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Legal Commentary

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A Big Step Forward - China May Enhance Drug Trial Data Protection

Comments on Implementing Measures for the Protection of Drug Trial Data (for Interim Implementation) (Draft for Comment)

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On April 26, 2018, the State Drug Administration issued for public comment the *Implementing Measures for the Protection of Drug Trial Data (for Interim Implementation) (Draft for Comment)* (the "**Implementing Measures**")[1]. Compared with the previous *Relevant Policies on Encouraging Innovation in Drug and Medical Equipment and Protecting the Rights and Interests of Innovators (Draft for Comment)* ("**Relevant Policies**")[2], and *Opinions on Deepening the Reform of the Evaluation and Approval System and Encouraging Innovations in Drugs and Medical Devices*[3], the Implementing Measures unprecedentedly expand the duration and scope of data protection for specialized drugs and, for the first time, implement data protection application, review, public notice of authorization, objection and revocation mechanisms.

I. High-standard drugs and drugs of the same variety may be granted 12 years of drug data protection

Compared with existing law and even recently promulgated opinions related to the protection of various types of drug data, the Implementing Measures further broaden the scope of data protection and extend the time of protection. These developments reflect the policy of promoting the research and development of innovative medicines and specialized drugs, while also setting out a high standard for drug trial data protection system. Comparisons between the

[1] *Implementing Measures for the Protection of Drug Trial Data (for Interim Implementation) (Draft for Comment)* (St. Drug Admin.; issued Apr. 26, 2018, for comment until May 31, 2018);

[2] *Relevant Policies on Encouraging Innovation in Drug and Medical Equipment and Protecting the Rights and Interests of Innovators (Draft for Comment)* (China Food and Drug Admin.; issued May 12, 2017, for comment until June 10, 2017)

[3] *Opinions on Deepening the Reform of the Evaluation and Approval System and Encouraging Innovation in Drugs and Medical Devices* (Gen. Office CCCPC, Gen. Office St. Council; promulgated Oct. 8, 2017) 2017 ST. COUNCIL GAZ. 29.

Implementing Measures and current laws and the Relevant Policies are as shown in the below:

<table>
<tr><th colspan="2">Existing law[4]</th><th colspan="2">Relevant Policies (2017)</th><th colspan="2">Implementing Measures (2018)</th></tr>
<tr><td rowspan="8">Innovative drugs</td><td rowspan="8">6 years</td><td>Innovative drugs</td><td>6 years</td><td>Innovative drugs</td><td>6 years</td></tr>
<tr><td>Innovative therapeutic biological products</td><td>10years</td><td>Innovative therapeutic biological products</td><td>12 years</td></tr>
<tr><td>Innovative orphan drugs</td><td>10years</td><td rowspan="2">Orphan drugs
(Including indications)</td><td rowspan="2">12 years</td></tr>
<tr><td>Improved new drugs for rare diseases</td><td>3 years</td></tr>
<tr><td>Innovative pediatric drugs</td><td>10 years</td><td rowspan="2">Pediatric drugs
(Including indications)</td><td rowspan="2">6 years</td></tr>
<tr><td>Improved new pediatric drugs</td><td>3 years</td></tr>
<tr><td colspan="2">Generic drugs that have successfully challenged patents and been sold in offshore markets but are being sold as first generics in China</td><td>1.5 years</td><td>Drugs that successfully challenge patents</td><td>To be determined</td></tr>
</table>

According to the Implementing Measures, innovative biological products that are brought to market in the China are entitled to up to 12 years of data protection, a period equivalent to that granted under U.S. law[5], which is even greater than 10 years in the EU and 8 years in Japan and Canada[6]. In addition, compared with the Relevant Policies, the Implementing Measures reduce the innovation requirements for orphan drugs and pediatric drugs, by stipulating a general 6-year protection period for those two drug types. Furthermore, Article 7 of the Implementing Measures also provides an "independent operation" rule, which stipulates that where different data protection periods are granted to the same drug, each period will be determined from the respective application approval date for such protection period[7]. Thus,

[4] According to Article 20 of Measures for Administration of Drug Registration (2007), "In accordance with the provisions of Article 34 of the Regulations for Implementation of the Drug Administration Law, for a period of 6 years from the date of approval of the original applicant, SFDA shall not approve a subsequent application that uses, without the consent of the original applicant, the undisclosed R&D data and other data generated by the original applicant approved to manufacture or market a drug containing new chemical ingredients unless the submitted data is generated by the subsequent applicant independently"

[5] See 42 U.S.C (United States Code) §262(7)(A): *"Approval of an application under this subsection may not be made effective by the Secretary until the date that is 12 years after the date on which the reference product was first licensed under subsection (a)."*

[6] Lei Zhang and Wei Xia, *Study on the Data Protection Clauses for TPP Biopharmaceutical*, Intellectual Property, issue 5 of 2016, p.119.

[7] Implementing Measures at Art. 7: "Protection periods granted for the same drug shall be calculated respectively from the date of approval of the corresponding drug registration applications."

under the new data protection system, applicants will be able to receive additional data protections for orphan drugs and pediatric drugs.

It is notable that, in order to accelerate the internationalization of drug R&D in China and encourage the introduction of specialized drugs, the Implementing Measures further provide that drug registration applications in China submitted with data obtained from international multi-center clinical trials conducted in China can be granted data protection for a designated period that is applicable for the corresponding drug type. However, if the drug registration application in China is later than the drug registration application in other countries or regions, the data protection period that may be awarded will only range from one to five years, depending upon the circumstances, and no protection will be awarded if the drug registration application in China is later than six years following that in other countries or regions[8]. In addition, in order to support the upcoming "acceptance of data from overseas clinical trials" system[9], and to strongly encourage applicants to carry out clinical trials on patients in China, the Implementing Measures also provide that a data protection period of only one fourth of the standard data protection period may be granted for drug registration applications in China solely based upon overseas trial data; a data protection period of one half of the standard may be granted where the underlying clinical trial data is supplemented by trials conducted in China[10].

II. Upon effectiveness, trial data protection applications to be submitted together with drug registration applications.

According to the Implementing Measures, trial data protection applications are required to be submitted together with drug registration applications and are subject to subsequent procedures, such as public notice of acceptance, technical reviews and public notice of authorization.

a. Application: drug registration applicants intending to obtain drug trial data protection should submit the trial data protection application together with the drug registration application,

[8] Implementing Measures at Art. 5, paras. 1 and 2: "Innovative drugs approved to enter the domestic market will be entitled to a data protection period of six years, and this data protection period will be doubled to 12 years for innovative biological products for curative uses. For the drugs or biological products for curative uses under applications for entry into the domestic market or for synchronous entry into the domestic market and other countries/regions by use of data of clinical trials conducted in China or data of international multi-center clinical trials conducted in China, a data protection period of 6 years or 12 years will be granted upon approval of their entry into market(s); for those data under applications for entry into the domestic market by use of data of international multi-center clinical trials conducted in China later than the applications for entry into other countries/regions, a data protection period of one to five years will be granted depending on circumstances, provided that no data protection period will be granted if the former applications are six years later than the latter ones."

[9] See Technical Requirements for Accepting Overseas Clinical Trial Data (Draft for Comment) promulgated by Center for Drug Evaluation, available at: http://news.163.com/17/1020/21/D17LIDSV000187VE.html.

[10] Implementing Measures at Art. 5, para. 3: "For the new drugs under applications for entry into the market by use of overseas data without clinical trial data for Chinese patients, a data protection period equivalent to one-fourth of the period calculated under the above method will be granted; if clinical trial data for Chinese patients are supplemented, a data protection period equivalent to one-second of the period calculated under the above method will be granted."

and provide a written statement to describe the reasons and term for trial data protection[11].

b. Acceptance: Upon acceptance of a drug registration application, the drug evaluation institution will publicize the trial data protection application submitted by the applicant for 30 days[12]. Publicizing of the application does not constitute an effective authorization of protection. During this period, the drug evaluation institution will normally review and approve the drug registration application of other applicants for the same-variety drug by use of data acquired on their own[13].

c. Review: the drug evaluation institution will review the applicant's data protection application at the same time when conducting a technological evaluation. If the data protection application complies with the rules, the drug evaluation institution will issue examination findings that specify the reasons for data protection and the period of protection[14].

d. Authorization: drug trial data protection rights will be granted concurrently once the drug registration application is approved and publicized. The *Catalog of Marketed Drugs* will include and publicize the reasons for protection, both the starting and ending dates, and will timely delete information of drugs whose data protection period has expired so that third parties can determine when it is appropriate to submit generic drug applications[15].

III. Notification and objection, guarantee of data exclusivity

The Implementing Measures will also allow data owners to exercise their data exclusivity rights and related remedies.

It should be noted that the drug trial data protection period is not the same as a market

[11] Implementing Measures at Art. 9, para. 1: "A drug registration applicant, if attempting to apply to the state drug administration for data protection, shall file an application for the protection of trial data for the concerned drug, specifying the length of the data protection period and reasons, when applying for registration to obtain the drug marketing authorization."

[12] Implementing Measures at Art. 9, para. 2: "After a drug registration application is accepted, the drug evaluation department of the state drug administration shall publicize the applicant's application for protection of trial data for 30 days."

[13] Implementing Measures at Art. 13: "Before a drug has its trial data protected, other applicants' applications for the registration of the same-variety drug by use of data acquired on their own may be proceeded with according to the evaluation and approval procedures, and those meeting requirements shall be approved."

[14] Implementing Measures at Art. 10: "When conducting a technological evaluation for the registration of a drug, the drug evaluation institution of the state drug administration shall concurrently evaluate the applicant's application for data protection; if the application is in compliance with the provisions, the drug evaluation institution shall specify reasons for protection and a protection period in an examination conclusion, and make an examination conclusion for the protection of trial data and marketing according to procedures."

[15] Implementing Measures at Art. 11: "The rights to protection of trial data of drugs shall become effective upon approval and publicity of the drug marketing and registration application, with data protection information and drug approval information publicized at the same time. The information on protection of trial data of drugs shall at least include reasons for protection of trial data of drugs, the starting and ending dates of the data protection period, and other information, and shall be set out and publicized in the Catalogue of Drugs for Marketing. Applicants applying for protection of trial data of drugs or any third parties may consult the Catalogue of Drugs for Marketing for protection status and protection period on their own. Upon expiration of the protection period for trial data of drugs, the relevant information shall be promptly deleted from the Catalogue of Drugs for Marketing."

exclusivity period. During the data protection period, the drug evaluation institution will not grant drug registration applications submitted based upon the trial data of data protection right holders, but will still examine and approve other drug registration applications submitted based upon independent data.

Relevant provisions of the Implementing Measures provide in that[16], during the data protection period, the data right holder must be notified within 30 days of when a drug registration applicant submits an application based on independent data for a drug that is of the same type as that of the holder. The data protection right holder can raise an objection within 30 days from the date of receipt of the notification. The drug evaluation institution will issue a decision on whether to accept the objection within 90 days. If the decision is not satisfactory, either the generic drug applicant or trial data protection right holder may file for administrative reconsideration or administrative litigation.

The above provisions essentially provide a channel for data protection right holders to exercise their data exclusivity rights. During the data protection period, a data protection right holder can challenge the data of subsequent applicants by filing objections. Further, they may resort to remedies such as initiating administrative reconsiderations or administrative litigation, if the drug evaluation institution decides to support a subsequent applicant's application by finding that the relevant data were sourced independently.

The trial data protection system in the Implementing Measures differs somewhat from how things are handled in the United States. Under U.S. drug trial data exclusivity, if the data protection right holder believes that its data exclusivity rights have been infringed because the U.S. Food and Drug Administration ("**FDA**") has approved an abbreviated new drug application (ANDA) within the trial data exclusivity period, the holder may seek administrative or judicial relief against the FDA's decision[17]. By contrast, the Implementing Measures may enable the data protection right holder to become aware of the possibility that a subsequent applicant may submit a drug registration application by relying on data from other sources at an earlier stage,

[16] Implementing Measures at Art. 14: "Within the trial data protection period, if an application is filed for the registration of the same-variety drug by use of the trial data acquired independently or upon consent of the marketing authorization holder, in addition to the required corresponding registration application materials, a written statement of the independent acquisition of the relevant data or authorization shall be submitted.
The drug evaluation institution of the state drug administration shall, within 30 days upon acceptance of the above application, notify the data protection right holder, who may, within 30 days upon receipt of the notification, raise an objection with the institution designated by the state drug administration. If there is no objection or no objection has been raised within the time limit, it shall be deemed that the above-mentioned statement of independent acquisition of data is recognized.
Where the data protection right owner raises an objection to the authenticity of the above-mentioned data acquired independently, the drug evaluation department of the state drug administration shall organize and complete data verification within 90 days. If the data are found to be problematic or suspected of being fraudulent, the data shall be dealt with in accordance with the relevant provisions on drug registration administration and it shall be notified to the data protection right holder."

[17] Tong Chu, *Study on Protection of Drug Trial Data under TRIPS Agreement* (First Edition), Intellectual Property Publishing House, January 2015, p. 112.

which would provide more protection to the holder.

IV. Prohibit abuse of rights, requirements on data disclosure, and cancellation of protection period

To prevent abuse of the trial data protection system, the Implementing Measures provide for a data disclosure system and a data exclusivity cancellation mechanism if no drug sales are made for a period of one year.

Regarding the disclosure system, the Implementing Measures stipulate that data protection right holders are required to disclose data under protection from the date of obtaining the data protection authorization[18]. This measure will not only prevent data fraud by subjecting the relevant data to public oversight, but will also help avoid duplicative experiments which may lead to wasted resources. However, it remains to be seen how this system will be specifically implemented, considering that the relevant data may include data right holders' trade secrets or the sensitive personal information of data subjects.

The Implementing Measures also provide for a data exclusivity cancellation mechanism if no drug sales are made for a period of one year. That is, if a drug that has obtained data protection has not been sold on the market for any reason for one year following the date of approval for sale, an interested party may file an application for cancellation of protection with the State Drug Administration[19], which, once verified, will cause the data protection period to be cancelled. After cancellation, other applicants can again submit drug registration and data protection applications for drugs of the same type[20]. The purpose of this mechanism is mainly to encourage the introduction of new drugs as early as possible for the benefit of the public. Therefore, drug R&D enterprises developing the same types of drugs should pay close attention to the sales status of approved drugs, and may again apply for data protection rights if the approved drugs have "no sales for one year." It should be noted that according to Article 4 of the Implementing Measures, if other applicants again submit drug registration and data protection applications, the applications must be entirely based on data acquired independently without reliance on the trial data of others or publicly released research results[21]. Such

[18] Implementing Measures at Art. 17, para. 1: "Data protection right holders shall voluntarily disclose their data under protection as of the date when the right is acquired."

[19] Implementing Measures at Art. 17, para. 2: "Where a drug under data protection has not been sold on the market within one year from the date of approval for marketing for its own reason, the relevant stakeholder may file an application for revoking the protection period with the state drug administration; if the situation is true upon verification, data protection shall be revoked."

[20] Implementing Measures at Art. 18: "Where the trial data protection of a drug is revoked, the state drug administration may, as of the date when the revocation decision is made, approve other applicants' applications for marketing and registration of the same variety; if an applicant files an application for the protection of drug data at the same time, the data meeting requirements shall be given the corresponding protection period in accordance with provisions."

[21] Implementing Measures at Art. 4: " For the purpose of the Measures, "trial data" refer to the non-clinical and clinical trial data contained in the data package of drug marketing and registration application documents

applications cannot be based upon trial data that have been previously published by the data protection right holder.

V. Patent challenge system not expressly provided, remains to be supplemented with a drug patent linkage system

Compared to the Relevant Policies, the Implementing Measures in their current form do not restrict data protection only to first generics once a successful patent challenge has been made. However, we tend to believe that the protection of "drugs that successfully challenge patents" will be further restricted based upon similar policies in the United States[22] and in consideration of the optimal distribution of pharmaceutical production resources. In addition, it is worth noting that the Implementing Measures fail to specify the definition of "successful patent challenge" and the corresponding protection period[23]. By referring to the 180-day market exclusivity period for new drugs under the U.S. *Drug Price Competition and Patent Term Restoration Act*[24], and the drug patent linkage system found in so-called "paragraph IV" certifications[25], we understand that "successful patent challenge" may imply a scenario where a generic drug applicant submits an application for registration together with a statement that potentially triggers litigation under the patent linkage system. The applicant certifies that it can prove through litigations that the patent for the branded drug is invalid, or prove that the applicant's generic drug, including its commercial manufacture, use, and sale, does not constitute patent infringement[26].

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submitted by a drug marketing applicant in accordance with requirements, which are related to the effectiveness of drugs but are not related to drug safety, and which shall meet the following requirements:
1. the data are required to be provided in the drug registration application materials submitted for obtaining the marketing authorization of drugs;
2. the data have not been publicly disclosed before a drug registration application is filed; and
3. the data are acquired independently without reliance on others' trial data or publicly released research results."

[22] Taoxi Lin, Na Yu and Lu Huang, *Research on the first generic drug system and patent challenge strategy of USA*, Chinese Journal of New Drugs, issue 19, Vol. 25, 2016, p. 2171.

[23] Implementing Measures at Art 3, para. 5: "The protection of trial data of drugs refers to the system under which the state drug administration shall, according to legal procedures, grant a certain data protection period to the following drugs for which applicants have obtained marketing authorization based on the test data acquired on their own:…(5) drugs that successfully challenge patents".

[24] See 21 U.S.C (United States Code) §355(j)(5)(B)(iv): *"…Subject to subparagraph (D), if the application contains a certification described in paragraph (2)(A)(vii)(IV) and is for a drug for which a first applicant has submitted an application containing such a certification, the application shall be made effective on the date that is 180 days after the date of the first commercial marketing of the drug (including the commercial marketing of the listed drug) by any first applicant."*

[25] See 21 U.S.C (United States Code) §355(b)(2)(A): "*An application submitted under paragraph (1)…shall also include— a certification, in the opinion of the applicant and to the best of his knowledge, with respect to each patent which claims the drug for which such investigations were conducted or which claims a use for such drug for which the applicant is seeking approval under this subsection and for which information is required to be filed under paragraph (1) or subsection (c)— (i) that such patent information has not been filed, (ii) that such patent has expired, (iii) of the date on which such patent will expire, or (iv) that such patent is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted…*"

[26] See 21 U.S.C (United States Code) §355(j)(2)(A)(iv): *"An abbreviated application for a new drug shall contain…a certification…(IV)that such patent is invalid or will not be infringed by the manufacture, use, or*

The Implementing Measures in their current form leave these relevant provisions blank because the drug patent linkage system is still at a preliminary stage in China. Aspects of the drug patent linkage system remain to be clarified, such as the specific declaration system for patent challenges, patent litigation linkage rules and the stay period[27]. Overall, the patent challenge system, after being promulgated, will be an effective tool to strike a balance between generic drugs and innovative drugs, and will provide a channel for generic drug applicants to seek data exclusivity protection by initiating patent litigations.

sale of the new drug for which the application is submitted..."

[27] Lin Wang, Rui Luo, *China May Establish a "Drug Patent Linkage System," How Should Companies Respond?* (Chinese), Han Kun Law Offices, May 27, 2017.

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