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China Life Sciences

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China FDA Calls for Comments on Key Policy Proposals

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On May 11-12, 2017, the China FDA (CFDA) issued four new draft policies for public comments, proposing further reforms in the current drug and medical device regulatory regime. The four draft policies aim to accelerate the review and approval of new drug and medical device applications (Circular No. 52), deregulate the conduct of clinical trials to encourage innovation (Circular No. 53), enhance post-market supervision throughout a product's entire life cycle (Circular No. 54), and protect the rights of innovators (Circular No. 55). The CFDA is soliciting public comments until June 10, 2017. Further legislative initiatives will be arranged if any parts of the draft policies contradict the current CFDA regulations. These draft policies, if adopted, are likely to further streamline and accelerate the market access of innovative products and will have a far-reaching impact on China's life sciences industry.

I. Circular No. 52 proposes the following key measures to accelerate the review and approval of new products:

- Expedited reviews and approvals for urgently needed therapies. Drugs and devices that offer new solutions for treating life-threatening diseases or address critical unmet medical needs can be eligible for conditional approvals, as long as early and mid-stage study data can indicate their efficacy and predict their clinical values. Companies receiving conditional approvals must develop a risk management plan and initiate confirmatory post-approval study as per the requirements in the conditional approvals. Innovative drugs and devices sponsored by the National Science and Technology Major Project can be eligible for expedited review and approval.

- Supportive regime for rare disease cures. Drugs and devices that offer new solutions for treating rare diseases, if already approved outside China, can be eligible for conditional approvals. Companies can complete the necessary stages of clinical study after receiving marketing authorizations. The health authorities will publish a catalogue of rare diseases and establish a rare disease patient registry.

- Cross-disciplinary and professionalized review system. The technical review for new drugs and devices will be led by a team of cross-disciplinary reviewers. Each new drug and device application will be assigned to a dedicated managing reviewer, who will be responsible for scheduling consultation meetings. The CFDA will require consultation meetings at all critical milestones of clinical studies, i.e., prior to initiation of phase I, after completion of phase II (and prior to initiation of phase III), after completion of phase III, and prior to the NDA application. Consultation meetings with expert panels will also be required to deliberate important but controversial technical questions. The technical review conclusions will be published in public, with an exception of company confidential information.

- Market access benefits. Hospitals will be encouraged to prioritize their procurement and use of new drugs with definite efficacy and reasonable prices. The government will support inclusion of innovative drugs in the basic medical insurance scheme, and the reimbursable drug list will be updated more frequently.

II. Circular No. 53 proposes the following new measures to remove certain governmental controls over clinical studies on new drugs and devices:

- Expansion of clinical study infrastructure.
    - Currently, hospitals need to be certified by the CFDA and the National Health and Family Planning Commission in order to become qualified clinical study sites. The draft policy proposed to revoke the certification system. All medical institutions that have the necessary infrastructure to conduct clinical studies can file for record with the CFDA. The CFDA will supervise clinical study sites through rigorous clinical study audits, and will not admit data generated in those studies that fail the audits.
    - Hospitals, medical research institutions and academic institutions will be incentivized to actively participate in clinical studies and research. The capabilities and quality of clinical studies and research will be considered for hospitals' and physicians' performance reviews and ratings.
    - Foreign companies and research institutions will be allowed to conduct phase I new drug clinical trials in China.
- Improvement in ethics committee reviews.
    - Currently, ethics committee (EC) review and approval is subsequent to the Center for Drug Evaluation (CDE)'s clinical trial authorization process. According to the proposed policy, companies can apply for EC review and approval in parallel to clinical trial applications, provided that the clinical study protocols are approved by the EC before the submission of clinical trial applications.
    - The proposed policy encourages mutual recognition of EC approvals. In the event of multi-center studies, the lead site's EC approval can be used as the basis for all EC reviews. The ECs of other participating sites can directly endorse the EC approval of the lead site, without repetitive reviews.
    - In addition to hospital-affiliated ECs, the proposed policy intends to encourage the formation of regional ECs, which will be responsible for the supervision of clinical studies, qualification of investigators, and the adjudication of appeals filed by sponsors or investigators.
- Streamlining clinical trial approval process. Like the IND mechanism in the U.S., companies need to submit a clinical trial application to the CDE, but only need to wait for 60 working days before initiating the study, unless the CDE rejects the application or issues a deficiency notice during the 60-day period. For certain high-risk medical devices that are subject to the clinical trial approval process, the CFDA must give its review opinions within 60 working days upon receiving the clinical trial application. Applicants will be automatically approved to conduct trials if the Center for Medical Device Evaluation (CMDE) does not reject the application or issue a deficiency notice during the 60-day period.
- Admission of foreign study data. Foreign clinical data can be admitted to support registration of drugs and medical devices in China, as long as (a) the trials comply with Chinese regulations, (b) the trials pass CFDA's on-site audits, and (c) applicants can provide clinical data to prove that no ethnicity difference affects the product's safety and efficacy.
- Expanded access to investigational products. Expanded access to investigational products may be allowed in phase II and phase III trials where the drug or device (a) is intended for treating life-threatening diseases with no effective treatments, and (b) shows probable benefits in early studies. Only a limited number of patients (not exceeding the number of study subjects as per the approved protocol) at each site can have such

compassionate use upon their informed consent. The safety data generated can be used to support marketing authorizations.

III. Circular No. 54 reinforces the CFDA's determination to enhance post-approval enforcement.

- Roll out the Marketing Authorization Holder (MAH) system. The MAH system has been piloted in 10 provinces since November 2015. MAHs are required to take all legal responsibilities for pre-clinical study, clinical studies, product manufacturing, quality of APIs and excipients, distribution, clinical use and adverse event reporting pertaining to the approved drugs. Meanwhile, contractual research, manufacturing, and service organizations (CRO, CMO, CSO, etc.) that are retained by MAHs are required to take both regulatory responsibilities by law and contractual liabilities. The CFDA is determined to roll out the MAH system nationwide.

- Improve adverse event reporting system. The CFDA will levy the primary adverse event reporting responsibilities and post-market product evaluation duties on the MAHs. Concealment, delayed reporting, or misrepresentation will be severely punished by the CFDA.

- Introduce regular and rigorous audits and inspections.

    - The CFDA will further strengthen its data integrity assessment of regulatory dossiers, continue its on-site audits on clinical trials, and take legal actions against data forgery (including criminal investigations by the police and prosecutors).

    - The CFDA and local FDAs will strengthen risk-based, on-site inspections and for-cause inspections for GxP compliance through the product's life cycle, and build a professional team of inspectors through recruiting and training initiatives.

- Regulate promotional activities. The CFDA will establish a Medical Representative Registration System, where all drug license holders will need to register their medical representatives. Medical representatives are allowed to conduct only academic promotion and technical consultation when interacting with physicians and are prohibited from engaging in drug sales.

- Enhance the infrastructure for technical reviews. The CFDA will procure services from qualified third parties to meet the capacity requirement for drug and device reviews. In addition, the CFDA plans to establish an Electronic Common Technical Document (eCTD) system to standardize the format of electronic submissions of drug and device applications. It aims to create a database of master files for each approved drug and device. Last but not least, the CFDA will step up its efforts toward international harmonization of technical standards and hopes to achieve mutual recognition of review and approval decisions.

IV. Circular No. 55 proposes to establish a patent linkage system and improve regulatory data protection. It also reiterates the confidentiality obligations of all government employees involved in the review and approval process.

- Establish patent linkage system. NDA applicants must submit a statement of patents pertinent to their drugs and either (i) an affidavit of non-infringement or (ii) a notice to relevant patent holders if the drugs may infringe any patents within 20 days after the submission of NDA applications. Patent holders can file infringement litigation within 20 days after receiving the notice or upon their knowledge of the CFDA's acceptance of the NDA applications, and inform the CDE accordingly. The CFDA can stay its NDA application for a period of up to 24 months from the date of receiving proof of court acceptance of the case, but the CDE can continue its technical review during this period. If the parties settle or a final court decision is issued during the 24-month period, the CFDA can reject or approve the NDA applications based on the

settlement agreement or the court decision. If the court does not issue any judgement after the 24-month period expires, the CFDA can approve the NDA applications.

- Improve regulatory data protection. NDA applicants can apply for regulatory data protection along with their submissions. The length of protection ranges from 1.5 years to 10 years starting from the date of NDA issuance, according to the degree of novelty and the therapeutic areas. The CDE will not approve NDAs for the same drugs during the protection period, except if the applicants can prove that they generate their data independently.

- Establish a "China Orange Book." The CFDA will publish a "China Orange Book" listing all approved drugs in China. The listing will contain the registration category of the approved drugs and their active ingredients, dosage forms, specifications, MAHs, and other regulatory exclusivity entitlements (i.e., patents, new drug monitoring periods, and regulatory data protection periods).

These draft CFDA policies introduce fundamental changes to the regulatory paradigm, and will considerably reshape the China strategy of life sciences companies. Companies need to carefully review the new policies, propose comments, and monitor the legislative progress.

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