Connecting a World of Pharmaceutical Knowledge

5 October 2012

State Food and Drug Administration
Department of Drug Safety and Inspection
26 Xuanwumen Xidajie
Beijing, 100053,
P.R. China

Subject: Submission of comments for *"Regulations on Inspection and Administration of Drug Manufacturing Enterprises Oversea (Opinion Soliciting Draft)"*
Document No. 82 2012 (20 August 2012)

Dear Sir/Madam:

ISPE welcomes the opportunity to comment on the *"Regulations on Inspection and Administration of Drug Manufacturing Enterprises Oversea (Opinion Soliciting Draft)",* and appreciates that SFDA is documenting the requirements for these inspections. The comments provided reflect the views and opinions of members from a number of global pharmaceutical companies.

In addition to the detailed comments provided, several general remarks and recommendations related to translations and inspection frequency are also captured in the document. We would request additional clarification of these items. We reiterate that we appreciate the SFDA's willingness to be transparent in documenting the requirements for overseas inspections. This will be mutually beneficial to the agency and to industry, and will help to clarify expectations prior to the subject inspections.

Our comments are attached.

Yours sincerely,

President/CEO, ISPE

ISPE Headquarters
600 N. Westshore Blvd. | Suite 900 | Tampa, FL 33609 | USA | TEL +1-813-960-2105 | FAX +1-813-264-2816
www.ISPE.org

国家食品药品监督管理局药品安全监管司关于《境外药品生产企业检查管理办法》征求意见的通知

企业名称：ISPE - International Society of Pharmaceutical Engineering	联系人：Jane R. Brown		email：jane.r.brown@gsk.com
一、对法规的总体意见			
General comment: We appreciate the SFDA documenting the requirements for the overseas manufacturing inspections. This will be mutually beneficial and helps to clarify expectations prior to the subject inspections. There are a few additional areas that we recommend be addressed to add further clarity: (1) Is it the expectation of the SFDA that the manufacturer provide translators to support the inspection process (before, during and after)?, (2) What is the intended frequency of inspections of overseas manufacturers and/or how will this be determined?, (3) Additional clarification may be needed with respect to the translation of documents that will be provided during the inspection (e.g., are all documents required to be translated or can the translation occur verbally using translators?), (4) We recommend that the term "agencies" be changed to "manufacturer" to eliminate potential confusion with the use of this term as it applied in other countries.			
二、具体意见			
法规原文	**修改意见 <<Comment>>**	**<<Proposed Language>>**	**修改依据或理由 <<Rationale>>**
第一条 根据《药品管理法》、《药品管理法实施条例》以及《国务院关于加强食品等产品安全监督管理的特别规定》等有关规定，为规范境外药品生产企业的检查工作，特制定本办法。 Article 1 In accordance with Drug Administration Law, Regulations for the Implementation of Drug Administration Law, as well as Special Rules of the State Council for the Safety Supervision and Administration of Food and Other Products, these Measures are instituted with a view to regulating the inspection of overseas drug manufacturers.	None	N/A	N/A
第二条 境外药品生产企业的检查工作是国家食品药品监督管理局组织的对注册审评、审批期间或已获得上市许可的进口药品生产现场的检查，旨在加强对进口药品监督管理，规范进口药品生产行为，确保进口药品质量安全。 Article 2 Inspection on overseas drug manufacturers refers to the inspection conducted by the SFDA on the manufacturing sites of imported drugs under registration evaluation, approval or already approved for marketing in order to enhance the supervision and administration of imported drugs, regulate the manufacturing of imported drugs and ensure the quality and safety of imported drugs.	1) There is no indication as to who covers the cost of these inspections i.e. SFDA, Marketing authorisation holder, or site being inspected. As this article indicates rational is based on strengthening administration by China, suggest cost is born by them. 2) Similarly this section does not indicate the expected frequency of such overseas visits. Nor does it relate the frequency of such visits to the expiry date of certificates of conformance mentioned in Amendments 15.1 and 15.2 3) The scope of this would appear to be a full inspection programme for every new or existing product supplied into Chinese market. Is there any opportunity to waive inspections through providing documentary evidence of satisfactory quality and inspection performance for existing products ?	1) State that the cost of these inspections ill be covered by SFDA 2) Relate the frequency of the visits to a stated expiry date on certificates of conformance detailed in Amendments 15.1 and 15.2 3) The inspection of drug manufacturer overseas means the SFDA will inspect the manufacturing site of import drugs which are being though the process of registration review, examination and approval. The inspection for import drugs which already acquired the marketing authorization may be waived through review of documentary evidence of satisfactory quality and inspection performance. This regulation is aimed to strengthen the administration of import drugs, discipline the manufacturing, and ensure the quality and safety of the import drugs.	N/A
第三条 本办法适用于所有取得国家食品药品监督管理局核发的《进口药品注册证》或《医药产品注册证》的境外药品生产企业，以及正在申请国家食品药品监督管理局《进口药品注册证》或《医药产品注册证》的境外药品生产企业。 Article 3 These Measures are applicable to all overseas drug manufacturers that have received Imported Drug License or Pharmaceutical Product License issued by the SFDA, together with overseas drug manufacturers that are applying to the SFDA for Imported Drug License or Pharmaceutical Product License.	1) It is not clear if the "drug manufacturers" is the same as the marketing authorisation holder? If so, then what is the inspection process if the manufacturing or exporting site is not the marketing authorisation holder? This is not explained here or in the rest of the document.	1) Clarify if “drug manufacturer” is the marketing authorization holder and, as necessary. indicate what the inspection process is if the inspected site does not belong to the marketing authorisation holder i.e., contract manufacture and analysis sites.	N/A

第四条　国家食品药品监督管理局根据注册审评、日常监督管理、口岸检验以及群**众**举报等各方面信息，确定需要实施现场检查的境外药品生产企业和品种名单，并**将**检查时间等相关信息提前告知境外药品生产企业驻中国境内的办事机构或者其委**托的中国境内代理机构**（**以下**简称代理机构）。 Article 4 According to the information from various sources such as registration evaluation, daily supervision and management, port inspection and public reporting, the SFDA shall draft a list of overseas drug manufacturers and drugs for site inspection and inform the offices of overseas drug manufacturers located in the People's Republic of China or their entrusted agent located in the People's Republic of China (hereinafter referred to as the "agencies") about relevant information such as inspection schedule in advance.	**1) We appreciate that the SFDA plan to provide advance notice of overseas inspections. Additional clarification regarding when this schedule would be available for the manufacturers would support that the desired timeframe for the inspection can be accommodated as scheduled. We propose that this timeframe be a minimum of 3 months in advance of the inspection start date unless there is a need to expedite based on SFDA concerns regarding patient safety. The notification should include the proposed scope, duration, number of inspectors and proposed dates.** **2) It appears that the term "agencies" may be a mistranslation of 代理机构 in this English version of the draft regulation. We believe the correct translation is "agents."** **3) The establishing of a list of approved drug suppliers should be through a process that is rigorous and robust and is neither influenced by nor dependent upon public activities.**	**Proposed revision: Article 4 According to the information from various sources such as registration evaluation, daily supervision and management, port inspection and public reporting, the SFDA shall draft a list of overseas drug manufacturers and drugs for site inspection and inform the offices of overseas drug manufacturers located in the People's Republic of China or their entrusted agent located in the People's Republic of China (hereinafter referred to as the "~~agencies~~" "Agents") about relevant information such as inspection schedule a minimum of 3 months in advance of the planned inspection or at a specific stated advance interval. The notification will include inspection scope, duration, number of inspectors, proposed dates of inspections, inspection discipline and instructions.** **3) Delete the reference to public reporting.**	**The advance notification benefits both the SFDA and the manufacturer in planning for the inspection. In addition, the advance notice of inspection may allow for the overseas manufacturer to adjust the manufacturing schedules to enable the inspectors to observe the production of the specific products in the scope of the planned inspection. This advance notice also supports that key personnel from the overseas manufacturer can be made available at the time of the inspection.** **The term "agencies" as currently written may cause confusion as to reference to a regulatory agency versus manufacturer.** **The establishing of a list of approved drug suppliers should be through a process that is rigorous and robust, and is neither influenced by nor dependent on public activities.**
第五条　代理机构负责与境外药品生产企业沟通联系，并负责及时向国家食品药品监督管理局药品认证管理中心提交所要求的相关资料。具体资料要求见附件。 Article 5 Agencies are responsible for communication and liaison with overseas drug manufacturers and timely submit related required documents to the SFDA's Center for Certification of Drug. Required documents are listed in the annex.	**1) We appreciate the SFDA's transparency in which documents they expect to be provided as part of the inspection. We recommend clarifying that these documents should include only those applicable to demonstrating compliance with GMPs, which excludes any financial or personnel related data (e.g., sales or cost of manufacture related data, salary, performance).** **2) If the drug manufacturer is not the marketing authorisation holder i.e. a contract site, will the SFDA also inform the marketing authorisation holder of the visit to the manufacturing site? Does the SFDA expect a representative of the marketing authorisation holder to be present during the inspection of a contract site?**	**1) 5 ~~Agencies~~ Agents are responsible for communication and liaison with overseas drug manufacturers and timely submit related required documents to the SFDA's Center for Certification of Drug. Required documents are listed in the annex.** **See also annex III for proposed language** **2) Clarify if "drug manufacturers" are the marketing authorization holders and, as necessary, the expectations as to marketing authorisation holder's representative being present during the inspection.**	**Financial and personnel related data are not required to demonstrate compliance with GMPs nor address patient safety related concerns.**
Article 5 (Continued)	**The Specific Materials requirements section/Annex raises two concerns:** **3) Line 3 refers to "self check". Expectations as to what is in scope of the inspection of "self check" is not detailed. Does SFDA intend to look at the site's self-inspection records, or as per other inspection agencies, only the process of performing these? If the actual self inspection records will not be reviewed by SFDA, this should be stated.** **4) Line 4 states that the specific material, such as the SMF, must be provided in Chinese. No mention is made as to who will pay for translation costs.**	**3) Clarify extent of review of site self inspection records by SFDA inspectors when undertaking overseas inspections.** **4) Clarify costs associated with translation of documents.**	

第六条　境外药品生产企业接到现场检查通知后，确有特殊原因须推迟现场检查的，应由其代理机构向国家食品药品监督管理局药品认证管理中心提出书面申请并说**明理由**。对于无故拒绝现场检查或不配合现场检查的企业，视为现场检查不通过。 Article 6 Upon receiving site inspection notification, where site inspection needs to be postponed for special reasons, overseas drug manufacturers shall have their agencies to submit written postponement requests to the SFDA's Center for Certification of Drug with explanations. Manufacturers that refuse site inspection without proper explanations or are not cooperative for site inspection shall be deemed as failed for site inspection.	**1) We respectfully request that specific examples of "special reasons" be provided. Some potential examples include local natural disasters, catastrophic failures or shutdown of manufacturing plants, planned closures of manufacturing facilities and periods of known inclement weather which could present safety issues for the inspectors and manufacturers staff.** **2) We would like to understand the SFDA process to request postponement and receive notification of SFDA acceptance of postponement including specific points-of-contact and timelines. In addition, we would appreciate clarification of the definition of "non-cooperation" and related consequences.**	**1 & 2) Upon receiving site inspection notification, where site inspection needs to be postponed for special reasons (which may include, but is not limited to local natural disasters, catastrophic failures or shutdown of manufacturing plants, planned closures of manufacturing facilities and periods of known inclement weather which could present safety issues), overseas drug manufacturers shall have their ~~agencies~~ Agents to submit written postponement requests at least 30 days prior to planned inspection to the SFDA's Center for Certification of Drug with explanations. Manufacturers that consistently refuse site inspection without proper explanations or are not cooperative for site inspection shall be deemed as failed for site inspection.**	**Changes to inspection timing may be mutually beneficial to both SFDA and manufacturers to support the safety of their staff and to ensure that the inspection can conducted as planned.** **Clarity of the postponement process is also mutually beneficial to both SFDA and manufacturers to support successful inspections without impacting product availability for the patients.**
第七条　被检查的境外药品生产企业应在现场检查期间安排被检查产品的批量生产。 Article 7 Drug manufacturers under inspection shall conduct the batch production of inspected goods during the period of site inspection.	**1) Coordination of production schedules with the period of inspection may not always be practical. This is particularly true for products manufactured in small quantities due to low market demands, products that are seasonal or for which there is a lack of availability of API, or products that are manufactured in campaigns with long lead times. . It is unrealistic to expect a firm to completely revise a manufacturing schedule in order to make one or more products coincident with an inspection. Witnessing production of similar products, placebos or mimic solutions may be a practical alternative to assess manufacturing capabilities. However, where many products are under consideration, the timescales could extend across many months and/or require many inspections. Instead, we suggest that the inspection should focus on the firm's overall quality system and less on a specific product, or range of products.** **3) The implication is that product specific i.e. marketing authorisation specific inspections will be performed and not systems inspections. Some clarification of this approach would be helpful i.e. are the inspections product specific or are the inspectors looking at the site quality system or both.**	**1) Where possible, drug manufacturer overseas under inspection should arrange batch production of the inspected products, or products using similar processes within the same facility, during the site inspection. However, a more suitable approach would be for the inspection to focus on the firm's overall quality system, rather than a specific product of range of products.**	**Evaluation of GMP compliance can be made by observation and assessment of "like" products or processes. The Quality Management system used to support GMP compliance of the manufacturer is usually applied across products to support ease of training and efficiency.**
第八条　现场检查实行组长负责制。检查组一般由2-5名检查人员组成。 Article 8 Site inspection shall practice leader responsibility system. An inspection team generally consists of two to five inspectors.	**1) The size of the inspection team and inspection duration should be commensurate with the scope of the inspection and the volume of products being distributed in China. In most cases, an inspection team of no more than 3 inspectors should be sufficient to assess GMP compliance and support timeliness of the manufacturer's response to inspectors requests.** **2) Language translation provision is not detailed.**	**1) Site inspection shall practice leader responsibility system. The inspection team size and duration should be commensurate with the scope of the inspection and the volume of products being distributed in China. 2) Clarify if the SFDA inspectors will speak the local language, provide their own interpreter' or whether they will rely on the site providing an interpreter.**	**The audit process should be viewed as a sampling of GMP records and processes to assess overall compliance with GMP requirements. Increasing the number of inspector may hinder the ability of the manufacturers inspection support staff to meet the timeliness expectations of the inspection team.**
第九条　现场检查首次会议由检查组组长主持，确认检查范围、检查日程以及企业**陪同人**员；宣布检查纪律及注意事项。 Article 9 The first site inspection meeting shall be chaired by leader of inspection team to confirm inspection scope, inspection agenda and companying staff; and to announce inspection discipline and instructions.	**1) See comments for Article 4 regarding scope and agenda being defined in advance (e.g., at the time of inspection notification). What is the expectation for attendance by the firm's staff at the opening meeting? This is primarily for planning purposes and to support an efficient inspection.** **2) In addition, to support mutually beneficial communication between SFDA and the manufacturer, we recommend that this article be modified to include that as SFDA discovers potential defects or findings, that these be shared with the manufacturer. This supports that the manufacturer has an opportunity to further explain or provide evidence of GMP compliance.**	**1) The first site inspection meeting shall be chaired by leader of inspection team to re-confirm inspection scope, inspection agenda and companying staff; and to re-affirm inspection discipline and instructions.** **2) "During the inspection, as potential defects or findings are discovered, the SFDA will share the concerns with the manufacturer. Inspected overseas drug manufacturers may provide explanations where they disagree and when necessary, inspection team may further verify relevant situations and revise the identification of defects according to the results of such verification."**	**Advance notice of planned inspection scope, agenda, duration and timing helps to support that the inspection team is able to address the most important areas of focus for the inspection.**

第十条 现场检查主要内容包括：药品注册申报资料、现场资料与实际生产过程的**一致性**；药品生产过程与《药品生产质量管理规范（2010年修订）》符合性等内容。 Article 10 Site inspection mainly includes: the consistency of drug registration application documents and site documents with actual manufacturing process; compliance between drug manufacturing process and GMP (revised in 2010), etc.	**1) We would like to request clarification on the specific regulations and guidance documents to which overseas manufacturers will be assessed.**	**1) Site inspection mainly includes: the consistency of drug registration application documents and site documents with actual manufacturing process, where practical; compliance between drug manufacturing process and GMP (revised in 2010) <<state specific regulations guidance that apply>>, etc.**	
第十一条 被检查的境外药品生产企业应及时提供检查所需要的相关资料。根据检查工作的需要，检查员可采取拍照、摄像等措施采集证据。如果企业拒绝拍照或摄像，检查员应将有关情况在检查报告中予以详细说明。必要时，检查人员可抽取样品**并**带回境内进行检验。 Article 11 Inspected overseas drug manufacturers shall timely submit required related documents for inspection. According to the needs of inspection, inspectors may collect evidence by taking photos and videos. Where manufacturers refuse to take photos or videos, inspectors shall make detailed notes about relevant situations in the inspection report. When necessary, inspectors may take samples and bring them back to the People's Republic of China for quality inspection.	**1) In most cases, photos are not required to effectively assess compliance with Chinese Good Manufacturing Practices. In the unlikely scenario taking photos may be warranted, there may be safety precautions that would first have to be considered. Therefore, pictures should be taken following company policies and safety controls. Videos may represent a violation to employee privacy. Personal transportation of samples by the inspectors may be in violation of transportation regulations. In addition, there are shipping requirements for temperature sensitive products.**	**1) Inspected overseas drug manufacturers shall timely submit required related documents for inspection. According to the needs of inspection, inspectors may collect evidence to support inspection findings. Photographs may be taken in accord with company policy and following safety precautions, where applicable. If necessary, inspectors may submit requests for samples for quality inspection. Whenever possible these requests should be submitted prior to initiation of inspection. As an alternative, manufacturers may ship samples to a designated location in the People's Republic of China.**	
第十二条 现场检查结束后，检查组应对现场检查情况进行分析汇总，确定企业的**缺陷**项目。分析汇总期间，企业陪同人员应回避。 Article 12 After the end of site inspection, inspection team shall make an analysis and summary of inspection and identify the defects of manufacturers. Company accompanying staff shall refrain from presence of analysis and summary meetings.	**1) We recognize the need for the inspection team to confer in private regarding any potential defects or findings. We recommend slight wording changes to clarify the intent of this article (may be due to translation issue).**	**1) Article 12 After the end of site inspection, inspection team shall make an analysis and summary of inspection and identify the defects of manufacturers. In preparation for the wrap-up meeting, the inspection team will meet in the absence of manufacturers staff to discuss and agree on findings / defects.**	**See Comments**
第十三条 末次会议由检查组向被检查的境外药品生产企业口头反馈检查中发现的**缺陷**项目。被检查的境外药品生产企业如有异议可予以解释，必要时检查组可进一步核实有关情况，并根据核实结果对缺陷项目进行修改。 Article 13 At wrap-up meeting, inspection team shall verbally report the defects identified during inspection to the inspected overseas drug manufacturers. Inspected overseas drug manufacturers may provide explanations where they disagree and when necessary, inspection team may further verify relevant situations and revise the identification of defects according to the results of such verification.	**1) See comments for Article 10 related to the inspection team communicating potential defects or findings at the time of discovery. The wrap-up meeting is the formal meeting at whichtime the defects are reviewed for a final time with the manufacturer.** **2) The intent of the inspection from a site point of view is to bring about improvement . Companies often have limited resources. Accordingly some categorisation by the inspectors of the perceived patient risk of the individual inspection findings would assist the company in the speed of response to each finding and targeting of company resources.** **3) It is not clear if the "the report of the defects" detailed in this amendment is the same as the "written report" given to the agency. Or if the later will include additional items. Will a copy of the written report given to the agency be available to the site inspected and or the marketing authorisation holder?**	**1) Article 13 At wrap-up meeting, inspection team shall verbally re-affirm the defects identified during inspection to the inspected overseas drug manufacturers.** **2) Insert " The inspection team will provide some form of categorisation of the inspection findings in line with patient risk."** **3) Clarify the nature of the "report" given to the site i.e. will it be in the form of a written summary or a verbal summary. Clarify if the site and the marketing authorization holder will be given a copy of the report.**	

第十四条　现场检查结束之日起2个月内，国家食品药品监督管理局药品认证管理中心将书面的现场检查报告反馈给代理机构。对于现场检查无明显缺陷项目或缺陷项目能立即整改到位的企业，国家食品药品监督管理局药品认证管理中心不再将书面的现场检查报告反馈给代理机构，直接按第十五条有关规定处理。代理机构在收到现场检查报告之后的1个月内，负责将被检查企业的整改报告提交国家食品药品监督管理局药品认证管理中心。因特殊原因，无法在规定期限内提交整改报告的，应提前向国家食品药品监督管理局药品认证管理中心申请并明确整改报告提交时限，但延长时限不得超过1个月。 Article 14 Within two months after the end of site inspection, the SFDA's Center for Certification of Drug shall provide written site inspection report to the agencies. For manufacturers with no obvious defects identified during site inspection or defects that can be rectified immediately, the SFDA's Center for Certification of Drug will not provide such written site inspection report to the agencies and will follow relevant stipulations of Article 15. Within one month after receiving site inspection report, the agencies shall be responsible to submit the rectification reports of inspected manufacturers to the SFDA's Center for Certification of Drugs. If the rectification reports cannot be submitted before prescribed deadline for special reasons, a request shall be submitted to the SFDA's Center for Certification of Drugs in advance with clear statement on the timeline for the submission of rectification reports, but the postponement shall not exceed one month.	**1) The response time for the site inspection report is challenging in that for most overseas manufacturers, the SFDA report and manufacturer's response must be developed and approved in the native language and then translated. Additional time for translations is needed to support accuracy of translation prior to response and subsequent submittal to the SFDA.** **2) In addition, we wish to clarify if the "rectification reports" are corrective and preventive actions with future due dates, or is there an expectation that all issues will be resolved within the period required to provide the report.**	**1) Within two months after the end of site inspection, the SFDA's Center for Certification of Drug shall provide written site inspection report to the ~~agencies~~ Agents. For manufacturers with no obvious defects identified during site inspection or defects that can be rectified immediately, the SFDA's Center for Certification of Drug will not provide such written site inspection report to the ~~agencies~~ Agents and will follow relevant stipulations of Article 15.** **2) Within 60 days after receiving site inspection report, the ~~agencies~~ Agents shall be responsible to submit the rectification reports (e.g., proposed corrective and preventive actions to address defects) of inspected manufacturers to the SFDA's Center for Certification of Drugs. If the rectification reports cannot be submitted before prescribed deadline for special reasons, a request shall be submitted to the SFDA's Center for Certification of Drugs in advance with clear statement on the timeline for the submission of rectification reports, but the postponement shall not exceed one month.**	**See comment**
第十五条　国家食品药品监督管理局药品认证管理中心在收到代理机构提交的整改情况报告后的1个月内，按照风险管理原则对检查情况进行综合评判。检查结论分为"符合要求"、"整改后符合要求"和"不符合要求"。判定原则如下： 一、药品生产及质量控制与申报资料一致，并能按照药品GMP要求组织生产的，判定为"符合要求"。 二、现场检查发现多项主要缺陷，提交的整改情况报告表明经整改后能按照药品GMP要求组织生产的，判定为"整改后符合要求"。 三、现场检查发现弄虚作假行为或影响产品质量的关键要素与申报资料不一致；存在严重缺陷或多项主要缺陷，表明被检查单位不能按药品GMP要求组织生产的，检查结论判定为"不符合要求"。 必要时，国家食品药品监督管理局药品认证管理中心可组织检查人员对企业整改情况再次进行核查。 Article 15 Within one month after receiving the rectification reports submitted by the agencies, the SFDA's Center for Certification of Drugs shall conduct a comprehensive evaluation on the inspection with the principle of risk management. Inspection conclusions fall into the categories of "compliant", "compliant after rectifications" and "non-compliant". Assessment principles are as follows: I. Manufacturers whose drug manufacturing and quality control are consistent with application documents and are able to organize manufacturing according to GMP requirements shall be rated as "compliant"; II. Manufacturers with major defects identified during site inspection and submitted rectification reports suggesting that manufacturing can be conducted in line with GMP requirements after rectification shall be rated as "compliant after rectification"; III. Manufacturers that are found to have falsification or have key elements that affect product quality that are inconsistent application documents; have serious defects or multiple major defects suggesting that inspected manufacturers cannot conduct manufacturing in accordance with GMP requirements shall be rated as "noncompliant".	**1) Some clarification as to the lenght of time the Conformance certificates are in effect is required. This dateshould be related to the frequency of inspection, as detailed above.** **2) There are many ways to interpret GMP requirements and different languages often make for difficulty in the justification of different interpretations. It is possible that site staff may not be able to fully articulate justifiable ways of working to inspectors during the visit due to language difficulties. For this reason, some form of appeals procedure to allow the manufacturer to provide futher explanation would be a useful addition. It would be appropriate to have this appeals process controlled by the centre for certification rather than the inspectors.** **3) If a site is out of compliance at time of inspection, but the inspectors determine that the faults can be rectified, it would appear that there are no concerns about materials made out of compliance. Manufacture and importation could continue, despite a failure to meet the prescribed GMP standards. There should be a process for suspending importation until rectification is complete and, potentially, a reinspection has occurred. Focussing on a particular kind of drug may permit other drugs with quality problems from the same site to continue to be imported.**	**1) Indicate how long the Certificates of conformance is in effect i.e. clarify the expiry date.** **2) An appeals process to allow a company a final chance of explanation and clarification of their ways of working would be a useful addition to this section.** **3) This section may need to be revised to accommodate the potential to suspend importation until rectification has been satisfactorily completed. Additionally, it may be necessary to suspend all imports from a firm or site rather than just 'this kind of drug'.**	**N/A**

第十六条 对检查结论为**"符合要求"**、**"整改后符合要求"的企**业，国家食品药品监督**管理局在**检查结论做出后的**1个月内**给代理机构反馈书面意见。对检查结论为**"不符合要求"的企**业，国家食品药品监督管理局给代理机构下发《警告信》，责令其暂停进口该药品，或暂停其药品注册审评、审批过程，直至下一次现场检查符合要求。**同**时通报各口岸药监局，暂停办理该药品《进口药品通关单》。已进口的药品，国**家食品**药品监督管理局根据情节的轻重，作出责令企业召回药品或其他处理决定。 Article 16 For manufacturers that are rated as "compliant" and "compliant after rectification", the SFDA shall provide written comments to the agencies within one month after the inspection conclusions are made. For manufacturers that are rated as "non-compliant", the SFDA shall issue a Warning Letter to the agencies demanding them to suspend the import of such drugs or directly suspend the process of registration evaluation and approval procedure for such drugs until requirements are met during the next site inspection. Meanwhile, the drug supervision bureaus of various ports shall be notified to suspend the issuance of Customs Form for Imported Pharmaceuticals. For imported drugs, the SFDA may demand that manufacturers recall the drugs or otherwise make other decisions depending on the severity of incidents.	**1) Replace "shall" with "may" before "issue a Warning Letter."**	**1) Allows for regulatory discretion to prevent possible drug shortages.**	
第十七条 特殊情况下，当现场检查发现被检查的境外药品生产企业存在严重缺陷，严重危害公众用药安全时，国家食品药品监督管理局可立即作出第十六第二款的**有**关决定。 Article 17 Under special situations, where overseas drug manufacturers are found to have serious defects that present grave hazards to public drug safety, the SFDA may immediately make relevant decisions of Article 16, Section 2.	**None**	**N/A**	**N/A**
第十八条 本办法自 年 月 日起开始实施，由国家食品药品监督管理局负责解释。 Article 18 These Measures shall come into force as of ¬_____, and the SFDA is responsible for explanations hereof.	**1) We request clarification as to the timeframe for implementation of these regulations.**	**1) Article 18 These Measures shall come into force as of ¬ March 15, 2013 (or later), and the SFDA is responsible for explanations hereof.**	**Overseas manufacturers with multiple facilities will need time to ensure that the site master files, product complaint and recall data have been translated intoChinese as required per this annex of this document.**
附件：具体资料要求			
一、现场主文件 现场主文件内容包括企业总体情况，生产质量管理体系，人员，厂房和设备，**文件**，**生**产，质量控制，分销、投诉、产品缺陷与召回，自检等九个方面。具体要**求按照**PIC/S关于现场主文件（site master file）**的最新要求撰写。**该项资料要求用中文表述，部分图表内容允许用英文填写。 I. Site master file Site master file includes the following nine aspects: overall company profiles; manufacturing quality management systems; staffing, workshops and equipment; documentation, manufacturing, quality control; distribution; complaint; product defect and callback; as well as self-inspection. Drafting shall follow the latest PIC/S requirements on site master file. The file shall be in Chinese language with the permission that some diagrams can be written in English.	**1) Many companies did not adopt the practice of a site master file in the past, as it was a "nice to have", but not a requirement in all markets. We believe this will continue to be a point of contention, as awareness of this new requirement will take some time to disseminate.** **2) It will be difficult for all foreign sites to maintain the Site Master File in Chinese since the files are typically maintained in English.**	**1) The details of the site master file should be written according to the latest requirements of the site master file of PIC/S.** **2) Replace "This document is demanded to be written in Chinese" with "Where possible, a copy of the file shall be available in Chinese."**	**Also, see comments for Article 18**

二、进口药品近三年进口到中国的基本情况 **包括**该品种近三年每年进口数量、口岸检验情况、不良反应情况、产品投诉情况**以及**产品召回情况。其中若发生因质量原因的投诉或召回该产品，需详细列明产**生投**诉或召回产品的原因及最终处理情况。要求该项资料用中文表述。若该品种正**在申**请国家食品药品监督管理局《进口药品注册证》或《医药产品注册证》，此项资料可不必提交。 II. Import of the drugs to China in recent three years Includes the annual quantity of the imported drugs, port inspection records, adverse reactions, product complaints and product callback in recent three years. Where quality complaints or callback of products have occurred, the reasons and final treatment of such complaints or callback shall be provided. This information shall be expressed in Chinese language. If such drugs are under the process of application for Imported Drug License or Pharmaceutical Product License, such information do not need to be submitted.	**1) We request clarification on the specific documents required for port inspection records. In addition, we would like to confirm that the product complaint and callback records are those for product distributed in China only.** **Further, we would like to confirm that these records would need to be available in advance of a planned inspection and not expected to be provided as part of an "Annual Product Review."** **As the sites are outside of China, it will be difficult for companies to have these documents available in Chinese**	**1) Includes the annual quantity of the imported drugs distributed in China, applicable port inspection records, adverse reactions, product complaints and product callback in recent three years. Where quality complaints or callback of products have occurred for product distributed in China, the reasons and final treatment of such complaints or callback shall be provided. Where possible, this information shall be expressed in Chinese language. If such drugs are under the process of application for Imported Drug License or Pharmaceutical Product License, such information do not need to be submitted.**	**See Comments**
三、进口药品近三年在全球其他国家生产销售基本情况 **包括在其他国家是否因不符合**GMP**而被停止**进口销售、是否因质量原因而召回产品。如有上述情况发生，需详细列明具体原因及最终处理情况。要求该项资料用**中文表述。若**该产品未在其他国家上市，此项资料可不必提交。 III. Manufacturing and sales of imported drugs in other countries over the past three years Includes whether products are suspended for import and sales for non-compliance with GMP or recalled for quality reasons. In the event of above situations, the specific reasons and final treatment shall be identified in detail. Such information shall be expressed in Chinese language. If such products are not marketed in other countries, this information do not need to be submitted.	**1) Request clarification of the term "sales", as it should pertain to product distributed in China only. It is the policy of most overseas manufacturers not to provide financial or personnel related data. However, we understand the need for transparency with the SFDA with respect to product issues that are discovered after release and distribution specific to commercial product distributed in China only.**	**1) III. Manufacturing of imported drugs in China over the past three years** **Includes whether products are suspended for import and distribution for non-compliance with GMP or recalled for quality reasons. In the event of above situations, the specific reasons and final treatment shall be identified in detail. Where possible, such information shall be expressed in Chinese language. If such products are not marketed in other countries, this information do not need to be submitted.**	**The information provided to the SFDA should be pertinent to those products imported and distributed in China.**