level of GCP compliance, and develop corrective action plans accordingly.

If you would like to discuss the foregoing or any other related matter, please contact Katherine Wang or your usual Ropes & Gray advisor.