Announcement on Issuing Regulations for the Administration of Overseas Inspection of Pharmaceuticals & Medical Devices (No. 101 of 2018)

In order to standardize the overseas inspection of pharmaceuticals & medical devices and ensure the quality of imported pharmaceuticals & medical devices, *Regulations for the Administration of Overseas Inspection of Pharmaceuticals & Medical Devices* Has been formulated by National Medical Products Administration (NMPA) and is hereby issued for implementation as of the date of issuance.

The announcement is hereby made.

National Medical Products Administration

December 26, 2018

Regulations for the Administration of Overseas Inspection of Pharmaceutical & Medical Devices

Chapter I General

Article 1 This *Regulations* has been developed in accordance with the requirements of *Drug Administration Law of the People's Republic of China*, *Medical Device Regulations* and applicable statutes to regulate the overseas inspection of pharmaceuticals & medical devices.

Article 2 This *Regulations* applies to the inspections of overseas processes in relation to the development and manufacturing of pharmaceuticals and medical devices that have been or are intended to be marketed within the territory of the People's Republic of China.

Article 3 For the purpose of this *Regulations*, overseas inspections of pharmaceuticals and medical devices refer to the inspections conducted by the National Medical Products Administration ("NMPA") to confirm the authenticity, reliability and compliance of the processes related to the overseas development and manufacturing of pharmaceuticals and medical devices.

Article 4 The NMPA is responsible for the overseas inspection and management of

pharmaceuticals and medical devices. Center for Food and Drug Inspection of NMPA (”CFDI”) is responsible for the specific organization and implementation of overseas inspections of pharmaceuticals and medical devices. Relevant departments handling inspection, review and evaluation of pharmaceuticals and medical devices assist in the conduct of overseas inspections.

Article 5 The NMPA discloses the basic situation and outcomes of inspection in accordance with the requirements of government information disclosure.

Article 6 Inspectors and the inspected organizations shall strictly abide by the anti-corruption requirements.

Article 7 Inspectors shall strictly abide by laws, regulations and inspection disciplines, and keep state secrets and the secrets of the organizations inspected.

Chapter II Inspection Tasks

Article 8 The NMPA determines the inspection tasks through risk assessment and random sampling taking into account recommendations of relevant departments on to-be-inspected products and their respective development and manufacturing sites. In the event a change in the inspection task(s) is indeed required due to regulatory purpose, adjustment(s) can be made to the inspection task(s) per provisions of the NMPA on management of foreign affairs involved in overseas inspection.

Where necessary as indicated, extended inspections can be conducted on the manufacturing sites, suppliers and/or other contract organizations of raw materials, excipients and/or packaging materials.

Article 9 The determination of inspection tasks shall consider risk factors in relation to medical products/medical devices such as registration review and approval, supervision and inspection, testing, complaint reports, and monitoring of adverse reactions and adverse events. Focus shall be placed on the following situations:

(I) Potential risks discovered during review and approval;

(II) Non-compliance of inspection or batch release, indicating that there are risks with the quality management system;

(III) Possible product safety risks as indicated by adverse reaction or adverse event monitoring;

(IV) Other violations of laws and/or regulations as indicated by complaint reports or other information;

(V) There are adverse records on the marketing approval holder, the medical device registrant or the filer (hereinafter referred to as “the holder”);

(VI) Presence of major problems with the holder's quality management system, as

evidenced by the findings of on-site inspection(s) conducted by foreign regulatory authorities;

(VII) There is a need of inspection again after rectification;

(VIII) Other situations for which overseas inspections are required.

Article 10 The CFDI shall send *Overseas Inspection Notice* (Annex 1) to the holder or their agent based on the overseas inspection tasks of the NMPA. The holder shall submit to the CFDI *Letter of Authorization* (see Annex 2 for corresponding requirements) and *Basic Information Form of Product under Overseas Inspection* (Annex 3) within twenty (20) working days, and site master files and other materials required for the inspection based on the *Listing of Site Master Files* (Annex 4) within forty (40) working days, as of the date of receipt of *Overseas Inspection Notice.*

The CFDI may retrieve technical materials relating to the inspection of the varieties depending on the need of inspection, and the technical information obtained shall be maintained confidential through necessary measures, and shall be included in the inspection files after the inspection.

The holder must appoint a domestic agent (where the agent of medical device shall be the agent of the medical device registrant or the filer) and issue an authorization in accordance with the relevant requirements. The agent is responsible for the liaison between the medicine regulatory authority and the holder, undertakes adverse medicine reactions or medical device adverse event monitoring, and is responsible for product traceability and recall. The agent shall perform the relevant responsibilities and obligations of the medical devices for domestic marketed medicines as prescribed by laws and regulations, and assist the medicine regulatory authorities to carry out investigations on the overseas development of products, the inspection of production sites and violations of laws and regulations.

In the event of a change in the agent, the holder shall, after completing the change procedures stipulated by laws and regulations, delegate the new agent to submit a new Letter of Authorization to the CFDI in a timely fashion. Said Letter of Authorization shall clarify that the termination date of authorization for the outgoing agent shall be start date of authorization for the new agent.

Article 11 Upon receipt of Basic Information Form of Product under Overseas Inspection, The CFDI preliminarily determines an inspection schedule based on the overall arrangement of the inspection work and serves an Overseas Inspection Pre-notice (Annex 5) to the holder.

The holder shall not postpone the inspection without justification. In the event there is indeed a need to postpone the inspection due to special circumstances, a written application accompanied by justifications shall be submitted to the CFDI within ten (10) working days as of the date of service of Overseas Inspection Pre-notice. In such case, the CFDI determines the final inspection date by comprehensive evaluation of the actual inspection work to judge whether there is any situation that rejects or obstructs inspection.

Article 12 The inspection team shall in principle consist of more than three inspectors, and the inspection team shall implement responsibility system of team leader responsibility. The inspectors shall be persons who have obtained the inspector qualification in accordance with law. Experts in relevant fields can be invited to participate in the inspection work depending on the needs of inspection work.

Article 13 The holder shall coordinate and cooperate with the overseas inspection work in an all-round manner to ensure the smooth progress of the inspection, without delay, obstruction, evasion or refusal of inspection.

Article 14 The holder shall be responsible for communicating with the relevant inspected organizations (including overseas production plants, research and development institutions, manufacturing sites of raw materials, excipients and packaging materials, suppliers or other contract organizations, etc.) to coordinate and check related matters.

Article 15 The working language for overseas inspection is Chinese that materials such as application dossiers and rectification report submitted by the holder shall be in Chinese language. During the inspection period, translators who can meet the inspection requirements shall be provided.

Chapter III Inspection

Article 16 The CFDI is responsible for formulating the overseas inspection plan, and the inspection team shall conduct on-site inspections in accordance with the inspection plan. When a change to the inspection plan is required, the inspection team shall report to the CFDI for approval before implementation.

The CFDI shall provide the inspection team with centralized pre-departure education to emphasize the anti-corruption discipline and foreign affairs discipline.

Article 17 At the beginning of the on-site inspection, the inspection team shall convene an initial meeting to notify the inspected organization of the composition of the inspectors, the purpose and scope of the inspection, the inspection schedule, and state the inspection precautions and the discipline for inspection.

The inspected organization shall introduce to the inspection team the registration, production, and quality management of the product(s) to be inspected, and clarify the responsible person for the site inspection.

Article 18 During the inspection, the inspected organization shall maintain the normal production status, open relevant places and areas to the inspection team, and cooperate with the inspection of relevant facilities and equipment; according to the inspection schedule, the inspected organization shall arrange the dynamic production of the key production processes of the inspected varieties, timely provide the documents, records, electronic data, etc. required for the inspection, and truthfully answer the inquiries of the inspection team.

Article 19 The inspection team may collect relevant evidence materials by means of copying, photographing and video depending on the needs of inspection.

Article 20 If samples need to be taken during the inspection, the inspection team shall sample and seal the samples with reference to the sampling procedures and attach samples.

The sealed sample shall be returned to the territory by the holder with the sample file or brought back to the territory for inspection. The holder shall ensure that the packaging and shipping conditions of the sample are such that the quality of the sample is not affected.

Article 21 If the inspection team finds that there is a serious quality risk, it shall immediately report to the CFDI and propose preliminary disposal. After receiving the report, the CFDI shall conduct a risk assessment in a timely manner and report relevant results to the NMPA.

Article 22 Before the inspection comes to an end, the inspection team shall convene the final meeting to communicate the inspection outcomes and problems identified through inspection to the holder. The holder may state the defense and the inspection team shall keep documentation thereof.

Article 23 The inspection report shall be signed by the entire inspection team for confirmation and shall be submitted to the CFDI within ten (10) working days from the date of the inspection team returning to China.

Chapter IV Review and Handling

Article 24 After on-site inspection is completed, the CFDI shall feed *Notice of Overseas Inspection Findings* (Annex 6) back to the holder or their agent in writing within twenty (20) working days as of receipt of the inspection report submitted by the inspection team.

Where testing is required, the testing agency shall complete the testing or study within the statutory time limit from the date of receipt of the sample, and the time of testing or study shall not be counted in the time limit for feeding back Notice of Overseas Inspection Findings.

If any objections to the inspection outcomes, the holder may present a written statement or justification to the CFDI within ten (10) working days as of the date of service of Notice of Overseas Inspection Findings to the holder or their agent. Failure of the holder to provide such statement or justification within the specified time limit of ten (10) working days shall be deemed as no objections. The holder's statement and justification shall be included in the inspection file.

Article 25 The holder shall submit to the CFDI a report of rectifications for defects identified during overseas inspection within fifty (50) working days from the date of service of Notice of Overseas Inspection Findings. Where rectifications for the defects cannot be completed within the prescribed time limit, the holder shall submit a detailed improvement and follow-up plan followed by corresponding updates until all the rectifications have been

completed.

Article 26 The CFDI shall conduct a comprehensive assessment of the on-site inspection report in conjunction with the rectifications made by the holder. The comprehensive assessment shall be completed within twenty (20) working days after receipt of the rectification report. The holder's statement or justification, if any, may be considered together in the comprehensive assessment. If necessary as indicated, inspection may be re-initiated for the rectifications. In the event risk consulting or supplementation of materials by the hold is required during the process of comprehensive assessment, relevant time taken will not be counted in the aforesaid time limit.

Article 27 The comprehensive assessment shall adopt the principles of risk assessment taking into account the nature and severity of the defects and the product category to assess the inspection outcomes. The principle of judgment is as follows:

(I) Conforming: no defects were found during on-site inspection.

(II) Conforming after rectification: on-site inspection has found that there are corrective measures for all major defects and general defects, indicating that the holder is able to take effective corrective measures and organize production per laws, regulations and technical specifications.

(III) Non-conforming: on-site inspection of the pharmaceutical product has found problems of non-compliance with regulatory requirements and technical specifications, such as data authenticity, inconsistency of product quality-affecting critical elements with the registration materials, presence of serious defects, inadequate corrective measures for major defects, infeasibility of the rectification plan, etc.; ; on-site inspection of medical device has found problems of non-compliance with regulatory requirements and technical specifications, such as data authenticity, inconsistency of product quality-affecting critical elements with the registration materials, presence of serious defects, inadequate corrective measures for major defects, infeasibility of the rectification plan, etc..

Article 28 In any of the following circumstances, the holder shall be deemed to have delayed, obstructed, restricted or rejected inspection and be directly judged as "non-conforming":

(I) Failure to provide the required authorization document(s) within the specified time limit after the date of service of *Overseas Inspection Notice*; failure to provide relevant documents and/materials required within the prescribed time limit;

(II) The holder obstructed or postponed the scheduled inspection twice;

(III) Refusal of the inspected holder to arrange for dynamic production;

(IV) Failure to cooperate with the procedures for overseas inspection;

(V) Failure to cooperate with an extended inspection;

(VI) The holder is found to delay, obstruct, restrict or reject the entry of the inspection personnel into the inspected place or area, or restrict the inspection time, or set unreasonable inspection conditions or disturb the inspection;

(VII) the holder is found to delay in providing or refuse to provide or deliberately cover critical information to be inspected;

(VIII) The holder is found to reject or restrict on-site collection of evidence-related materials, or refuse to perform notarization certification procedures or submit notarized certification documents for evidence-related materials;

(IX) Other circumstances that do not cooperate with the inspection.

Article 29 After comprehensive assessment, the CFDI shall form a report of overseas inspection review, which shall be submitted to the NMPA together with relevant inspection records and documents.

When discovering any potential major quality hazards requiring emergency measures in the on-site inspection report of the inspection team or during comprehensive assessment, the CFDI shall immediately send a report to the NMPA.

Article 30 For the varieties that are in the stage of registration review and approval or belong to the category of registration review and approval, the NMPA will, taking into the conclusion(s) from comprehensive assessment, adopt corresponding measures in accordance with *Drug Administration Law of the People's Republic of China*, *Medical Device Regulations, Drug Registration Regulations*, *Regulations on Medical Device Registration* and *Regulations on Registration of In vitro Diagnostic Reagents*.

For the varieties that have been marketed in China, the NMPA will, with consideration given to the conclusion(s) from comprehensive assessment, order corresponding risk control measures against the holder, including interviews, making rectifications within a specified time limit, issuing a warning letter, suspending the filing of drug import customs clearance, suspending the import of the medical device involved, suspending the sale and use of the medical device involved, overseeing the product recall and even revoking import approval certificates.

If the comprehensive judgment is that the requirements are not met, and the inspection reveals that the enterprise has illegal activities or the product has potential safety hazards, the NMPA shall promptly adopt risk control measures and make information disclosure per law. For those who have major quality hazards and need to take urgent measures, the NMPA shall immediately take risk control measures and handle the case in accordance with law.

Article 31 In the case of discovering suspected violations of law, the inspectors shall fix the evidence in time, and the NMPA shall organize investigation and handling in accordance

with law.

Article 32 The holder shall establish a product traceability system to ensure efficient recall of products being distributed and used in the country when product recall is required as evidenced by problems identified during inspection.

Article 33 After the risk factors are eliminated or rectifications have been made, the holder may submit an application to the NMPA for on-site inspection, which can be initiated again as appropriate after review. If the requirements of laws, regulations and technical specifications are met, the relevant risk control measures shall be lifted.

Chapter V Supplementary Provisions

Article 34 The on-site inspection of processes in relation to product development and manufacturing for holders located in the Hong Kong Special Administrative Region, the Macao Special Administrative Region and the Taiwan region shall be carried out in reference to this *Regulations*.

Article 35 On-site inspections for the raw material, excipient and/or packaging material manufacturing sites or suppliers of home-made products located outside China shall be conducted in reference to this *Regulations*.

Article 36 Site master files defined in this *Regulations* are part of the quality management system documents, describing the enterprise's quality management policies and activities, the implementation of manufacturing and/or quality control of medical products/medical devices at designated sites, the performance of relevant operations in adjacent or nearby buildings ,etc.

Article 37 This *Regulations* shall be interpreted by the NMPA.

Annexes:

1. Overseas Inspection Notice
2. Relevant Requirements for Holder's Authorization of Agency for Overseas Inspection Affairs
3. Basic Information Form of Product under Overseas Inspection
4. Listing of Site Master Files (for Pharmaceuticals / Medical Devices)
5. Overseas Inspection Pre-notice
6. Notification of Overseas Inspection Outcomes

Annex1

Overseas Inspection Notice

This is to notify that per work arrangements of the National Medical Products Administration (NMPA), the product(s) of your company has (have) been included among the list of overseas development/manufacturing sites to be inspected Relevant requirements for overseas inspection are now notified as follows:

I. Basic Information

Company name (holder)：

Product name:

Acceptance number / registration number / filing number:

II. Relevant requirements for overseas inspection

1. The holder included in the aforesaid list shall appoint a domestic agent (where the medical device registrant and the filer shall designate his agent as the inspection agency) within China and issue a letter of authorization in accordance with the relevant requirements. Please send the original Letter of Authorization to the Center for Food and Drug Inspection within twenty (20) working days from the date of service of this notice.
2. Each authorized agent shall specify two fixed contacts, with contact information provided, including mobile phone, landline, fax, email, etc., to ensure smooth communication on preparations for the inspection.
3. Please fill out Basic Information Form of Product under Overseas Inspection within twenty (20) working days from the date of service of this notice, submit it online and send two (2) sets of paper documents affixed with seal to the CFDI. Please provide proposals on the time you are available for on-site inspection, and you are required to arrange for dynamic production of the product under inspection during the inspection period.
4. Please submit to the CFDI the Chinese and English versions of the site master files online and two (2) sets of paper documents within forty (40) working days from the date of service of this notice. The paper site master files shall be printed and stamped with the official seal and sent to the CFDI.

III. CFDI Contact Information

Contact:

Fax:

E-mail address:

Address:

Zip code:

Annex 2

Relevant Requirements for Holder's Authorization of Agency for Overseas Inspection Affairs

In order to ensure effective communication between the National Medical Products Administration (NMPA) and the holder on overseas on-site inspection work and follow-up measures, the holder is required to set up an agent with full authorization for the inspection= affairs. The relevant requirements are as follows:

I. The holder shall appoint a domestic agent (where the medical device registrant and the filer shall designate his agent as the inspection agency) and issue a Letter of Authorization as required. The agent is responsible for the liaison between the medicine regulatory authority and the holder, undertakes monitoring of adverse drug reactions (ADRs) or medical device-related adverse events, and is responsible for product retrospective recall. The agent shall perform the relevant responsibilities and obligations of the domestic marketed medicine medical device as stipulated by laws and regulations, and assist the medicine regulatory authority to carry out investigations on the overseas development of the product, the inspection of the production site and the violation of laws and regulations.

II. The Letter of Authorization shall be signed or stamped by the person in charge of the holder. The contents of the Letter of Authorization must clearly describe the authorization items, and at least shall include the authorization to submit the inspection materials to the Chinese Medicine regulatory authority, cooperate with the support of on-site inspections, and implement the follow-up requirements. The legal person of the agent, the specific address, contact person and contact information shall also be specified in the Letter of Authorization.

III. In the process of overseas on-site inspection where extended inspection of the manufacturing sites, suppliers and/or other contract organizations of raw materials, excipients, and/or packaging materials , the Letter of Authorization shall specify that the agent also has the authorization to assist in supporting the extended inspection.

IV. The Letter of Authorization must be notarized by a law firm or lawyer of the place where the holder is located, and certified by the local Chinese embassy or consulate. The certification document shall be in both Chinese and foreign versions that have the same effect of authorization.

V. When the agent submits the Letter of Authorization, it shall also submit a photocopy of Registration Certificate of Foreign Resident Representative Office in China or a photocopy of the agent's Business License, either of which shall be stamped with the official seal of the agent.

VI. In the event of a change in the agent, the holder shall, after completing the change procedures stipulated by laws and regulations, delegate the new agent to submit a new Letter of Authorization to the CFDI in a timely fashion. Said Letter of Authorization shall clarify that the termination date of authorization for the outgoing agent shall be the start date of authorization for the new agent. .

Annex 3

Basic Information Form of Product under Overseas Inspection – For Pharmaceuticals

<table>
<tr><td>Product name</td><td colspan="2">Chinese
English</td><td>Acceptance number or import registration certificate number</td><td></td></tr>
<tr><td>Dosage form</td><td colspan="2"></td><td>specification</td><td></td></tr>
<tr><td>Current registration status</td><td colspan="4">☐ Marketed ☐ Re-registration ☐ Application for production
☐ Application for clinical trial ☐ Supplementary application</td></tr>
<tr><td>company name (Holder)</td><td colspan="4">Chinese:
English:</td></tr>
<tr><td rowspan="4">Site 1*</td><td>Name</td><td colspan="3">Chinese
English</td></tr>
<tr><td>Production activities</td><td colspan="3"></td></tr>
<tr><td>Production address</td><td colspan="3">Chinese
English</td></tr>
<tr><td>Country</td><td colspan="3"></td></tr>
<tr><td rowspan="4">Site X</td><td>Name</td><td colspan="3">Chinese:
English:</td></tr>
<tr><td>Production activities</td><td colspan="3"></td></tr>
<tr><td>Production address</td><td colspan="3">Chinese:
English</td></tr>
<tr><td>Country</td><td colspan="3"></td></tr>
<tr><td rowspan="2">Agency</td><td>Name</td><td colspan="3"></td></tr>
<tr><td>Address</td><td colspan="2"></td><td>Postcode</td><td></td></tr>
<tr><td>Contact A</td><td></td><td>Contact number</td><td></td><td>Mobile Phone</td><td></td></tr>
<tr><td>E-mail</td><td colspan="3"></td><td>Fax</td><td></td></tr>
<tr><td>Contact B</td><td></td><td>Contact Number</td><td></td><td>Mobile phone</td><td></td></tr>
<tr><td>E-mail</td><td colspan="3"></td><td>Fax</td><td></td></tr>
<tr><td>Proposed inspection schedule 1</td><td colspan="3"></td><td>Remarks</td><td></td></tr>
<tr><td>Proposed inspection schedule X</td><td colspan="3"></td><td>Remarks</td><td></td></tr>
<tr><td colspan="5">Imports in the last five years**</td></tr>
</table>

Year	Import lot number	Import Volume	Import inspection	Remarks

Previous applications			
Acceptance number	Application content	Approval status	Remarks

Attachments	1. Product's manufacturing process and related process production cycle, corresponding production location 2. Imported drug registration certificate (if applicable)
statement	The electronic materials submitted are consistent with the submitted paper materials.
other	Is there any change in the product recently or is any change planned for the product in the near future? □ No □ Yes _____

Official seal

Date (MM DD, YYYY)

Form Completion Instructions:

*Factory: including all factories involved in production activities such as production, packaging, inspection, and release.

**Imports in the past 5 years; additional documents can be attached if there was great number of batches.

Basic Information Form of Product under Overseas Inspection – For Medical Devices

<table>
<tr><td>Name of product with a registration certificate</td><td colspan="2">Chinese
English</td><td>Registration number / filing number</td><td colspan="2"></td></tr>
<tr><td>Name of product under registration application</td><td colspan="2">Chinese
English</td><td>Acceptance number</td><td></td><td>❑ Initial registration
❑ Change of registration
❑ Registration renewal</td></tr>
<tr><td>Company name</td><td colspan="5">Chinese
English</td></tr>
<tr><td rowspan="3">Factory 1</td><td>Name</td><td colspan="4">Chinese
English</td></tr>
<tr><td>Production address</td><td colspan="4">Chinese
English</td></tr>
<tr><td>Main process</td><td colspan="4"></td></tr>
<tr><td rowspan="3">Factory 2</td><td>Name</td><td colspan="4">Chinese
English</td></tr>
<tr><td>Production address</td><td colspan="4">Chinese
English</td></tr>
<tr><td>Main Process</td><td colspan="4"></td></tr>
<tr><td rowspan="3">Research and development</td><td>Name</td><td colspan="4">Chinese
English</td></tr>
<tr><td>R&D address</td><td colspan="4">Chinese
English</td></tr>
<tr><td>Country</td><td colspan="4"></td></tr>
<tr><td rowspan="2">Agent</td><td>Name</td><td colspan="4">Chinese
English</td></tr>
<tr><td>Correspondence address</td><td colspan="4"></td></tr>
<tr><td>Contact A</td><td></td><td>contact number</td><td></td><td>Mobile phone</td><td></td></tr>
<tr><td>Department and position</td><td></td><td>E-mail</td><td></td><td>Fax</td><td></td></tr>
<tr><td>Contact B</td><td></td><td>Contact number</td><td></td><td>Mobile phone</td><td></td></tr>
<tr><td>Department and Position</td><td></td><td>E-mail</td><td></td><td>Fax</td><td></td></tr>
</table>

<table>
<tr><td colspan="2">Proposed inspection schedule 1</td><td colspan="5"></td></tr>
<tr><td colspan="2">Proposed inspection schedule 2</td><td colspan="5"></td></tr>
<tr><td colspan="2">Proposed inspection schedule 3</td><td colspan="5"></td></tr>
<tr><td colspan="2" rowspan="4">Number of products imported into China in the past 3 years</td><td rowspan="2">Product name</td><td rowspan="2">Registration number</td><td colspan="3">Import volume</td><td rowspan="2">Remarks</td></tr>
<tr><td></td><td></td><td></td></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>Attachment</td><td colspan="6">Product’s production process and corresponding production location
Copy of import registration certificate / Xu Zi registration certificate (including attachments)</td></tr>
<tr><td>statement</td><td colspan="6">The electronic materials are consistent with the submitted paper materials.</td></tr>
<tr><td>other</td><td colspan="6">For example, whether there is any change in the product recently or any change is planned for the product in the near future.</td></tr>
</table>

Official seal

Date (MM DD, YYYY)

Annex 4

List of Site Master Files (For Pharmaceuticals)

1. Company overview

1.1 Company's contact information

- Company name, registered address;
- Names and addresses of the company's product plant(s) and buildings & workshops within the plant(s);
- Company's contact information and 24-hour emergency contact number (in case of product problems or recalls);
- Site identification number, such as GPS details, D-U-N-S number (Data General Numbering System) (a unique identification number provided by Dun & Bradstreet) or any other geo-location system.

1.2 Licensed pharmaceutical production activities at the site

- Provide a copy of the valid production permit document issued by the competent regulatory authority in Listing Attachment 1; if necessary, reference to the Eudra GMP database. In the event a production permit is not issued by the regulatory authority, explanation shall be provided.
- Brief description of production, import, export, distribution and other activities licensed by the competent regulatory authority, including dosage forms/production activities permitted by foreign authorities not mentioned in the permit document.
- Please provide in Listing Attachment 2 a list of products currently produced at the site; the aforesaid products are not included in Listing Attachment 1 or in the Eudra GMP database.
- Information on GMP inspections received by the site in the past five years, including inspection time and the name and country of the regulatory authority that implemented the inspections. If any, please provide a copy of the current GMP certificate or refer to the Eudra GMP database in Listing Attachment 3.

1.3 Other production activities at the site

- If the factory has non-pharmaceutical production activities, please specify.

2. Company's quality management system

2.1 Company's quality management system

- Briefly describe the operation of the company's quality management system and the standards referenced;
- Responsibilities related to quality systems, including the senior management;
- Information about the certification and approval of the factory’s quality system, including the date of certification and approval, the content of approval, and the name of the approving authority.

2.2 Finished product release procedure

- Describe in detail the qualification requirements of the authorized person responsible for the batch qualification and release procedures;
- Outline the batch qualification and release procedures;
- Responsibilities of the authorized quality person(s) in pending inspection and release, as well as responsibilities in assessing compliance with marketing approval
- If involvement of several authorized persons, describe the work arrangements among these authorized persons;
- Describe in detail the use of process analytical technology (PAT) and/or real-time release or parametric release in the process.

2.3 Management of suppliers and contractors

- Briefly describe the company's supply chain and external audit projects;
- Briefly describe the system(s) for qualifying contractors, API manufacturers and other critical material suppliers;
- What measures are in place to ensure that the variety manufactured is in compliance with the TSE (transmissible spongiform encephalopathy) guidelines.
- Control measures taken on suspected or identified fake/counterfeit medicines, products to be packaged (e.g., unpackaged tablets), APIs or excipients;
- Commissioned production and commissioned inspections and other project commissions;
- A list of contract manufacturers and laboratories shall be provided in Listing Attachment 4, including address and contact information, as well as a supply chain flow chart for outsourced production and quality control activities, for example, sterilization of the inner packaging material for aseptic processing, starting material inspection, etc.
- Briefly describe the responsibilities of the principal and the trustee in product

release (when not covered in Article 2.2).

2.4 Quality Risk Management (QRM)

- Briefly describe the enterprise's quality risk management (QRM) methods.
- The scope and focus of quality risk management, including quality risk management activities at the company level, and risk management activities carried out locally within the company. Any activity that uses the Quality Risk Management (QRM) system to evaluate supply continuity shall be described.

3. Personnel

- The company's organizational chart of quality management, production and quality control and their respective responsible persons, including senior management and authorized personnel, with their positions/titles listed (Listing Attachment 5);
- Number of employees engaged in quality management, production, quality control, storage and distribution.

4. Plant and equipment

4.1 Plant

- Briefly describe the production plant, including the site area and the name of each building. Where the varieties produced in different buildings are oriented to the local and different markets such as the European Union and the United States, the building(s) for specific markets shall be clearly indicated in the chart (if not specified in 1.1)
- Briefly describe the scale of the production area, accompanied by general layout of the plant area and layout plan and flow diagram of the production area, with the scale indicated (no construction or engineering drawings are required). The cleanliness class of the room and the pressure difference between adjacent rooms should be clearly indicated to show production activities carried out in the room (e.g., compounding, filling, storage, packaging, etc.) (Listing Attachment 6); the floor plan of the warehouse and the storage area (if available), including special areas for storage and handling of highly toxic, hazardous and sensitive materials.
- Please provide a brief description of special storage conditions (if any), but no need to indicate them on the floor plan.

4.1.1 Brief description of the heating, ventilation and air conditioning (HVAC) system

- Briefly describe the design philosophy of the HAVC systems, such as air supply, temperature, humidity, pressure difference, as well as ventilation rate, return air,

etc. (%).

4.1.2 Brief description of the water system

- Water quality design standards;
- Listing Attachment 7 Schematic diagram of water system.

4.1.3. Briefly describe other related utilities such as steam, compressed air, nitrogen, etc.

- 4.2 Equipment

4.2.1 List main instruments and equipment used for production and laboratory testing in Listing Attachment 8.

4.2.2 Cleaning and disinfection

- - Briefly describe the surface cleaning, disinfection methods and verification of equipment, instruments and tools that are in immediate contact with pharmaceutical products, e.g., manual cleaning, automatic online cleaning, etc.).

4.2.3 Critical computerized systems related to pharmaceutical production quality

- - Briefly describe critical computerized systems related to pharmaceutical production quality (excluding programmable logic controllers (PLCs)).

5. Documentation

- Describe the company's documentation system (e.g., electronic, paper);
- If documents and records are all stored outside the production facility (if any, including pharmacovigilance data), please provide the directory of externally stored documents/records, the name and address of the storage location, and the time required to retrieve the documents from outside the facility.

6. Production

6.1 Product type

(Refer to Listing Attachment 1 or Listing Attachment 2):

- Type of variety produced
  - List of dosage forms manufactured at the factory (including human and veterinary products)
  - List of investigational medicinal products (IMPs) manufactured at the factory. If the manufacturing site is different from that of the marketed products, please provide the production area and production personnel information.
- Treatment of toxic or hazardous substances (e.g. highly active and/or highly sensitizing medical products);

- Please describe the dedicated equipment or products produced/manufactured by stage (if any);
- If any please describe the application of process analytical technology (PAT) and outline the application of related technologies and computerized systems.

6.2 Process validation

- Briefly describe the principles of process validation;
- The principle of rework or reprocessing.

6.3 Material management and warehousing

- Handling of starting materials, packaging materials, bulk products and finished products, including sampling, inspection, release and storage;
- Disposal of non-conforming materials and products.

7. Quality control

- Describe quality control activities such as physical and chemical testing, microbiology and biological testing.

8. Distribution, complaints, product defects and recalls

Distribution (part of the manufacturer's responsibilities)

- Type of distributor (including whether the distributor holds a business license or manufacturing license, etc.) and its region (EU/EEA, USA, etc.);
- Describe the system used to identify the customer/recipient to demonstrate that the customer is legally eligible to receive the medicine;
- Briefly describe the measures that ensure that the product meets the storage requirements during transportation, such as temperature monitoring/control;
- Product distribution management and methods to ensure it is traceable;
- Measures to prevent products from flowing into illegal supply chains.

9. Complaints, product defects and recalls

- Briefly describe complaint handling, product defects and recall systems.

10. Self-inspection

- Briefly describe the enterprise’s self-inspection system, focusing on the selection criteria for scope involved in the self-inspection plan, implementation of self-inspection implementation and rectifications.

Related listing attachments:

Listing Attachment 1	A copy of the valid manufacturing permit document
Listing Attachment 2	Directory of all dosage forms produced, including the INN name or generic name of the drug substance used (if any)
Listing Attachment 3	A copy of the valid GMP certificate
Listing Attachment 4	List of contract manufacturers and laboratories, including address and contact information, as well as the supply chain flow chart for outsourcing activities
Listing Attachment 5	Organizational Chart
Listing Attachment 6	Production area plan, including material and personnel flow chart, production flow chart of each type (dosage form) product
Listing Attachment 7	Schematic diagram of water system
Listing Attachment 8	List of key production equipment and laboratory equipment and instruments

List of Site Master Files (For Medical Devices)

1 Company overview

1.1 Contact Information

Company name:

Registered address:

Contact information (including 24-hour contact number in case of product defects or recalls):

1.2 Basic information of the company

Brief description of company history:

Production plant address (if there are multiple addresses, they should be specified one by one and match with the production process flow chart of the inspected product):

1.3 Enterprise product information

1.3.1 The name of product with the registration certificate, and the registration certificate number (attached with the certificate)

1.3.2 Name and acceptance number of the product under review

2 Company's quality management system

2.1 Briefly describe the operation of the company's quality management system and the standards referenced;

2.2 Responsibilities of the top management and senior management in the quality management system

2.3 Brief description of inspections of the medical device quality system received by the factory in the past 2 years: inspection time, the authority performing the inspection and inspection conclusions, etc.

3 Management of suppliers and contractors

3.1 Brief description of the company's supplier requirements and their audits

3.2 Brief description of the contractor(s) and its (their) control measures, commissioned / contract production, commissioned / contract testing and its entrusted matters, the responsibilities of the principal and the trustee in the release of products, the list of the commissioned / contract manufacturer (testing laboratory), including the address, contact information.

4 Personnel

4.1 Factory Organization Chart / Quality Organization Chart

4.2 Names and positions of the senior management

4.3 Number of personnel engaged in quality management, production operation and quality inspection

4.4 Brief description of personnel training and health management

5 Plants and facilities

5.1 Production plant overview

5.1.1 Area of the production plant

5.1.2 Functionality and area of each building

5.1.3 Floor plan of the production plant

5.2 Production area

5.2.1 Production area plan

5.2.2 Identify the processes involved in each area

5.2.3 Identify the cleanliness class of each area

5.3 Storage area

5.3.1 Functions of the storage area

5.3.2 Storage area

5.3.3 Special storage conditions

5.4 Heating, ventilation and air conditioning (HVAC) system

5.4.1 Air supply and return air

5.4.2 Temperature, humidity, pressure difference

5.5 Water system

5.5.1 Purified water, water for injection

5.5.2 Water specifications

5.6 Brief description of other utilities such as steam, compressed air, nitrogen, etc.

6 Equipment

6.1 Brief description of the main production processes and equipment used in relation to the product inspected;

6.2 Brief description of the main test items and test equipment related to the product

inspected;

6.3 Computer system

7 Documentation

Briefly describe the document control system. (If documents and records are stored outside the production facility, please provide the directory of externally stored documents/records, the name and address of the storage location, and the time required to retrieve the documents from outside the facility.)

8 Production

8.1 Flow chart and brief description of the production process of the inspected variety (including cleanliness class/contract production/testing, etc.).

8.2 Principle of rework or reprocessing

9 Material storage management

9.1 Control of raw materials, excipients, parts, bulk products and finished products.

9.2 Status identification, area segmentation, management of non-conforming products

10 Quality control

10.1 Provide a brief description of quality control activities such as physical and chemistry tests, microbiology and biological testing

10.2 Process inspection

10.3 Finished product inspection and release

10.4 Sample retention

11 Sales, complaints, product defects and recalls

11.1 Brief description of product sales methods and after-sales services, methods and measures to ensure product traceability

11.2 Brief description of complaint handling, product defects and recall procedures

12 Internal audit

Brief description of internal audit, management review and CAPA

13 Brief description of the company’s product development management

14 Data authenticity statement

Annex 5

Overseas Inspection Pre-notice

This is to notify that per the work arrangements of the National Medical Products Administration (NMPA), the product(s) of your unit is (are) included among the tasks of overseas development/manufacturing site inspection. Upon review of *Basic Information Form of Product under Overseas Inspection* and relevant materials submitted by your company, the on-site inspection has been preliminarily scheduled for your company. Relevant arrangements are hereby notified as follows.

Company name (holder):
Product name:
Acceptance number / registration number / filing number:
Site inspection location:
Proposed on-site inspection time:

The above time and location are preliminarily determined. The inspection location and/or the inspection time may be adjusted during the process of inspection due to needs of inspection, in which case, you will be further notified.

Your company is supposed not to postpone the scheduled inspection without justification. If there is indeed a need to postpone the inspection due to special circumstances, a written application accompanied with justification should be presented to the CFDI within ten (10) working days as of the date of service of this notice. In such case, the CFDI determines the final inspection date by comprehensive evaluation of the actual inspection work to judge whether there is any situation that rejects or obstructs inspection.

It is hereby notified.

CFDI contact information

Contact:
Fax:
Mailbox:
Address:
Postcode:

Annex 6

Notice of Overseas Inspection Findings

Task number:

<table>
<tr><td rowspan="2">Medicine holder/medical device registrant or filer</td><td>Name</td><td colspan="3"></td></tr>
<tr><td>Address</td><td colspan="3"></td></tr>
<tr><td rowspan="2">Manufacturer</td><td>Name</td><td colspan="3"></td></tr>
<tr><td>Production address</td><td colspan="3"></td></tr>
<tr><td>Product inspected</td><td colspan="4"></td></tr>
<tr><td>Registration number / filing number (or acceptance number)</td><td colspan="4"></td></tr>
<tr><td>Inspection type</td><td colspan="4"></td></tr>
<tr><td>Inspection basis</td><td colspan="4"></td></tr>
<tr><td rowspan="4">Agency</td><td>Name</td><td colspan="3"></td></tr>
<tr><td>Address</td><td colspan="3"></td></tr>
<tr><td>Contact</td><td colspan="3"></td></tr>
<tr><td>Phone</td><td></td><td>E-mail</td><td></td></tr>
<tr><td>Authority performing inspection</td><td colspan="2"></td><td>Time of inspection</td><td></td></tr>
<tr><td rowspan="3">Inspection team</td><td>Team leader</td><td colspan="3"></td></tr>
<tr><td>Inspectors</td><td colspan="3"></td></tr>
<tr><td>Expert(s)</td><td colspan="3"></td></tr>
<tr><td colspan="5">Basic inspection information</td></tr>
<tr><td colspan="5">Inspection findings</td></tr>
<tr><td colspan="5">On-site inspection found a total of XX defects:</td></tr>
<tr><td colspan="5">(The following is an example: product risk control measures and rectification requirements recommended in light of inspection findings)
The defects listed in this Form are only the defects found in this inspection and do not represent all the defects existing with the enterprise. Your company has the responsibility to carry out production activities in accordance with existing laws, regulations and technical standards of China in relation to pharmaceuticals / medical devices to ensure the quality of pharmaceuticals and medical devices exported to China.
For the above defects, your company has the responsibility to investigate and identify their cause(s) and make corrections as soon as possible. In the meanwhile, your company shall initiate product risk assessment to identify whether there are potential safety hazards. If any potential safety hazard has been identified, recall of the products involved should be performed per provisions of Drug Recall Regulations and Medical Device Recall Regulations. Please submit a rectification report on the problems found in the inspection to the CFDI within fifty (50) working days from the date of service of this notice. If rectification for the identified defects cannot be completed within the specified time limit, a detailed improvement and follow-up plan shall be submitted to the CFDI. When necessary as indicated, the NMPA will organize a re-inspection on your company's rectifications.</td></tr>
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