State Food and Drug Administration Drug Safety Supervisory Department Notice Seeking Opinions Concerning 《Foreign Drug Manufacturing Enterprises Inspection Administrative Measures》 Shi Yao Jian An Han [2012] No. 82

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To all relevant entities:

In order to standardize the task of inspecting foreign drug manufacturing enterprises, SFDA has organized the drafting of《Foreign Drug Manufacturing Enterprises Inspection Administrative Measures》 (Draft for Public Comment) and hereby publishes the draft for public comment on SFDA web site so as to publicly solicit comments. If any entity or individual has any comments or suggestions, please provide the feedback to SFDA's Drug Safety Supervisory Department before October 8, 2012.

Contact person:	Ye Jia Hui
Telephone:	010-88330812，88330854
Fax：	010-88330810
Email：	ajgmp @ sda.gov.cn
Enclosures:	Specific data requirements

State Food and Drug Administration Drug Safety Supervisory Department
August 20, 2012

《Foreign Drug Manufacturing Enterprises Inspection Administrative Measures》(Trial)（Draft for Comments）

Article 1 These Measures are formulated in accordance with the relevant regulations such as the《Drug Administrative Law》、《Drug Administrative Law Implementing Rules》and《Special Rules of the State Council Concerning the Strengthening of the Supervision of the Safety of Food and other Products》, in order to standardize the task of inspecting foreign drug manufacturing enterprises.

Article 2 The task of inspecting foreign drug manufacturing enterprises refers to SFDA-organized on-site inspection of manufacturing sites for imported drugs that are in the process of undergoing review and evaluation or review and approval for registration or have already obtained marketing authorisation, the purpose of which is to strengthen the supervision and management of imported drugs and standardize the manufacturing activities of imported drugs, in order to ensure the quality and safety of the imported drugs.

Article 3 These Measures apply to all foreign drug manufacturing enterprises that have obtained the 《Imported Drug Registration Certificate》or the 《Medical or Drug Product Registration Certificate》approved and issued by SFDA, and foreign drug manufacturing enterprises that are in the course of applying for the《Imported Drug Registration Certificate》or the《Medical or Drug Product Registration Certificate》from SFDA.

Article 4 SFDA shall determine the list of the foreign drug manufacturing enterprises and product types that require on-site inspections according to information from all aspects such as review and evaluation for registration, day-to-day supervision and management, port inspection, reports from the general public, and shall provide advance notification of the inspection time and other relevant

information to the representative offices of these foreign drug manufacturing enterprises in China or the agency organizations in China entrusted by them (hereinafter referred to as the “agency organizations”).

Article 5 The agency organization shall be responsible for handling communications and contacts with the foreign drug manufacturing enterprise, and it shall also be responsible for submitting to SFDA Drug Certification Management Center the required relevant materials in a timely manner. Please see the enclosures for the detailed data requirements.

Article 6 Upon receipt of the on-site inspection notice, foreign drug manufacturing enterprises that have special reasons for requiring postponement of the on-site inspection shall have its agency organization submit a written application with an explanation of the reasons to SFDA Drug Certification Management Centre. Enterprises that refuse to have on-site inspections without any reason or do not cooperate with the on-site inspection shall be deemed as not having passed the on-site inspection.

Article 7 The foreign drug manufacturing enterprises being inspected shall arrange for batch manufacture of the product being inspected during the period of on-site inspection.

Article 8 The on-site inspections shall be conducted on a system whereby responsibility lies with the team leader. Each inspection team shall generally be composed of 2-5 inspection personnel.

Article 9 The initial meeting for the on-site inspection, which shall be chaired by the team leader of the inspection team, shall confirm the scope of the inspection, the inspection schedule, the accompanying enterprise personnel; the inspection disciplinary rules and items of note shall be announced during the initial meeting.

Article 10 The on-site inspection shall primarily consist of: whether the drug registration submission materials and on-site materials are consistent with the actual manufacturing process as well as whether the drug manufacturing process conforms to the《Drug Manufacturing Quality Management Standards (GMP) (2010 Revision)》.

Article 11 The foreign drug manufacturing enterprise being inspected shall provide the necessary relevant information in a timely manner. According to the needs of the inspection task, the inspection personnel may collect evidence by means of taking photographs and recording videos. If the enterprise refuses to allow the taking of photographs or the recording of videos, the inspection personnel shall provide a detailed explanation of the relevant circumstances in the inspection report. When necessary, the inspection personnel may collect samples and take them back to China for testing.

Article 12 Upon completion of the on-site inspection, the inspection team shall conduct analysis and summary of the circumstances of the on-site inspection, determine the defective items of the enterprise. During the period of the analysis and summary, the accompanying enterprise personnel shall recuse themselves.

Article 13 In the final meeting the inspection team shall provide verbal feedback to the foreign drug manufacturing enterprise being inspected of the defective items discovered in the inspection. If the foreign drug manufacturing enterprise being inspected has any objections, it may provide explanations. When necessary the inspection team may further verify the relevant situation and make amendments to the defective items in accordance with the verified results.

Article 14 Within two months of the completion of the on-site inspection, SFDA Drug Certification Management Center shall provide feedback to the agency organization in the form of a written on-site inspection report. With respect to enterprises where no obvious defective items have been uncovered in the on-site inspection or where the defective items can be immediately rectified, SFDA Drug Certification Management Center shall not provide feedback to the agency organization in

the form of a written on-site inspection report, but shall handle the matter directly in accordance with the relevant provisions of Article 15.

The agency organization shall be responsible for submitting the rectification report of the enterprise being inspected to SFDA Drug Certification Management Center within one month of receiving the on-site inspection report. If the rectification report cannot be submitted within the stipulated period due to special reasons, an application to seek an extension of the deadline specifically stating the date of submission should be submitted to SFDA Drug Certification Management Center in advance, and the period of extension shall not exceed one month.

Article 15 Within one month of receiving the report setting out the rectification situation submitted by the agency organization, SFDA Drug Certification Management Centre shall conduct a comprehensive evaluation with respect to the inspection situation in accordance with risk management principles. The inspection conclusions can be divided into three categories: "Compliant with requirements", "Compliant with requirements after rectification" and "Not compliant with requirements". The judging principles are as follows:

I. In instances where the drug manufacturing and quality control are consistent with the submitted materials, and the manufacturing can be organized in accordance with the drug GMP requirements, the enterprise shall be judged as being "Compliant with requirements".

II. In instances where multiple major defects are discovered during the on-site inspection, and the submitted rectification situation report states that the manufacturing can be organized in accordance with the drug GMP requirements after rectification, the enterprise shall be judged as being "Compliant with requirements after rectification".

III. In instances acts of fraud are discovered during the on-site inspection or if key factors affecting product quality are inconsistent with the submitted materials; or in instances where there exist severe defects or multiple major defects indicating that the entity being inspected cannot organize manufacturing in accordance with the drug GMP requirements, the enterprise shall be judged as being "Not compliant with requirements".

When necessary, SFDA Drug Certification Management Centre may organize the inspection personnel to conduct another inspection with respect to the rectification situation of the enterprise.

Article 16 With respect to enterprises with inspection conclusions of "Compliant with requirements" or "Compliant with requirements after rectification", SFDA shall provide feedback to the agency organization the written opinion within one month after the inspection conclusion is made.

With respect to enterprises with the inspection conclusion of "Not compliant with requirements", SFDA shall issue to the agency organization a 《Warning Letter》, ordering it to suspend importation of the drug, or suspend the process of review and evaluation or review and approval for registration until it complies with requirements in the next on-site inspection. At the same time, the food and drug administration of each port shall be notified to stop processing the《Imported Drug Customs Clearance Form》for this drug. With respect to the drugs that have already been imported, SFDA shall determine, based on the severity of the circumstances, to issue an order to recall or otherwise dispose of the drug.

Article 17 Under special circumstances, if it is discovered during an on-site inspection that serious defects exist in the foreign drug manufacturing enterprise being inspected, such that the safety of the public in respect of drug use would be severely impaired, SFDA may immediately make the relevant decisions in accordance with Article 16, paragraph 2.

Article 18 These Measures shall take effect from [DATE], and SFDA shall be responsible for the interpretation thereof.

Enclosures: Specific data requirements:

The following data must be provided in two counterparts, printed on A4 paper and bound together.

I. Site Master File

Content of Site Master File includes nine aspects, i.e., the general situation of the enterprise, manufacturing quality management system, personnel, plant and equipment, documents, manufacturing, quality control, distribution, complaints, product defects and recalls, self-inspection. Specific requirements shall be drafted in accordance with the newest PIC/S requirements concerning Site Master Files. Such materials shall be provided in Chinese, and part of the content in the graphs and tables may be provided in English.

II. Basic situation concerning importation of the imported drug into China during the last three years.

This includes the import volume of each year, ports inspection situation, adverse effect situation, product complaint situation and product recall situation with respect to the product over the past three years. If there has been any complaint concerning or recall of the product due to quality reasons, the reasons for the occurrence and final disposition of the complaint or recall shall be described in detail. Such information shall be provided in Chinese. If the application with SFDA for an 《Import Drug Registration Certificate》 or 《Medical and Drug Product Registration Certificate》 is pending, this item needs not to be submitted.

III. Basic situation with respect to the manufacture and sale of the imported drug in other countries worldwide during the last three years.

This should include the information if import and sale of the product has been halted due to failure to achieve GMP compliance or if the product has been recalled due to quality reasons. If the aforementioned circumstances have occurred, the specific reasons for the occurrence and final disposition should be provided in detail. Such information shall be provided in Chinese. If such product is not on the market in other countries, this item need not be submitted.