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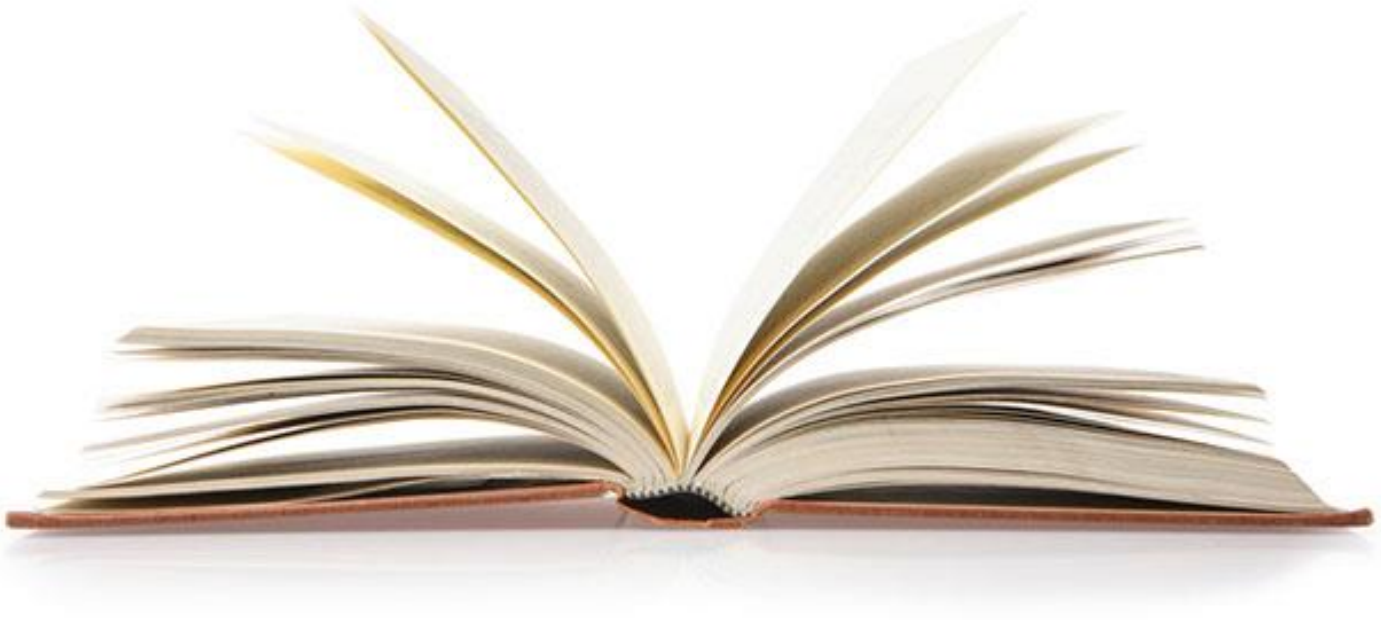
Recent developments on China IP and Regulatory

February 5, 2018



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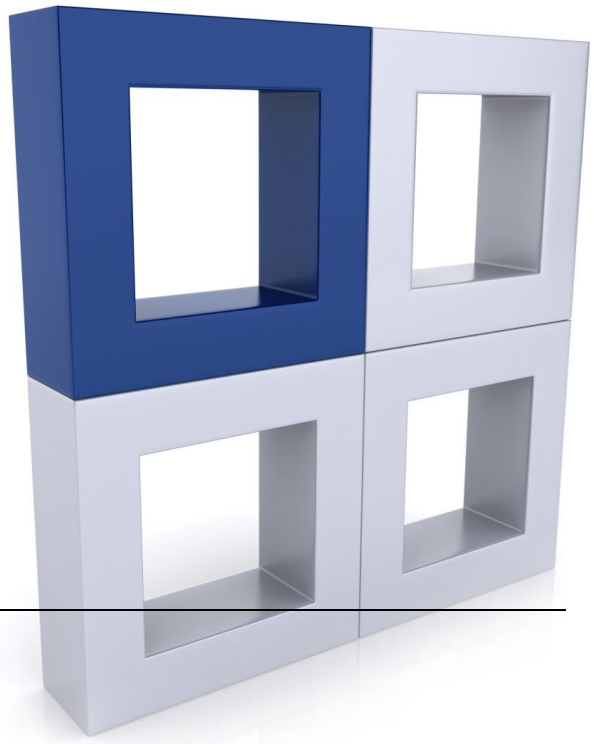

Legislative Developments

China Marketed Chemical Drug Catalog – Chinese Version of the "Orange Book"

The Center for Drug Evaluation (**CDE**) of the CFDA issued a Chinese version of the "Orange Book" – the "China Marketed Chemical Drug Catalog" (**Catalog**) on November 28, 2017. Patent information related to marketed chemical drugs is listed in the Catalog. This may be the first step in establishing a patent linkage system in China. The current Catalog incorporates 189 marketed chemical drugs. The Catalog generally includes the following information relating to a marketed chemical drug: its active ingredient, its brand name, recommended dosages, the ATC code, the registration/approval number, the registration/approval date, the market authorization holder name, the manufacturer name, and the designated drug category.

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Regulations on Review and Approval of Active Pharmaceutical Ingredients, Pharmaceutical Adjuvants, and Pharmaceutical Packaging Materials together with Pharmaceutical Drug Products (Draft for Comments)

An active pharmaceutical ingredient (**API**) will no longer be reviewed and approved separately. Instead, it will be reviewed together with its pharmaceutical product (according to the "Regulations on review and approval of active pharmaceutical ingredients, pharmaceutical adjuvants, and pharmaceutical packaging materials together with pharmaceutical drug products (drug products) (Draft for Comments)" issued by the CFDA on December 4, 2017.

A drug Market Authorization Holder (**MAH**) shall be responsible for the quality of its pharmaceutical drug product, and shall choose appropriate suppliers based on the quality requirements of the pharmaceutical drug product for the API, pharmaceutical adjuvants, and pharmaceutical packaging materials. API suppliers shall register with the CFDA and submit relevant annual reports with the CFDA on a drug product to drug product basis.

During the review of a new drug application (**NDA**), CFDA may conduct an on-site inspection of the pharmaceutical drug product producer and API supplier.

During the review and the approval process, if there are changes in the any of the API, the MAH shall evaluate the effects such changes may have on the drug product and conduct studies accordingly. If the changes are deemed significant, the MAH shall submit a new NDA. Additionally, if such changes will cause changes in the drug product, the MAH shall conduct studies and evaluate the risks involved in the changes in the drug product. It shall not continue the clinical trial until the studies are completed and the ethical requirements are met. For an approved drug product, if there are changes in the API, such changes shall be processed according to the relevant regulations and technical guidelines of the CFDA. If there are changes in either the pharmaceutical adjuvant or the pharmaceutical packaging material, the providers must evaluate and study the changes unless otherwise regulated. Furthermore, for a marketed drug product, the MAH shall submit a supplemental NDA if there is a new supplier and the CDE will review both the drug product and the new API supplier together.

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Adjustment of Review and Approval of Clinical Trial Application (Draft for Comments)

The CFDA issued a "Notice on Adjustments on the Review and Approval of Drug Clinical Trials (Draft for Comments)" (**Draft**) on December 11, 2017. The Draft proposes to make several adjustments to the Review and Approval of Drug Clinical Trials. The main change is that if a CTA is not questioned or rejected by CFDA, it is deemed to be approved (similar to the current US FDA practice).

The CDE, within 5 days of the receipt of the CTA materials, shall finish its procedural review. For an application that meets all requirements, the CDE shall issue a notice of acceptance. For an application that does not meet all the requirements, the CDE will ask the applicant to provide supplemental materials within 60 days of the acceptance. If the applicant fails to do so, the application will be deemed abandoned. After submitting its CTA materials, if the applicant does not receive a rejection or any questions from the CDE within 60 days of the acceptance, the applicant can initiate the drug clinical trial according to the submitted application.

Before filing a CTA, an applicant can request a conference with the CDE to discuss the planned clinical trial by submitting an application for a meeting. Upon receiving the application, the CDE shall set up a conference date with the applicant and the applicant shall submit meeting materials 30 days before the conference. CDE shall conduct a preliminary review on the meeting materials. The CDE will inform the applicant the preliminary review result and answer the questions asked by the applicant. If the applicant believes its questions have been answered and the conference is no longer needed, it can cancel the conference. During the conference, the CDE and the applicant will discuss key technical questions of the clinical trial and whether current data supports the feasibility of the clinical trial. If major defects exist in the clinical trial plan to ensure the safety of the clinical trial subjects, the applicant will be required to conduct further studies before the clinical trial.

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Guidelines for Conditional Approvals for Urgently Needed Drugs (Draft for Comments)

The CFDA circulated "Guidelines for Conditional Approvals for Urgently Needed Drugs (Draft for Comments)" (Draft) on December 13, 2017. If an applicant meets certain conditions, an urgently needed drug may be conditionally approved for marketing to provide early access to innovative drugs addressing severe life-threatening diseases where no effective cure exists. The CFDA may grant conditional approvals if any of the followings occurs: (A) the surrogate endpoint or intermediate clinical endpoint indicates the efficacy and clinical values of the innovative drugs; (B) the early and mid-stage study data indicates the innovative drugs' efficacy and can predict their clinical values (however a confirmatory clinical study must be completed after the conditional approval is issued); or (C) any orphan drugs that have been approved for marketing outside of China.

According to the Draft, drugs meeting the following requirements can apply for conditional marketing: (1) drugs used to prevent or treat serious diseases or reduce the progression of a disease to a less serious degree, including drugs for orphan diseases; and (2) the current treatment of such disease has unmet clinical needs, including: (i) no approved treatment exists; or (ii) one or more approved treatments exist but one of the following occurs: (a) there is a significant improvement in the outcome of the innovative drugs compared to the existing treatments; (b) the drug is clearly effective on patients that are intolerant to or unresponsive to the existing treatments; (c) the drug can be used with other key drugs that cannot be used together with the existing treatments; (d) the drug has the same effects but can effectively avoid serious side effects; and (e) the drug can improve patients' compliance of the existing treatments or meet new public health needs.

For an orphan drug that has been approved for marketing outside of China, the applicant can apply for conditional approval based on the data used to support the foreign marketing approval. Once the CDE grants such conditional approval, the applicant shall finish the ethnicity difference studies and other clinical trials required by the CFDA as soon as possible. As for the timing of such conditional approval application, it should be submitted together with the corresponding NDA.

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Regulation for Compassionate Expanded Clinical Trial "Named Patient Program" (Draft for Comments)

The CFDA, on December 13, 2017, circulated "Regulation for Compassionate Expanded Clinical Trial "Named Patient Program" (Draft for Comments)" (**Draft**). The Draft details the requirements and procedures for expanded access to clinical trial drugs via a "Named Patient Program." Such use is intended for patients with life-threatening diseases or diseases having severe adverse impacts on their quality of life without any existing effective treatments who do not meet the enrollment criteria and require early intervention, including: (1) patients ineligible for new drug clinical trials; (2) patients unable to participate due to their locations, clinical trial times and other reasons; (3) drugs whose clinical study has been completed but has not yet been approved for marketing in China and the available data indicates that the drug is effective and safe for use on targeted patients in China.

The drug applicant shall submit an expanded access to clinical trial drug application with the CDE of the CFDA for approval. The application shall include informed consents from the patients, for whom the benefit of using the drugs shall, based on the evaluation of their doctors, outweigh the risks. Additionally, the experimental data generated from the expanded access to clinical trial drugs cannot be used as primary data for the drug's market approval, but can be used as supporting data. The CDE, upon receiving the application, shall make a decision within 30 days. The following factors will be considered by the CDE: whether the patients are among the targeted patients; whether there is preliminary data indicating effectiveness and safety of the drug; and whether the expanded access to the clinical trial drug will affect the drug's development and registration in China.

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Notice on Drug Market Authorization Holder ("MAH")'s Responsibility to Report Adverse Events (Draft for Comments)

New proposed regulations shift the burden of reporting adverse events from the drug manufacturer to the drug MAH as the CFDA is promoting the MAH system. The CFDA circulated a "Notice on Drug MAH's Duty to Report Adverse Reactions (Draft for Comments)" (**Draft**) on December 27, 2017. The Draft sets out detailed responsibilities of a drug MAH in reporting adverse reactions and adverse events of its drug.

The MAH shall report any adverse events of its drug to the National Drug Adverse Reaction Monitor System, including adverse reactions of normal dosage use and adverse events that are caused by drug qualities or any other reasons such as overdose, prohibited use, misuse, etc. Drug distributors shall report such adverse reactions and adverse events to the MAH and in turn, the MAH shall timely report them to the National Drug Adverse Reaction Monitor System. Second, the MAH shall monitor adverse reactions and adverse events of the drug, and collect information from doctors, pharmacists and patients. It shall also voluntarily collect data regarding adverse reactions and adverse events from clinical trials, marketing programs, academic papers and online forums. Third, the MAH shall analyze all adverse reactions and events and file an annual report to the Provincial Drug Adverse Reaction Monitor Agency.

The MAH shall conduct recall on any of its drugs that may have safety and quality issues.

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Notice on Increasing the Damage in Intellectual Property Right Infringement Cases

The Supreme People's Court is aiming to increase the damage award in intellectual property infringement cases as indicated in its first paper in 2018 issued on January 2: "Notice on Making the Full Use of the Role of Trial Function to Create a Good Legal Environment for Entrepreneurs to Innovate and Start Businesses" (**Notice**). The Notice is a response to the State Council's September 8, 2017 "Opinions on Establishing a Good Environment for Entrepreneurs' Growth to Carry Forward the Spirit of Excellent Entrepreneurs and Better Make the Full Use of the Roles of Entrepreneurs." The Notice aims to protect entrepreneurs' intellectual property rights by raising the damage levels in intellectual property right infringement cases. The Supreme People's Court hopes to establish an IP judicial guideline to improve the compensation level in intellectual property right infringement cases. It further states that courts, in adjudicating infringement cases, shall use the market value of the underlying intellectual property right as a guideline. The guideline will primarily try to compensate the loss of the intellectual property right owners and supplement it with **punitive damages**. Currently, no detail regarding the new guideline has been disclosed.

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