HEALTH

Drugs and Medical Devices

Agreement Between the
UNITED STATES OF AMERICA
and CHINA

Signed at Beijing December 11, 2007

NOTE BY THE DEPARTMENT OF STATE

Pursuant to Public Law 89—497, approved July 8, 1966 (80 Stat. 271; 1 U.S.C. 113)—

". . .the Treaties and Other International Acts Series issued under the authority of the Secretary of State shall be competent evidence . . . of the treaties, international agreements other than treaties, and proclamations by the President of such treaties and international agreements other than treaties, as the case may be, therein contained, in all the courts of law and equity and of maritime jurisdiction, and in all the tribunals and public offices of the United States, and of the several States, without any further proof or authentication thereof."

CHINA

Health: Drugs and Medical Devices

Agreement signed at Beijing December 11, 2007;
Entered into force December 11, 2007.

AGREEMENT BETWEEN THE DEPARTMENT OF HEALTH AND HUMAN SERVICES OF THE UNITED STATES OF AMERICA AND THE STATE FOOD AND DRUG ADMINISTRATION OF THE PEOPLE'S REPUBLIC OF CHINA ON THE SAFETY OF DRUGS AND MEDICAL DEVICES

The Department of Health and Human Services ("HHS") of the United States of America ("United States") and the State Food and Drug Administration ("SFDA") of the People's Republic of China ("China") (hereinafter referred to together as "the Parties"):

Understanding the mutual benefits of protecting the public health through improved cooperation between the Parties with regard to monitoring and regulating the safety of drugs and medical devices;

Desiring to work together to better ensure the safety and quality of Drugs, Excipients, and Medical Devices; and

Recognizing that such cooperation can improve the health of the citizens of both the United States and China and enhance confidence in the regulation of Drugs, Excipients, and Medical Devices in both countries;

Have agreed as follows:

Article I Purpose

The purpose of this Agreement is to establish methods of cooperation between the Parties that will provide the Food and Drug Administration within HHS ("HHS/FDA") with additional information about products exported from the customs territory of China to the United States, provide SFDA with increased sharing of information about products

exported from the United States to China, and encourage further regulatory cooperation between the Parties regarding Drug and Medical Device regulation.

Article II General Principles

A. The Parties shall engage in regulatory cooperation regarding the export of Drugs, Excipients, and Medical Devices from the customs territory of China to the United States and Drugs, Exipients, and Medical Devices produced in the United States and exported to the customs territory of China as set out in Article VI and as further defined in Work Plans to be agreed upon by the Parties.

B. The Parties shall engage in information-sharing to improve their mutual understanding of, and to gain greater confidence in, each Party's regulatory system as set out in Article V and as further defined in Work Plans to be agreed upon by the Parties. As specified in Article V, each Party shall share relevant information with the other Party, including on relevant laws, regulations, areas of jurisdiction, and public health and safety.

C. The Parties shall engage in regulatory cooperation regarding improving the authenticity, quality, safety, and effectiveness of Drugs, Excipients, and Medical Devices as set out in Articles IV and VI and as further defined in Work Plans to be agreed upon by the Parties.

D. The Parties shall commit to annual meetings between senior Agency leaders to discuss and evaluate progress under this Agreement, among other things.

Article III Definitions

For purposes of this Agreement the following definitions shall apply:

A. "API" or "Active Pharmaceutical Ingredient" means any substance or mixture of substances intended to be used in the manufacture of a drug (medicinal) product and that, when used in the production of a drug, becomes an active ingredient of the drug product. Such substances are intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease or to affect the structure and function of the body.

B. "Counterfeit Drugs and Medical Devices" means a product that is deliberately and fraudulently mislabeled with respect to identity and/or source. Counterfeiting can apply to branded and generic products and may include products with correct ingredients, with wrong ingredients, without active ingredients, with incorrect quantity of active ingredient, or with fake packaging.

C. "Designated Drugs and Designated Medical Devices" means a Drug (including APIs) and Excipients or Medical Device, respectively, designated for inclusion in each phase of implementation, based on criteria established in Article IV. A.

D. "Drug" means any material commonly used for human pharmaceutical use. The term includes the following materials:

1. Finished-dosage forms (including both over-the-counter ("OTC") and prescription drugs);
2. Drug substance, or active pharmaceutical ingredients ("APIs");
3. Biologic drugs (e.g., vaccines and monoclonal antibodies); and
4. Products taken by mouth intended to supplement the diet that:

(i) bear or contain one or more of the following dietary ingredients: a vitamin; a mineral; an herb or other botanical; an amino acid; a dietary substance for use in humans to supplement the diet by increasing the total dietary intake; or a concentrate, metabolite, constituent, extract or combination of any of the above; and

(ii) meet any one of the following characteristics:

-are not clearly labeled as dietary supplements; or

-contain claims to diagnose, cure, mitigate, treat, or prevent disease; or

-contain substances that are regulated by HHS/FDA as APIs.

E. "Excipient" means any components other than APIs that are commonly used in a pharmaceutical product. These components may include vehicles and additives, such as dyes, flavors, binders, emollients, fillers, lubricants, and preservatives.

F. "Firm" means any business within the customs territory of China or within the United States that is engaged in the manufacture (including processing) and distribution (including export) of Drugs, Excipients, and Medical Devices.

G. "HHS/FDA Requirements" means any U.S. laws, regulations or other requirements, including any amendment adopted after the date of entry into force of this Agreement,

concerning Drugs, Excipients, and Medical Devices that are administered or enforced by HHS/FDA.

"SFDA Requirements" means any Chinese laws, regulations or other requirements, including any amendment adopted after the date of entry into force of this Agreement, concerning Drugs, Excipients, and Medical Devices that are administered or enforced by SFDA.

H. "Medical Device" means any instrument, apparatus, machine, implant, *in vitro* reagent, or similar or related article, intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease in humans, or intended to affect the structure or any function of the human body, and which is not a drug.

I. "SFDA-Registered Firm" means a Firm that SFDA has determined meets SFDA Requirements and that is registered with SFDA.

"HHS/FDA-Registered Firm" means a firm that complies with U.S. registration and listing requirements and that is registered with HHS/FDA.

J. "Facility" means any Firm's site within the customs territory of China or in the United States that is engaged in manufacturing, producing, processing, packing, testing, holding, transporting, distributing, or exporting Drugs, Excipients, and Medical Devices.

Article IV Import/Export Tools

A. Determination of Designated Drug and Designated Medical Devices

This Article will be implemented in a phased approach, beginning with a defined list of Designated Drugs and Designated Medical Devices. The Parties shall conduct a formal evaluation of the implementation of this Article for the products designated in paragraph 2 at the conclusion of the 12-month period described in Article VII.D and annually thereafter. Based on the Parties' determination of the success of this program, the Parties may agree to add or delete specific Drugs, Excipients, and Medical Devices. Timing for the evaluation will be established through the Work Plan.

1. *Factors.* The Parties shall consult on the designation of which products to include in each phase, as appropriate, based on the following factors:

a. potential or actual, direct or indirect risk to the public health associated with the product, based on testing, inspection results or other relevant information;
b. the rate of refusal of admission in either Party's country or of problems associated with the product before, during or after entering the domestic commerce of the other Party's country, including product recalls, safety alerts and enforcement actions;
c. fraudulent or deceptive labeling or indications of any substitution or additions of a substance to a product or an ingredient of a product that reduces the quality of the ingredient or product or makes it appear of greater value than it is, without clearly revealing such substitution or addition to the recipient in the importing country;
d. promotion or advertising of products intended for consumers of the importing country, beyond the products' approved indications for use; and
e. the feasibility of implementing an effective and timely Work Plan with respect to the product.

2. *First Phase – Designated Drugs and Designated Medical Devices.*

The Parties agree that the first phase shall include products designated by each Party. Designated Drugs shall include any substance or chemical that may be used as an API for any Designated Drug under this Agreement, even if the entity manufacturing or distributing the substance or chemical does not identify the product as an API. Details on these designations shall be determined through the Work Plan. Designated Drugs and Designated Medical Devices shall include:

a. SFDA-Designated Drugs:
   i. Recombinant Human Insulin
   ii. Lysine Fat and Lysine Salt
   iii. Cefoperazone and its salts
   iv. Paclitaxel injection
   v. Penicillin and its finished dosage form
   vi. Diagnostic kit for blood screening, specifically, for HIV/AIDS and Hepatitis B & C
b. SFDA-Designated Medical Devices:
   i. Intraocular Lenses

ii. Cardiac pacemakers

c. HHS/FDA-Designated Drugs:

i. Gentamicin sulfate

ii. Atorvastatin

iii. Sildenafil

iv. Dietary supplements intended for erectile dysfunction or sexual enhancement

v. Human Growth Hormone

vi. Oseltamivir

vii. Cephalosporins manufactured in facilities that also manufacture non-cephalosporin drugs

viii. Glycerin

d. HHS/FDA-Designated Medical Devices:

i. Glucose test strips

ii. Condoms

B. <u>Registration and Collaboration on Designated Drugs and Designated Medical Devices</u>

1. With respect to Designated Drugs and Designated Medical Devices:
   a. For those designated by HHS/FDA, SFDA shall require that all Firms that manufacture Designated Drugs and Designated Medical Devices intended for export to the United States are registered by SFDA.
   b. For those designated by SFDA, HHS/FDA shall provide SFDA with the following available information as agreed to in the Work Plan:
      i. the facilities that manufacture the products;
      ii. information from the product approval or clearance package;
      iii. recalls, warning letters, and enforcement actions; and
      iv. reported post-marketing adverse events
2. HHS/FDA shall consult with SFDA to assist SFDA in understanding HHS/FDA Requirements for Designated Drugs and Designated Medical Devices.
3. HHS/FDA and SFDA shall review the HHS/FDA Requirements for the Designated Drugs and Designated Medical Devices and the SFDA Requirements for the Designated Drugs and Designated Medical Devices to understand the differences and identify the means to ensure the quality, safety, and authenticity

of Designated Drugs and Designated Medical Devices, given different regulatory systems.

4. SFDA shall maintain documents on file related to reviews, inspections, testing, recalls, compliance, and any other assessment of a Firm of Designated Drugs and Designated Medical Devices. SFDA shall make such records available to HHS/FDA within 7 work days of an HHS/FDA request.

C. Future Collaboration on Registration and Certification

The Parties agree to pursue activities to better understand the differences and the gaps between HHS/FDA and SFDA requirements and establish mechanisms to address those gaps. Specifically, SFDA shall actively create conditions to enable SFDA to certify that HHS/FDA Requirements are met for firms producing Designated Drugs and Designated Medical Devices intended for export to the United States. Once these new conditions mature for SFDA, the Parties may agree to modify this Agreement to include provisions that provide for the certification of products, exported from the customs territory of China to the United States, to HHS/FDA requirements, and for appropriate export control mechanisms.

D. Product Integrity and Security

1. The Parties shall cooperate on the establishment of the pedigree (chain-of-custody) systems, as follows, for those Drugs designated under Article IV A. that are identified in the Work Plan as being at risk for counterfeiting;
   a. The Parties shall establish and implement measures, including pedigree requirements, to further ensure the integrity and security of Designated Drugs. The Parties shall collaborate with each other on the establishment of such pedigree requirements for both domestic and exported Designated Drugs.
   b. The Parties shall establish and implement pedigree systems. The pedigree shall include information on Designated Drugs and their manufacturers as follows:
      i. product information (drug name, manufacturer, product registration or identification number);
      ii. item information (unique product serial number, dosage form, strength, container size, lot number, expiration date);

iii. information about each party to the transaction (including company name, street address, license number, contact person, and telephone number); and

iv. transaction information (date product was shipped from seller, date received by purchaser).

c. Each Party shall establish and implement standards for a comprehensive electronic tracking system for each unique package.

2. The Parties shall also work on the following product integrity and security measures for all Drugs:

a. Each Party shall enhance enforcement against entities that fail to provide a pedigree, provide a false pedigree, or fail to comply with any other provisions related to the integrity or security of Drugs.

b. Each Party shall develop a program to inform and educate supply-chain stakeholders and the public on how to avoid and minimize their risk of receiving a misbranded, adulterated or Counterfeit Drug or Medical Device, and how to report suspect drugs, excipients, medical devices and suspicious parties.

c. SFDA and HHS/FDA shall respond rapidly to, and investigate reports of, Drugs, Excipients, and Medical Devices suspected of being misbranded, adulterated, or counterfeited. SFDA and HHS/FDA shall also notify each other of any such reports and the steps they have taken or plan to take to investigate the report. SFDA and HHS/FDA shall also report Counterfeit Drugs to the World Health Organization (WHO).

d. Each Party shall take steps to adopt and implement regulations and practices (e.g., good distribution practices) and guidelines (e.g., pharmacovigilance, rapid response for counterfeits) consistent with those established by the World Health Organization (WHO) including with respect to Counterfeit Drug identification and prevention, including the enforcement of laws and regulations that encompass APIs, Excipients, and finished-dosage forms misidentified as to source and composition. Details of the collaboration on standards shall be determined through the Work Plan.

e. Each Party shall endeavor to enhance cooperative activities with its appropriate law-enforcement and regulatory authorities to actively

investigate and prosecute individuals or entities that manufacture, sell, distribute, handle, test, trade, or export misbranded, adulterated, or Counterfeit Drugs, Excipients, and Medical Devices. Each Party shall actively participate in the WHO's International Medical Products Anti-Counterfeiting Taskforce (IMPACT), and the Permanent Forum on International Pharmaceutical Crime (PFIPC).

Article V Information Sharing

The Parties shall exchange information related to Drugs, Excipients, and Medical Devices and their respective regulatory systems concerning Drugs, Excipients, and Medical Devices, on a timeframe and with updates as agreed to in the Work Plan, as follows:

A. A Party may provide information to the other Party in the English or Chinese language.

B. The Parties shall exchange copies of and other relevant information concerning their respective laws and regulations.

C. HHS/FDA and SFDA shall provide each other with copies of all relevant HHS/FDA and SFDA Requirements, updated as appropriate, with respect to Designated Products.

D. Each Party shall provide to the other Party a list of all registered API manufacturers, and the products they manufacture, in its respective country.

E. Each Party shall notify the other Party of serious adverse health consequences or death relating to product safety, manufacturing conditions, recalls, serious adverse event reports, and other instances or the gross deception of consumers. Each Party shall promptly respond to requests from the other Party for information concerning any such risk, including contact information for the Firms or other entities concerned. The Work Plan shall include specific commitments to ensure the timeliness of any such notification or response.

F. HHS/FDA shall work with SFDA to better understand the Global Harmonization Task Force (GHTF) National Competent Authority Reporting (NCAR) program, to support both Parties' actively reporting any serious adverse events that involve medical devices into the NCAR program.

G. Each Party shall notify the other Party of its determination that a shipment of Drugs, Excipents, or Medical Devices has been shipped to the other Party's country, for which there is a reasonable probability that the use of, or exposure to, the product will cause serious adverse health consequences or death. The notification shall:
   1. Be in writing;
   2. Be made within 24 hours of the determination;
   3. Include the reasons for the determination; and
   4. Include, as it becomes available, other information that may assist the other Party to identify the shipment and the supplier.

H. Within 30 calendar days of entry into force of this Agreement, each Party shall provide the other with a list of Firms that manufacture Drugs and Medical Devices in its country and are registered in its country, and the products each Firm manufactures. SFDA shall provide to HHS/FDA the list of Drug, Excipients, and Medical Device manufacturers in the customs territory of China that SFDA has determined to be out of compliance with SFDA Requirements, when such a list becomes available.

I. Within 30 calendar days of a request from HHS/FDA, SFDA shall provide HHS/FDA inspection reports requested by HHS/FDA for SFDA-Registered Firms that manufacture or distribute Drugs, Excipients, or Medical Devices that have been or will be exported to the United States. SFDA shall notify HHS/FDA within 10 calendar days of becoming aware of inspection results that indicate significant deficiencies or fraud associated with firms that manufacture or distribute Drugs, Excipients, or Medical Devices that SFDA determines have been or will be exported to the United States. Once HHS/FDA has addressed any remaining remote access issues, HHS/FDA will grant SFDA access to an electronic database of HHS/FDA inspection results.

J. Each Party shall notify the other Party of any Counterfeit Drug, Excipient, or Medical Device found in its country, including information about the source and distribution.

Article VI Regulatory Cooperation

The Parties shall accomplish the following tasks, as it relates to Drugs, Excipients, and Medical Devices:

A. Develop and set out in the Work Plan specific steps and measures to prevent and control Counterfeit Drugs, Excipients and Medical Devices.

B. Develop appropriate regulatory cooperative activities, including training programs and scientific discussions or cooperation, intended to support the long-term stability and effectiveness of the registration and certification programs. For each training or other cooperative activity that requires travel or other organizational costs, each Party shall bear the cost for its respective participants. Appropriate regulatory cooperative activities may include:

   1. development and coordination of the training programs for Chinese inspectors;
   2. technical exchanges and training relating to the use of Good Clinical Practice (GCP)s to ensure the safety of human subjects and the collection of valid clinical data; and
   3. training and exchange on the development of evaluation review methods, inspection techniques, establishment of computer databases, evaluation report standard formats, and the development of technical guidance documents, and laws and regulations.

C. The Parties shall cooperate on the implementation of standards.

   1. The Parties shall develop through the Work Plan details of collaboration on the establishment of internationally-recognized standards. These standards may include:
      a. the International Pharmaceutical Excipients Council's standards for excipients;
      b. International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) Guidelines, including ICH Q7A Current Good Manufacturing Practice Guideline for APIs;
      c. Pharmaceutical Inspection Cooperation Scheme (PIC/S) GMP Standards for Finished-Dosage Form Pharmaceuticals; and
      d. Global Harmonization Task Force Standards, including ISO 13485 medical device requirements.
   2. Upon request, HHS/FDA shall provide assistance to SFDA regarding internationally-recognized standards.

D. Each Party shall develop a streamlined process for facilitating (e.g., issuing a letter of invitation) an inspection by a Party in the other Party's country no later than 5 calendar days after receipt of such a request from a Party. Such inspection may be

conducted with or without providing advance notice (as specified in the request) to the establishment concerned. The performance measure for this activity shall be the number of days that elapse between the Party's request and the other Party's response in facilitating the inspection.

E. Each Party may request the other Party to conduct an investigation regarding any Drug, Excipient, or Medical Device, exported from the other Party's country to the Party's country, that the Party has reason to believe may pose a risk to public health or safety. The Party shall respond to the requesting Party within 3 calendar days of the receipt of the request, informing the requesting Party of its decision on whether or not to conduct an investigation. If the decision is to conduct an investigation, the Party shall notify the requesting Party within 15 calendar days from the decision to conduct the investigation of:

1. information relating to the source of the health or safety risk;
2. steps taken to remedy the risk; and
3. the outcome of any remediation.

The Work Plan shall set out requirements and performance measures related to investigations under this paragraph.

F. HHS/FDA may fully participate in any annual or other SFDA inspection of any SFDA- or HHS/FDA- Registered Firm in the customs territory in China exporting to the United States.

G. Except in extraordinary circumstances, each Party will observe the following procedures: each Party shall publish on its website(s) all proposed regulations and other measures related to Designated Drugs and Designated Medical Devices and allow a reasonable period of time for all interested parties to submit comments. Each Party shall consider such comments and, at the time final regulations are adopted, address in writing significant, substantive comments received from interested persons during the comment period and explain any substantive revision made to the proposed regulations. Both Parties shall also publish on its website all final regulations and measures related to Designated Drugs and Designated Medical Devices and allow a reasonable amount of time before implementation and enforcement. Both Parties shall also publish all of the information listed above in the relevant government publication (i.e., HHS/FDA, the *Federal Register*). Pending the designation of a

single relevant government publication for this purpose in China, SFDA shall ensure its website is kept current, so as to assure transparency in rulemaking.

H. HHS/FDA shall report any science and technology cooperation to the Joint Commission on Scientific and Technological cooperation established under the Agreement between the Government of the United States of America and the Government of the People's Republicp of China on Cooperation in Science and Technology, signed at Washington January 31, 1979.

Article VII Administration

A. Within 15 calendar days of the date of entry into force of this Agreement, each Party shall notify the other Party in writing of its primary points of contact for coordinating all bilateral activities under this Agreement, including coordinating meetings, exchanging information, and sending and receiving notifications.

B. The Parties hereby establish a Working Group. Within 30 calendar days of the date of entry into force of this Agreement, each Party shall identify relevant policy and technical experts of each Party to serve on the Working Group.

C. Within 60 calendar days of the date of entry into force of this Agreement, the Working Group shall hold its first meeting to develop a Work Plan that:

1. further details specific activities each Party shall perform pursuant to this Agreement within the first 12-month period following the date of entry into force of this Agreement and time lines for the completion of each such activity; and
2. includes, as appropriate, performance measures to evaluate the success of each such activity.

D. Within 120 calendar days of the date of entry into force of this Agreement, the Working Group shall finalize the Work Plan for the first 12-month period following the date of entry into force of this Agreement. The Parties shall assess the Work Plan at the conclusion of the 12-month period.

E. For each subsequent 12-month period, the Working Group shall meet to develop a Work Plan that further details specific activities that each Party shall perform pursuant to this Agreement within that period and, as appropriate, that includes performance measures to evaluate the success of each such activity. The Parties shall assess each such Work Plan at the conclusion of the relevant period.

F. The Work Plan for each 12-month period, when adopted by the Parties, shall include binding commitments for the effective and timely implementation of this Agreement. Each Party shall make the Work Plan for the first 12 months, and each subsequent year, publicly available on its respective website.

G. Within 180 calendar days of the date of entry into force of this Agreement, high-level representatives of the Parties shall meet to discuss and review the implementation of and progress under this Agreement and related matters.

H. Thereafter, the high-level representatives of the Parties shall meet on an annual basis to discuss and review the implementation of and progress under this Agreement and related matters. Unless the Parties otherwise agree, the location of these annual meetings shall alternate between the United States and China. The Parties may convene additional technical or program-level meetings on an as-needed basis in any mutually agreeable location.

I. For each provision in this Article, each Party shall notify the other Party within 24 hours of determining it will be unable to meet an agreed-upon deadline, for such reasons as U.S. or Chinese holidays, or for any other reason, and will provide the reason for the delay. The Parties may then agree to modify the timelines and establish a new delivery date. Such notification shall occur through the designated points of contact established as per Article VII. 1.

Article VIII Performance Measures

A. The Parties shall evaluate and discuss progress under this Agreement on an annual basis, including the effectiveness of SFDA's registration program established pursuant to the Work Plan. HHS/FDA may base its evaluation of such progress on, among other things, the following:

1. the rate of refusal by HHS/FDA of Drugs, Excipients, and Medical Devices exported from the customs territory of China and offered for import into the United States, as compared to the overall rate of refusal in calendar year 2007 or other relevant period by HHS/FDA of Drugs, Excipients, and Medical Devices exported from the customs territory of China and offered for import into the United States; and

2. the volume, frequency and significance in terms of public health hazard of recalls of Drugs, Excipients, and Medical Devices in the United States, including Counterfeit Drugs and Medical Devices, exported from the customs territory of China and offered for import into the United States as compared to the volume, frequency and significance of such recalls in 2007 or other relevant period.

B. SFDA may base its evaluation of such progress on, among other things, the following:
   1. a rate of refusal of Designated Drugs and Designated Medical Devices approved by HHS/FDA offered for import into the customs territory of China, as compared to the overall rate of refusal in the previous calendar year;
   2. the overall percentage of Designated Drugs and Designated Medical Devices exported from the customs territory of the United States and offered for import into the customs territory of China that are determined as unqualified based on the supervised sample testing; and
   3. the volume frequency, and significance in terms of public health hazard of recall of drugs and medical devices in China, including Counterfeit Drugs and Medical Devices, exported from the United States and offered for import into the customs territory of China as compared to the volume, frequency and significance of such recalls in the previous calendar year.

Article IX Final Provisions

A. Nothing in this Agreement precludes the Government of United States or the Government of China from taking any measure to protect the public health or the citizens of its respective country. HHS/FDA and SFDA affirm that it shall work with its country's national, state, provincial, or municipal bodies, as appropriate, to implement this Agreement fully.

B. Nothing in this Agreement shall be construed to affect the rights or obligations of the United States or China under any other agreement in force between the United States and China.

C. HHS/FDA actions with regard to Drugs, Excipients, and Medical Devices shall be governed by HHS/FDA Requirements and all other existing U.S. laws and regulations.

D. SFDA actions with regard to Drugs, Excipients, and Medical Devices shall be governed by SFDA Requirements and all other existing Chinese laws and regulations.

E. The Parties shall endeavor to resolve any dispute regarding the implementation or interpretation of this Agreement through timely consultations.

F. This Agreement shall enter into force upon signature by both Parties and shall remain in force for a period of two years, unless terminated by either Party. On the last day of the two-year period, and of each subsequent two-year period, the Agreement shall automatically be renewed for another two-year period, unless either Party notifies the other Party that it wishes to terminate the Agreement at least 60 calendar days prior to the last day of the two-year period. In addition, either Party may terminate the Agreement upon 60 calendar days' written notice to the other Party. The Parties may amend this Agreement at any time by mutual written agreement.

DONE at Beijing, this 11th day of December, 2007, in duplicate in the English and Chinese languages, each text being equally authentic.

FOR THE DEPARTMENT OF HEALTH AND HUMAN SERVICES OF THE UNITED STATES OF AMERICA

FOR THE STATE FOOD AND DRUG ADMINISTRATION OF THE PEOPLE'S REPUBLIC OF CHINA

中华人民共和国国家食品药品监督管理局与美利坚合众国卫生与人类服务部关于药品、医疗器械安全的协议

中华人民共和国（以下简称“中国”）国家食品药品监督管理局（“SFDA”）与美利坚合众国（以下简称“美国”）卫生与人类服务部（“HHS”）（以下简称“双方”）：

理解到通过促进双方在药品、医疗器械监测和监管方面的合作，保护公众健康的共同利益；

愿意共同努力，以更好地确保药品、辅料和医疗器械的质量和安全；及

认识到这种合作可以改善中美两国人民的健康水平，并增强对两国药品、辅料和医疗器械监管的信心；

协议如下：

第一条　目的

本协议旨在双方之间建立合作机制，对从中国关税区出口到美国的产品，向 HHS 下属的食品药品监督管理局（HHS/FDA）提供额外的信息，同时对美国出口到中国的产品，向 SFDA 提供更多的信息共享，并在药品、辅料和医疗器械方面开展进一步监管合作。

第二条　一般原则

一、双方应依照第六条，以及经双方同意在工作计划中进一步确定的内容，对从中国关税区出口到美国的药品、辅料和医疗器械，以及从美国生产并出口到中国关税区的药品、辅料和医疗器械，开展监管合作。

二、双方应依照第五条，以及经双方同意在工作计划中进一步确定的内容，开展信息共享，促进双方的理解并对彼此的监管体系树立更大的信心。按照第五条规定，双方应分享相关信息，包括法律、法规、权限范围、以及公共健康和安全。

三、双方应依照第四条和第六条以及经双方同意在工作计划中进一步明确的内容，开展监管合作，促进药品、辅料和医疗器械产品的真实、质量、安全和有效。

四、双方应召开部门高级领导人年度会议，对本协议以及其他事项的进展进行讨论和评估。

第三条　定义

本协议适用以下定义：

一、“活性药物成分”，是指用于生产药品并在用于制药时成为药品活性成分的任何一种物质或物质的混合物。此种物质在疾病的诊断、治愈、症状缓解、治疗或疾病的预防中有药理活性或其它直接作用，或者能影响机体的功能和结构。

二、“假冒药品和医疗器械”是指故意和欺骗性地错误标识产品的特征和/或来源。假冒适用于品牌产品和非专利产品，并且包括成分正

确，成分错误，没有活性成分，活性成分含量不正确，或伪造包装的产品。

三、“指定药品和指定医疗器械”是指依照第四条第一款设定的标准，包含在每个实施阶段的指定药品（包括活性药物成分/原料药）和辅料，或医疗器械。

四、“药品”是指普遍用于人体的任何药用物质。该术语包括以下物质：

（一）制剂（包括非处方药（OTC）和处方药）；

（二）原料药，或活性药物成分（APIs）；

（三）生物药品（如：疫苗和单克隆抗体）；及

（四）以及用于补充膳食的口服产品。这种产品

1.具有或包含一种或多种以下膳食成分：维生素，矿物质，草药或其他植物，氨基酸，在人体内使用、通过增加总的饮食摄入量来补充饮食的膳食物质，或者浓缩物、代谢物、要素、提取物或任何一种上面物质的组合；并且

2.符合以下特点之一：

(1)没有明确的标签说明作为饮食补充剂；或

(2)声称用于诊断，治愈，减缓，治疗或预防疾病；或

(3)含有 HHS/FDA 作为活性药物成分/原料药监管的物质。

五、“辅料”是指除活性药物成分/原料药之外，在一个药品中普遍使用的所有成分。这些成分包括赋形剂和附加剂，如染料、增味剂、黏合剂、缓和剂、填充剂、润滑剂和防腐剂。

六、“公司”是指中国关税区或美国境内从事药品、辅料和医疗器械生产（包括加工）和经营（包括出口）的企业。

七、“HHS/FDA 要求”是指美国所有法律、法规或其他规定，包括在本协议生效后通过的任何由“HHS/FDA”执行或实施的关于药品、辅料和医疗器械的修订文件。

“SFDA 要求”是指中国任何法律、法规或其他规定，包括在本协议生效后通过的任何由 SFDA 执行或实施的关于药品、辅料和医疗器械的修订文件。

八、“医疗器械”是指用于疾病或其他状况的诊断，或治愈、减轻、治疗或预防疾病在人体的发生，或用于影响人体的结构或任何功能的非药品的任何工具、仪器、机械、植入物、体外诊断试剂或类似、相关物品。

九、“在 SFDA 注册的公司”，是指 SFDA 确定符合其要求并向 SFDA 注册的企业。

“在 HHS/FDA 注册的公司”，是指遵守美国注册和目录要求并向 HHS/FDA 注册的公司。

十、“设施”是指中国关税区或美国境内从事药品、辅料和医疗器械制造、生产、加工、包装、检验、储存、运输、经销或出口的公司的任何场地。

第四条　进口与出口工具

一、确定指定药品和指定医疗器械

本条款的执行将分步骤进行，由指定药品和指定医疗器械目录名单开始着手。双方应遵照第七条第四款规定于最初 12 个月结束时以及其后每年，就本条款对第二段指定产品的执行结果进行正式评估。双方可

以协商同意增加或撤除名单中的某一药品、辅料和医疗器械。评估时间表将通过工作计划确定。

（一）因素：

根据以下因素，双方应通过协商适当确定每个阶段的指定产品：

1.根据检验、检查的结果或其他相关信息，该产品对公共卫生造成潜在的或实际的、直接的或间接的风险；

2.各方拒绝一定产品进入另一方市场的比率，或该产品在进入另一方国内市场之前、之中或之后发生问题的比率，包括产品召回、安全性警告和其他执法措施。

3.通过欺诈性、欺骗性的标签或适应症，在产品或产品成分中替换或增加某种物质，使产品成分或产品的质量降低或使其看起来有更高价值，却没有向进口国的接货方明确通报有关增加或替代的情况。

4.向进口国消费者进行的促销或广告宣传超越批准的适应症信息。

5.有效及时地执行与该产品有关的工作计划的可行性。

（二）第一阶段——指定药品和指定医疗器械

双方同意第一阶段应当包括双方指定的产品。指定药品包括任何可被用作本协议项下的指定药品之活性药物成分的物质和化学品，即使生产和经销该物质和化学品的企业未将产品明确为活性药物成分。指定产品的详细内容应由工作计划确定。这些产品包括：

1.SFDA 指定的药品：

(1)合成人胰岛素

(2)赖氨酸脂和赖氨酸盐

(3)头孢哌酮及其盐

(4)紫杉醇注射液

(5)青霉素和制剂

(6)各种血源筛查用诊断试剂，特别是用于艾滋病毒/艾滋病和乙型及丙型肝炎的诊断试剂

2. SFDA 指定的医疗器械：

(1)人工晶体

(2)心脏起搏器

3. HHS/FDA 指定的药品：

(1)硫酸庆大霉素

(2)阿托伐他汀

(3)西地那非

(4)用于治疗勃起功能障碍或增强性功能的膳食补充剂

(5)人体生长激素

(6)奥司他韦

(7)用生产非头孢菌素类药品的设施生产的头孢菌素

(8)甘油

4. HHS/FDA指定的医疗器械：

(1)葡萄糖测试条

(2)安全套

二、指定产品的注册和合作

（一）对于指定的药品和医疗器械产品：

1. 对于 HHS/FDA 指定的产品，SFDA 应要求所有生产出口至美国的指定药品和医疗器械的企业向 SFDA 进行登记。

2. 对于 SFDA 指定的产品，HHS/FDA 应依照工作计划中所同意的，向 SFDA 提供以下可获得的信息：

(1)产品的生产设施；

(2)产品批准信息或放行结果；

(3)召回、警告信和执行措施；及

(4)已报告的上市后不良事件。

（二）HHS/FDA 应与 SFDA 进行协商，为 SFDA 理解 HHS/FDA 对于指定药品和指定医疗器械的要求提供帮助。

（三）HHS/FDA 与 SFDA 应审核 HHS/FDA 对于指定药品和指定医疗器械的要求和 SFDA 对于指定药品和指定医疗器械的要求，了解彼此的差异；如果双方监管体系确实存在不同，应明确保证指定药品和指定医疗器械的质量、安全性和真实性的方法。

（四）SFDA 应保留对指定药品和指定医疗器械企业的审评、检查、检验、召回、执法和任何其他评估的证明文件。如 HHS/FDA 要求，SFDA 应在七个工作日内向 HHS/FDA 提供相关文件记录。

三、未来在注册和认证方面的合作展望

双方同意继续努力，以更好地理解 HHS/FDA 的要求和 SFDA 的要求之间的差异与差距，并努力建立解决这些差距的机制。特别是 SFDA 应积极创造条件，使 SFDA 能够对生产用于出口至美国的指定药品和指定医疗器械的企业是否符合 HHS/FDA 的要求进行认证。一旦这些新条件成熟，双方可同意对本协议作出调整，增加有关按照 HHS/FDA 的要求就中国关税区出口到美国的产品进行认证和适当的出口控制机制方面的条款。

四、产品一致性和安全性

（一）双方应按照工作计划确定存在被仿冒风险的第四条第一款的指定药品，并在建立追溯系统（监管链）方面开展合作。

1.双方应建立并实行包括指定药品追溯要求在内的相关措施， 以进一步确保指定药品的一致性和安全性。双方应相互合作，设定同时适用于国内和出口指定药品的追溯要求。

2.双方应建立并实行追溯系统。追溯系统应包括如下指定药品及其生产商的信息：

(1)产品信息（药品名称、生产企业、产品注册或识别码）；

(2)项目信息（唯一产品序列号、剂型、规格、包装尺寸、批号、失效日期）；

(3)涉及交易各方的信息（包括企业名称、街道地址、许可证号、联系人和电话）；及

(4)交易信息（卖方交运日期和买方收货日期）。

3.针对每一特定包装，各方应建立并执行全面电子追踪系统的标准。

（二）双方应就所有药品的产品一致性和安全措施开展合作；

1.对无法提供溯源信息、提供虚假信息或者不遵守任何其他有关药品一致性、安全性规定的实体，各方应加大执法力度。

2.各方应开展项目，告知和教育供应链利益攸关方和公众如何避免收到标识不符、掺假或假冒的药品或医疗器械，如何将这种风险降到最低，以及如何举报可疑药品、辅料、医疗器械和嫌疑人。

3.SFDA 和 HHS/FDA 应对被怀疑为标识不符、掺假或假冒的药品、辅料和医疗器械迅速做出反应，并对举报展开调查。SFDA 和 HHS/FDA 应将此类举报以及对举报采取的措施或调查计划通报对方。SFDA 和 HHS/FDA 还应向世界卫生组织（WHO）报告假药信息。

4.各方应采取措施，采用并执行有关法规、规范（例如良好销售质

量管理规范）、指南（例如药物警戒、对假冒药品的快速反应），相关文件应与世界卫生组织（WHO）制定的包括假药的识别和预防，以及来源不明和成分不符的活性药物成分/原料药、辅料和制剂执法的文件保持一致。有关标准方面的合作细节，应通过工作计划予以确定。

5.各方应努力加强与本国有关执法和监管部门的合作，积极调查和起诉生产、销售、分销、处理、检验、交易或出口标识不符、掺假或假冒药品、辅料和医疗器械的个人或实体。

6.各方应积极参加 WHO 国际医药产品打假工作组（IMPACT）和国际药品犯罪永久论坛（PFIPC）的活动。

第五条　信息共享

双方应根据工作计划协定的时间表遵照以下规定，相互交换及更新关于药品、辅料和医疗器械及其监管体系的有关信息：

一、一方可向另一方提供英文或中文的信息。

二、双方应交换各自涉及药品和医疗器械安全性、有效性和质量的法律法规副本以及其他相关信息。

三、针对指定产品，HHS/FDA 和 SFDA 应向对方提供所有相关的 HHS/FDA 和 SFDA 要求，并适时更新。

四、一方应向另一方提供在本国注册登记的全部活性药物成分生产商及其产品的清单。

五、一方应向另一方通报由于产品安全、生产条件、召回、严重不良事件报告和其他情况，或因严重欺骗消费者行为所造成的严重不良健康后果或死亡事件。一方应尽快对另一方所要求的任何此类风险相关信

息做出反应，包括公司或其他相关实体的联系信息。工作计划应包括详细的规定以确保任何此类通报或反应的及时性。

六、HHS/FDA 应与 SFDA 合作，以加深对全球协调工作组（GHTF）的国家主管当局报告（NCAR）项目的了解，并支持双方主动向 NCAR 项目报告任何涉及医疗器械的严重不良事件。

七、对已经运往对方国家的药品、辅料或医疗器械，一方如果有合理的可能性认定相关产品的使用或接触会造成严重不良健康后果或死亡事件，应向另一方通报其认定结果。这种通报应当：

1. 采用书面形式；

2. 在认定后 24 小时之内进行；

3. 包括认定原因；及

4. 如有可能，包括其他可以帮助对方确定装运情况和供应商的其他信息。

八、在本协议生效后 30 个历日内，双方应互相提供设在本国并在本国注册的药品和医疗器械的生产厂商名单及其产品目录。如果可能，SFDA 应向 HHS/FDA 提供中国关税区内已经确定未能遵守 SFDA 规定的被吊销药品、辅料和医疗器械生产许可证的厂商名单。

九、在 HHS/FDA 提出要求后 30 历日内，SFDA 应根据要求向 HHS/FDA 提供有关注册公司的检查报告，所述公司生产或者销售的药品、辅料或医疗器械已经或者即将出口美国。对上述生产或销售的药品、辅料或医疗器械的具有重大缺陷或欺诈的，SFDA 应该在知晓检查结果 10 个历日内向 HHS/FDA 进行通报。一旦 HHS/FDA 解决了任何现存的远程获取问题，HHS/FDA 将允许 SFDA 进入 HHS/FDA 检查结果电子数据库。

十、各方应当通报在各自国内发现的任何假冒药品、辅料或医疗器械，包括有关来源及分销的信息。

第六条　监管合作

双方应就有关药品、辅料和医疗器械方面完成下列任务：

一、在工作计划中设定具体的步骤和措施，预防和控制假冒药品、辅料和医疗器械。

二、开展适当的监管合作活动，包括培训项目和科学研讨或合作，目的在于支持注册及认证机制长期稳定及有效。对于各项涉及旅行和其他组织费用的培训和其他合作活动，双方各自负担参加人员的费用。适当的监管合作活动可以包括：

1.建立并协调对中国检查员的培训；

2.就药品临床质量管理规范（GCP）开展技术交流及相关培训，保证人体受试者的安全，并收集有效的临床数据；及

3.在审评方法、检查技术、建立计算机数据库、评价报告的标准格式、建立技术指导文件及法律法规方面，开展培训和交流。

三、双方应在标准的实施方面开展合作。

（一）双方应在工作计划中确定关于建立国际认可的标准的合作细节。这些标准可以包括：

1.国际药用辅料协会的辅料标准；

2.人用药物注册技术要求国际协调会议（ICH）指南，包括 ICH　Q7A 活性药物成分/原料药的现行良好生产质量管理规范指南；

3.药品检查合作计划(PIC/S)的药品制剂 GMP 标准；及

4. 全球医疗器械标准和法规协调组织标准，包括 ISO 13485 对医疗器械的要求。

（二）应 SFDA 要求，HHS/FDA 应在采用国际认可的标准方面向 SFDA 提供帮助。

四、在收到一方要求的 5 个历日之内，对方应建立精简的程序，以协助（例如发邀请信）一方在对方国家进行检查。对相关企业的检查可在提前通知或未提前通知（根据要求的具体说明）的情况下进行。该项活动将依据一方提出要求和另一方回应协助检查之间需要的天数予以评估。

五、如果一方有理由认为从另一方国家出口到本国的任何药品、辅料或医疗器械会对公共健康及安全带来风险，可要求对方进行调查。一方应就对方的要求，在收到要求的 3 个历日内给予回应，说明是否决定调查；如果决定调查，应当在决定调查的 15 个历日内向对方通报以下信息：

1. 关于健康或安全风险来源的信息；

2. 弥补风险所采取的步骤；及

3. 任何补救措施的结果。

对本条所述的调查，由工作计划明确有关要求和评估手段。

六、HHS/FDA 可完全参与 SFDA 对中国关税区内向美国出口产品的在 SFDA 或 HHS/FDA 注册的公司的任何年度或其他检查。

七、极端情形除外，各方应遵照以下程序：双方应在其网站上发布所有涉及指定药品和指定医疗器械的法规建议案和其他规定，以使所有利益相关方有合理的时间做出评议。双方应考虑这些评议意见，并在通过最终法规时以书面形式指出在评议期内收到的来自利益相关方的重

大和实质性评议意见，解释对于法规建议案的任何实质性修改。双方也应在其网站上发布有关指定药品和指定医疗器械的所有最终法规和其它措施，并在实施前留出合理的时间。双方应将上述信息公布在相关政府出版物上（如 HHS/FDA 的联邦政府公报）。在中国未指定单一的相关政府出版物之前，SFDA 应确保其网站随时更新以确保政策制定的透明度。

八、HHS/FDA 应将任何科技合作报告科技合作联委会。该联委会系根据美利坚合众国政府和中华人民共和国政府于 1979 年 1 月 31 日在华盛顿签署的科技合作协议设立的。

第七条　执行

一、本协议生效后 15 个历日内，双方应以书面形式将主要联络人通知对方。联络人负责协调本协议下的所有双边活动，包括协调会议、交换信息，以及发送和接受通知。

二、双方为此建立一个工作组。本协议生效后 30 个历日内，双方应各自确定相关政策和技术专家作为工作组成员。

三、本协议生效后 60 个历日内，工作组应召开第一次会议以制定工作计划：

1. 进一步根据本协议细化双方在协议生效后最初 12 个月内的具体活动，以及每项活动的完成时限；及

2. 适当时包括执行测评以评估每项活动的成效。

四、本协议生效后 120 个历日内，工作组应确定最初 12 个月的工作计划。双方应在 12 个月结束时对工作计划进行评估。

五、此后每 12 个月，工作组均应开会制定工作计划，进一步细化双方根据本协议在该期间进行的具体活动，并且适当时包括工作测评以评估每项活动的成效。双方应在该期间结束时对工作计划进行评估。

六、每 12 个月的工作计划经双方同意后，应包括使本协议得到有效和及时执行的具有约束力的承诺。各方均应制定最初 12 个月和此后年度的工作计划，并在各自的网站上对外公布。

七、本协议生效后 180 个历日内，双方高层代表应会面以讨论和审评本协议执行情况和进展以及相关事宜。

八、此后，每年举行一次双边高层会晤，讨论并审议本协议执行情况和进展以及相关事宜。除非双方另有商定，年度会议应轮流在中国和美国举行。双方根据需要，可在任何商定的地点举行另外的技术或项目层面的会议。

九、针对本条各项规定，一方应在确定无法保证商定时限的24小时内通知对方，告知延误的原因，例如中美两国假期的不同或任何其他理由，并提供新的双方同意之提交日期。该通报应通过第七条第一款确定的指定联络人完成。

第八条　执行评估

一、双方应根据本协议，每年评估并讨论协议的进展，包括 SFDA 依照工作计划建立的注册机制的有效性。HHS 可以基于以下和其他事项评估进展情况：

1.与 2007 历年或其他相关时期 HHS/FDA 对从中国关税区出口和用于进口到美国的药品、辅料和医疗器械的总拒绝率相比，从中国关税区

出口和用于进口到美国的药品、辅料和医疗器械的被 HHS/FDA 拒绝的比率。

2. 与 2007 年和其他相关时期相比，从中国关税区出口和提供进口到美国的药品、辅料和医疗器械，包括假冒药品和医疗器械，因危害公共健康被召回的数量、频率及影响。

二、SFDA 基于以下和其他事项评估进展情况：

1. 与上一年总拒绝率相比，经 HHS/FDA 批准的用于进口到中国关税区的指定药品和指定医疗器械的拒绝率。

2. 基于抽样检验结果，从美国关税区出口并用于进口到中国关税区的指定药品和指定医疗器械被确定为不合格产品的总比率。

3. 与上一年相比，从美国关税区出口的和用于进口到中国关税的药品、辅料和医疗器械，包括假冒药品和医疗器械产品，因危害公共健康被召回的数量、频率及影响。

第九条　最终条款

一、本协议的所有内容都不排除美国政府和中国政府采取措施保护本国公民或公众健康。HHS/FDA 和 SFDA 确认，在适当的条件下，与国家、州、省或市级机构协作，全面实施本协议。

二、本协议的解释不应影响美国或中国任何其他已生效协议下的权利和义务。

三、HHS/FDA 对药品、辅料和医疗器械采取的措施应符合 HHS/FDA 要求和所有其他现行的美国法律法规。

四、SFDA 对药品、辅料和医疗器械采取的措施应符合 SFDA 要求和

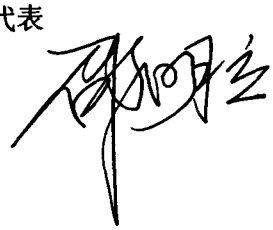
所有其他现行的中国法律法规。

五、双方应通过及时协商，努力解决涉及本协议实施和解释的任何争议。

六、本协议在双方签署后生效，有效期2年，除非任何一方终止协议。协议将在2年期限届满以及随后每2年期限届满的最后一天，自动延续至另一个2年，除非任何一方在2年期限最后一天结束前的至少60个历日前通知另外一方希望终止协议。此外，各方均可提前60个历日以书面通知对方终止协议。双方可以在相互书面同意后于任何时间修改本协议。

本协议于2007年12月11日在北京签署，一式两份，以中英文书就，两种文本同等作准。

中华人民共和国
国家食品药品监督管理局
代表



美利坚合众国
卫生与人类服务部
代表