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ALERT

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CFDA Solicits Comments on Drug Registration Rules

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The China Food and Drug Administration ("CFDA") recently published long-awaited and comprehensive revisions ("Revisions") to the Drug Registration Rules ("DRR"). The Revisions are now open to public comments until August 26, 2016. Since the DRR is the most important regulation for seeking approval of drugs in China, the pharmaceutical industry is advised to review the Revisions carefully and offer feedback on proposed changes.

The Revisions are said to be a response to the State Council's 2015 announcement (See our Alert dated August 21, 2015) on the reform of the drug and device approval system. As a result, the Revisions contain some of the State Council's requested reforms, including simplifying the drug approval process and imposing severe penalties on false data submitted during drug registration.

Overall, key changes proposed in the Revisions can be divided into the following four categories:

1. Changes that may affect Clinical Trials

- **Remove explicit reference to international multicenter studies**: Unlike the DRR, the Revisions do not distinguish an international multicenter study from a drug registration study. The China arm of an international multicenter study, if the data of which will eventually be used for applying the marketing approval in China, must be approved by the CFDA in advance. Companies can include China in any stage of the drug development process when conducting an international multicenter study, rather than having to wait until Phase 2 of the clinical study program.

- **Remove the validity term of clinical trial approval**: The Revisions would remove the current DRR requirement that a clinical trial must be launched within three years from the approval date. The Revisions do, however, propose that a clinical trial approval will become invalid if the clinical hold issue can't be resolved for more than 18 months.

- **Add procedures for removing a clinical hold**: The Revisions propose that, if a suspended clinical trial can resolve the clinical hold issues, the drug applicant must obtain an ethics committee ("EC") approval first, and then submit a written application regarding the removal of clinical hold to the CFDA. The Revisions also add that both the EC and the principal investigator may request to suspend or terminate an ongoing trial, if there are any unexpected serious adverse events.

2. Changes that may affect Drug Regulatory Approval Process

- **Abolish the statutory technical review time limit**: Under the DRR, the Center of Drug Evaluation ("CDE") must complete the technical review within a statutory timeline. The Revisions, however, explicitly exclude the technical review timeline from the entire drug registration timeline, as well as the inspection and testing timeline. Furthermore, at the beginning of each year, the Revisions specify the CDE would need to publish a statistical report regarding the technical review, the on-site inspection and registration testing timeline of the preceding calendar year. In addition, the CDE would provide an estimate of the technical review timeline at different stages for the current year.

- **Prohibit any separate API marketing application**: Under the Revisions, an active pharmaceutical ingredient ("API") marketing application would have to be bundled with a drug product marketing application. In other words, the CFDA would reject any API marketing application that is submitted separately without identifying the relevant drug product marketing application.

- **Simplify the license renewal procedure**: According to the Revisions, a drug approval holder must submit the renewal application no later than three months before the drug registration approval expires. If the CFDA fails to reach a decision prior to the expiration date, the renewal application will be automatically approved.

- **Limit the scope of changes to pending applications**: There is no available procedure for making changes to approved clinical trials in the current DRR. In its 2013 draft amendments (See our Alert dated November 18, 2013) to the DRR, the CFDA had proposed that an applicant for an investigational new drug approval could make changes to the approval holder, the manufacturing process, the manufacturing site and the product specification by filing a supplementary application. The Revisions, in contrast, specify that an applicant can make only non-significant changes during the clinical trial process—although the Revisions do not define "non-significant changes." In terms of reviewing the marketing approval application, the Revisions further require that any changes in the conditions of manufacturing, quality control and use must be made through a new application, rather than a supplementary application.

3. Changes that may affect the Administrative Exclusivity

- **Eliminate the linkage between patent protection and the drug approval process**: In the current DRR, any applicant must submit a drug application two years prior to the expiration date of any third-party patent in China, and the CFDA cannot approve an application before the patent expires. Under the Revisions, any applicant can submit a marketing authorization application, regardless of the existence of third-party patents. This change is proposed in response to the Bolar Exemption provisions in the PRC Patent Law.

- **Limit the exclusivity scope during the new drug monitoring period**: The current DRR prohibits the CFDA from accepting any applications for clinical study authorizations on a new drug during its monitoring period. However, the Revisions limit the exclusivity by only prohibiting the CFDA from accepting any marketing approval application of the same drug. In other words, the Revisions would allow the CFDA to accept and review *other clinical trial authorization applications* of the same drug during the monitoring period. Additionally, the Revisions would allow the CFDA to approve a third-party marketing approval application during the monitoring period, but only if the new drug has not yet been placed in the market within two years from the start of the monitoring period.

- **Grant administrative exclusivity to approved TCM new drugs**: Currently, a traditional Chinese medicine ("TCM") manufacturer can apply for a TCM protection certificate separately from the drug registration procedure. If any TCM obtains a protection status designation, then only the TCM protection certificate holder can manufacture the TCM during the protection period. The Revisions propose that any TCM new drug will be granted a protection designation automatically upon the approval date of such new drug. At the same time, the CFDA will refuse to accept any marketing approval application of the same TCM.

4. Changes that may affect the Drug Applicant's Rights and Obligations

- **Specify the qualified applicant for CADN application**: Any new Chinese Approved Drug Names ("CADN") must be approved by Chinese Pharmacopoeia Commission ("CPC"). However, the Revisions specify that CDE, not the drug applicant, shall submit the CADN proposal regarding the new drug to CPC. Once CPC makes a determination regarding the new CADN, it will notify only the CDE.

- **Impose evaluation requirement for contract research or manufacturing organizations**: According to the Revisions, if a drug applicant contracts a third party to provide drug development services or produce drug samples, the drug applicant must conduct an evaluation of the service provider's quality system by itself or another evaluation agency.

- **Outsource drug registration testing to private testing institutions**: Currently, only the National Institute for Food and Drug Control and its provincial counterparts can conduct the drug registration tests. The Revisions allow qualified private testing institutions to handle drug registration tests.

- **Appoint a dedicated person for regulatory filings**: The Revisions ask the applicants for a dedicated regulatory specialist to handle the registration applications and to communicate with the CFDA on behalf of the applicants. If the CFDA discovers any misrepresentation or falsification of data or samples in the dossiers, the responsible regulatory specialist will be blacklisted.

The Revisions unveiled many material changes to the drug registration system and will significantly impact the future business strategy of pharmaceutical companies in China. It remains unclear whether these changes will be adopted. We recommend that pharmaceutical companies closely monitor the progress of the Revisions and propose their comments by the deadline.

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